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Cluster Headache and Other Trigeminal Autonomic Cephalalgias

IHC-OR-001

Evaluation of genetic associations in a multicentre UK cohort of 880 Cluster Headache patients

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Objective: The genetic variation predisposing patients to CH remains elusive. The majority of genetic studies have been association studies in candidate genes with a putative role in CH. We sought to evaluate reported genetic associations with CH, through examination of SNPs in the genes HCRTR2 (rs2653349 and rs3122156), CLOCK (rs12649507) and ADH4 (rs1126671). Also to examine previous GWAS findings in an independent cohort

including analysis of candidates rs12668955 within ADCYAP1R1, rs1006417 upstream of the LRFN5 gene and rs147564881 in MME.

Methods: A multicentre study involving six headache centres in the UK between 2016 and 2019. Patients diagnosed with episodic or chronic CH by a neurologist in concordance with the ICHD3b criteria were recruited to the study. DNA was extracted from peripheral blood or saliva and genotyped using the Illumina Infinium Global Screening Array. SNPs of interest were identified and screened for association.

Results: Overall, approximately 880 cases and 5,000 controls were screened for previously associated variants in candidate genes. Genotype analysis did not identify a statistically significant association between any previously implicated candidate variant and cluster headache

Conclusion: This is the largest cohort to date examining genetic associations with CH. Our findings do not support previous reports identifying associations between CH and variants in plausible candidates. Whilst this may represent population-specific effects, these findings highlight the importance of independent replication studies, using sufficiently powered datasets and a hypothesis-free approach. It outlines the requirement for multi-centre, collaborative efforts for patient recruitment in future studies

Disclosure of Interest: None Declared

Headache Pathophysiology – Basic Science

IHC-OR-002

Molecular characterization of human trigeminal ganglia at single-cell resolution

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Objective: Pain experienced in migraine involves the sensitization of trigeminal afferent neurons, but the extraordinary cellular diversity within trigeminal ganglia has limited our understanding of the molecular substrates

through which this process occurs. The aim of this study is to leverage recent advances in single-cell genomics to identify genes that are selectively expressed in subtypes of trigeminal nociceptors which could inform the design of novel and more selective migraine therapeutic targets.

Methods: Post-mortem bilateral trigeminal ganglia were obtained from three individuals. Nuclei were extracted and individually sequenced using 10X Genomics droplet-based RNA sequencing. Graph clustering was used to bioinformatically group cells with similar gene expression patterns. The expression of known marker genes was used to validate the cell type of each cell cluster. Once cell types were assigned, we performed differential expression and identified the entire set of genes that are selectively enriched in each cell type. Novel genes were validated by in situ histochemistry.

Results: We obtained 39,000 human trigeminal ganglia nuclei that met quality metrics. Bioinformatic analysis demonstrated that 24% of the nuclei derived from neurons, 22% from satellite glia, 8% from Schwann cells, 39% from dura, and 7% from vascular cells. Of the neurons, 25% were peptidergic C-fibers, 28% were non-peptidergic C-fibers, and 47% were A-fibers. Approximately 60% of CGRP+ cells were peptidergic C-fibers and 40% were A-fibers. We identified 20 genes that are significantly enriched in CGRP+ peptidergic nociceptors compared to other neuronal subtypes. There was significant overlap between the CGRP+ nociceptor-enriched genes in human and mice.

Conclusion: We have generated the first single-cell atlas of human trigeminal neurons, glia, dura, and vascular cells. Analysis of these data identified genes that are selectively expressed in CGRP+ nociceptors, which could both inform the design of more selective migraine therapeutics as well as help predict potential off target effects. Ongoing studies are aimed at characterizing the role of CGRP+ nociceptor-specific genes on their activity and neuropeptide release.

Disclosure of Interest: None Declared

IHC-OR-005

PKC- δ -positive cells in the central amygdala contribute to chronification of migraine in a mouse model

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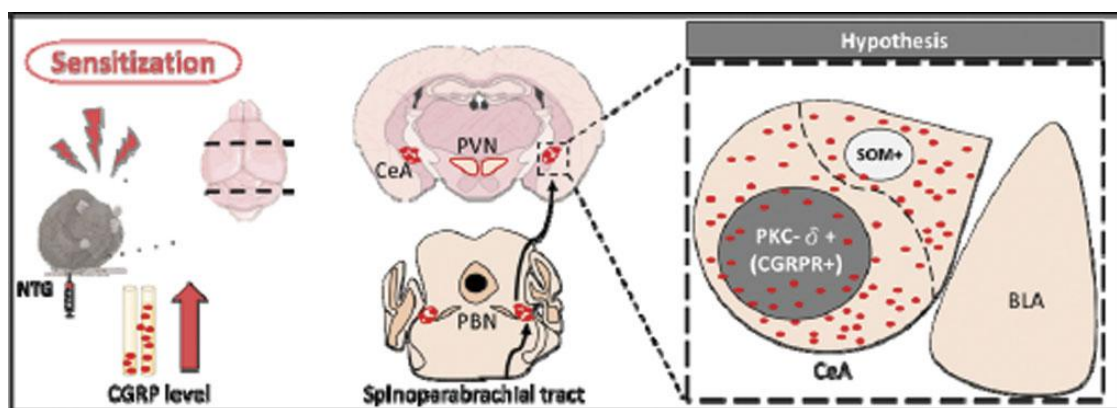
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Objective: The molecular mechanism underlying the chronification of migraine remains elusive. We aimed to investigate the maladaptive modifications of pain circuits in chronic migraine (CM) in a mouse model.

Methods: We gave C57BL/6 mice intermittent intraperitoneal injections of nitroglycerin (NTG, 10–20 mg/kg) for 9 days (i.e., totally 5 NTG injection/study days) to simulate migraine attacks. Pre- and post-injection mechanical hyperalgesia was measured by von Frey test. Approach-avoidance and active avoidance assay were used to measure the comorbid anxiety-like behaviors after chronic NTG induction. Besides, we used pERK immunostaining to identify neurons that were sensitized during the chronification of migraine, and explored their relationship with CGRP-containing and the somatostatin (SOM) or protein kinase c-delta (PKC- δ) neurons in the central nucleus of the amygdala (CeA). Finally, we used chemogenetics to manipulate the PKC- δ (+) GABAergic neurons in the CeA.

Results: With chronic low-dose (10 mg/kg) NTG injections, mice displayed persistent mechanical hyperalgesia. Under repetitive high-dose (20 mg/kg) NTG injections, the mice developed sustained mechanical hyperalgesia 2



Abstract number: IHC-OR-005

weeks beyond injection and also exhibited anxiety-like behaviors by burying more marbles in comparison with controls. Besides, we found that the level of pERK at the CeA significantly increased after the development of mechanical hyperalgesia. The level of CGRP was also increased at the CeA and the parabrachial nucleus (PBN). Furthermore, we found that the pERK (+) cells in the CeA were predominantly PKC- δ (+) neurons colocalized with CGRP receptor. Moreover, chemogenetic inhibition of PKC- δ (+) neurons in CeA alleviated the mechanical hypersensitivity after chronic NTG induction in PKC- δ -Cre mice.

Conclusion: Our results suggest that PKC- δ (+) neurons within the CeA might be responsible for the chronification of migraine. These PKC- δ (+) neurons might be activated and sensitized by CGRP through the spinoparabrachial tract after chronic NTG induction.

Disclosure of Interest: None Declared

IHC-OR-007

Local Thalamic Inhibition and Migraine

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Objective: The thalamus is a key centre for the integration of sensory information from the head and body. Abnormal thalamic activation is observed prior to and during migraine attacks and during experimental models of central sensitization, highlighting the thalamus as a key hub in the neural networks that regulate migraine biology. At the level of the thalamus, sensory information is regulated by two complimentary mechanisms. Feedback GABAergic inhibition from the thalamic reticular nucleus and feedforward local-circuit GABAergic interneurons (INs) that act to regulate thalamocortical activity. We have recently demonstrated that local thalamic INs, but not those from extra-thalamic sources express Sox14 and that their optogenetic activation is sufficient to inhibit thalamocortical relay neurons. Hypothesising that dysregulation of local thalamic INs may play a role in migraine-related pain processing and central sensitization we sought to demonstrate the impact of their loss of function on orofacial and hind-paw mechanical sensitivity.

Methods: Mechanical sensitivity in the periorbital and hind paw region was assessed for Sox14 knockout mice (N = 6/5 respectively) and their wild type littermate controls (N = 6/5 respectively) using von-Frey filaments. Mice were habituated to the apparatus 2 days prior to behavioural testing and mechanical thresholds tested on 2 separate occasions. On each occasion, the 50% withdrawal thresholds were calculated. Knock out and control

thresholds were then compared using the students t-test with $p < 0.05$ considered significant.

Results: In comparison to WT littermate controls, Sox14 KO mice showed a significant decrease in mechanical withdrawal thresholds in both the periorbital (0.84 ± 0.4 g vs 0.01 ± 0.01 g; $p < 0.0001$) and hind paw regions (0.90 ± 0.07 g vs 0.09 ± 0.003 g; $p < 0.0001$).

Conclusion: Our data confirms that the neuronal defects caused by Sox14 loss-of-function result in increased orofacial and hind paw mechanical sensitivity, highlighting a potential role for Sox14-expressing neurons in modulating migraine-associated pain processing and central sensitization. We now seek to refine our model by selectively ablating Sox14 INs from the ventrobasal complex of the thalamus – which in addition to being a key relay centre for nociceptive signalling has recently been recognised as a site of multisensory integration.

Disclosure of Interest: None Declared

IHC-OR-010

Glyceryl trinitrate-induced non-headache symptoms indicative of an impending migraine-like attack: a case-control study

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Objective: Spontaneous and pharmacologically-provoked migraine attacks are frequently preceded by non-headache symptoms called premonitory symptoms (PMS). Here, we systematically evaluated non-headache symptoms in migraine patients and non-headache controls following glyceryl trinitrate (GTN) infusion.

Methods: In 34 women with migraine without aura and 24 age-matched women without migraine, we conducted a semi-structured interview asking for 21 possible PMS every 15 minutes in the 5 hours after GTN infusion ($0.5 \mu\text{g}/\text{kg}/\text{min}$ over 20 min).

Results: Migraine-like headaches occurred in 28/34 (82.4%) migraineurs. All migraineurs and 13/24 (52.4%) controls reported at least one item from the list of 21 possible PMS, irrespective of whether or not a migraine-like headache was provoked. Concentration difficulties ($p = 0.011$), yawning ($p = 0.009$), nausea ($p = 0.028$), and photophobia ($p = 0.001$) were more frequently reported by those who developed a migraine-like attack versus non-headache controls. Concentration difficulties were exclusively reported by those who developed a migraine-like attack. Yawning and nausea were the earliest symptoms reported based on calculated interquartile ranges, followed by photophobia and concentration difficulties that occurred nearer to onset of migraine-like headache.

Conclusion: GTN may induce PMS items, irrespective of a subsequent migraine-like headache. Yawning, nausea, photophobia and, in particular, concentration difficulties, in that temporal order, seemed most specific for an impending GTN-induced migraine-like headache.

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IHC-OR-011

PACAP-38 and PACAP(6–38) degranulate rat meningeal mast cells via the orphanMrgB3-receptor

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Objective: Pituitary adenylate cyclase activating peptide-38 (PACAP-38) provokes migraine attacks in migraineurs. The infusion causes long-lasting flushing and heat sensation that can be treated with oral antihistamine. Degranulation of rat peritoneal mast cells was provoked by several isoforms of PACAP via previously unknown receptor pharmacology.

PAC₁-receptor splice variants have been cloned and characterized by ligand binding and signal transduction. The Mas-related G-protein coupled receptor member X₂ (MrgX₂) was found to be present in human mast cells. The rat counterpart is MrgB₃. Both receptors mediate basic secretagogues-induced mast cell degranulation.

We hypothesized that PACAP mediated degranulation of rat meningeal and peritoneal mast cells were either caused by a splice variant of the PAC₁-receptor or via MrgB₃-receptors.

Methods: Degranulation of meningeal mast cells was investigated in the hemisected skull model after toluidine blue staining followed by microscopic quantification.

Presence of mRNA encoding PAC₁-receptor splice variants and the MrgB₃-receptor in rat mast cells was investigated by RT-PCR analysis. The effect of PACAP isoforms on PAC₁- and MrgB₃-receptor expressing *Xenopus laevis* oocytes were made by two-electrode voltage-clamp electrophysiology.

Results: PACAP-38 and PACAP(6–38) are more potent mast cell degranulating agents than PACAP-27 in the meninges. This support our previous findings in rat peritoneal mast cells.

Presence of mRNA encoding the PAC₁-receptor and its different splice variants could not be detected in peritoneal mast cells by RT-PCR, whereas the orphan MrgB₃-receptor was widely present.

In PAC₁-receptor expressing oocytes both PACAP-38, PACAP-27 and maxadilan were equipotent, however, only PACAP-38 degranulated mast cells significantly. We confirmed PACAP(6–38) to be a PAC₁-receptor antagonist, and we show that it is a potent mast cell degranulator and have agonistic effect on MrgB₃-receptors expressed in oocytes.

Conclusion: The present study provides evidence that PACAP-induced mast cell degranulation in rat is mediated through MrgB₃-receptor with the order of potency being: PACAP-38 = PACAP(6–38) >> PACAP-27 = maxadilan.

Disclosure of Interest: None Declared

IHC-OR-016

Spontaneous cortical spreading depolarization and early mortality in an Scn1a-L263V familial hemiplegic migraine mouse model

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Objective: Familial hemiplegic migraine type 3 (FHM3) is a migraine with aura subtype caused by autosomal dominant mutations in the *SCN1A* gene encoding the voltage-gated sodium channel Na_v1.1. Variable effects of FHM3-associated mutations on Na_v1.1 channel functioning in heterologous expression systems stress the need to establish their consequences *in vivo*.

Methods: We generated a transgenic mouse model with a heterozygous missense mutation L263V in the *Scn1a* gene, a mutation previously identified in FHM3 patients, using a Crispr/Cas9 strategy. Parallel continuous video and electrophysiological monitoring were used to detect cortical spreading depolarization (CSD) and/or seizures. Cortical electrical stimulation was used to assess CSD threshold in freely behaving mice.

Results: *Scn1a*^{L273V} mice did not exhibit overt behavioral abnormalities, but died at juvenile to young adult age often following sudden behavioral activity lasting seconds. Treatment with GS967, a sodium channel blocker that was effective in various sodium channelopathies, markedly improved survival. A subset of *Scn1a*^{L273V} mice displayed spontaneous CSD events that invariably spread in caudo-rostral direction. Preliminary data indicate that electrical threshold for CSD was reduced, yet propagation rate remained unaffected.

Conclusion: Our findings indicate that *Scn1a*^{L273V} mice may serve as a valuable model for the preclinical study of migraine.

Disclosure of Interest: None Declared

Headache Pathophysiology – Imaging and Neurophysiology

IHC-OR-008

Increased neural connectivity between the hypothalamus and cortical resting state functional networks in chronic migraine

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Objective: Resting-state functional MRI studies suggest that abnormal functional integration between interconnected cortical networks characterizes the brain of migraineurs. The aim of this study is to investigate the functional connectivity between the hypothalamus, the brainstem –the supposed generators of migraine –, and the areas that encompass the following networks involved in the pathophysiology of migraine: the default mode network (DMN) and the dorsal attention system (DAS).

Methods: Twenty patients with chronic migraine (CM) without medication overuse and 20 healthy subjects (HS) were prospectively recruited. All study participants underwent 3T MRI scans using a 7.5-minute resting state

protocol. Using a seed-based approach, we performed a ROI to ROI analysis choosing hypothalamus as seed and areas belonging to the DMN and the DAS, and brainstem as target region of interests.

Results: Compared to HS, CM patients showed significant increased neural connectivity between the hypothalamus and brain areas belonging to DMN and DAS. We haven't detected any connection abnormalities between the hypothalamus and the brainstem. The correlation analysis showed that the severity of migraine headache correlates positively with the connectivity strength of the hypothalamus and negatively with the connectivity strength of the middle prefrontal cortex, which belongs to the DMN.

Conclusion: These data provide evidence for hypothalamic involvement in large-scale reorganization at the level of the functional networks during chronic migraine and in proportion with the severity of perceived migraine pain.

Disclosure of Interest: None Declared

IHC-OR-014

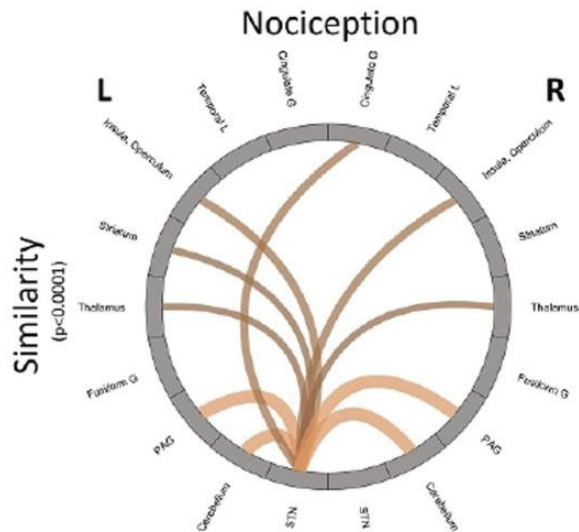
Partial Similarity reveals dynamics in brainstem-midbrain networks during trigeminal nociception

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Objective: Functional imaging studies help us understand the role of brainstem and midbrain regions in human trigeminal pain processing without solving the question how these regions dynamically interact. Such connectivity changes are important for cycling diseases such as cluster headache and migraine. We aim at describing connectivity and its dynamics using Partial Similarity, a novel analytical approach specifically developed to estimate the communication between individual hubs of networks in contrast to the overall communication within that network.

Methods: 29 healthy volunteers received 15 trials of gaseous ammonia as nociceptive trigeminal input and 15 air puffs as control condition while recording brainstem fMRI. After preprocessing, data was analyzed by a GLM, modeling each trial individually. Resulting beta-values entered Similarity and Partial Similarity analysis to retrieve functional connectivity dynamics from the spinal trigeminal nucleus (STN), the first central hub of trigeminal pain processing, to brainstem and midbrain areas. Similarity uses Spearman correlation of trial-to-trial variance as a measure of general connectivity while Partial Similarity achieves direct connectivity by correcting for general communication across the brain.



Results: Similarity reveals 9 clusters connected to the STN (see figure) while Partial Similarity shows 10 clusters with positive and 3 with negative correlations to the STN. Both measures show connectivities to hubs of the pain matrix while the contralateral crossing to higher cortical areas is only revealed using Partial Similarity analysis.

Conclusion: Uncovering connectivity in human fMRI is a challenging field as to date only few methods exist. While commonly used DCM and PPI both work on raw time courses, depend on the height of BOLD amplitude, and are further hindered by a long list of assumptions and constraints, common correlation analysis may lead to overestimating of results. Here we introduce a new way to delineate network connectivity with the potency to overcome aforementioned limitations. While we concentrate on the first hub of the trigeminal driven network in the CNS, further research will reveal the dynamical connectivity of all hubs in the network and identify structures which would be missed using only one of these tools.

Disclosure of Interest: None Declared

IHC-OR-017

Impaired parasympathetic modulation on heart rate variability in patients with chronic migraine

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Objective: Autonomic nervous system (ANS) dysfunction, especially altered parasympathetic modulation as evaluated by heart rate variability (HRV), has long been found in patients with episodic migraine (EM), as well as in some chronic pain conditions. However, whether ANS dysfunction exists in patients with chronic migraine (CM) remained inconclusive. We hypothesized that CM would have impaired ANS/parasympathetic function.

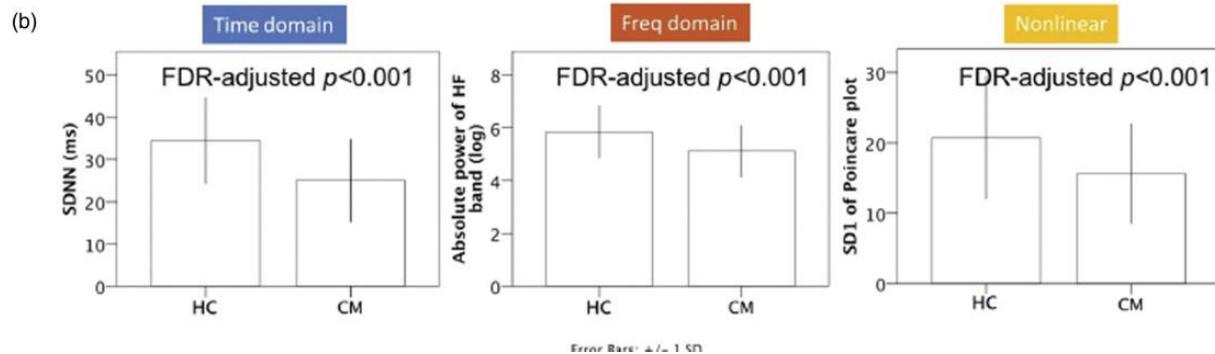
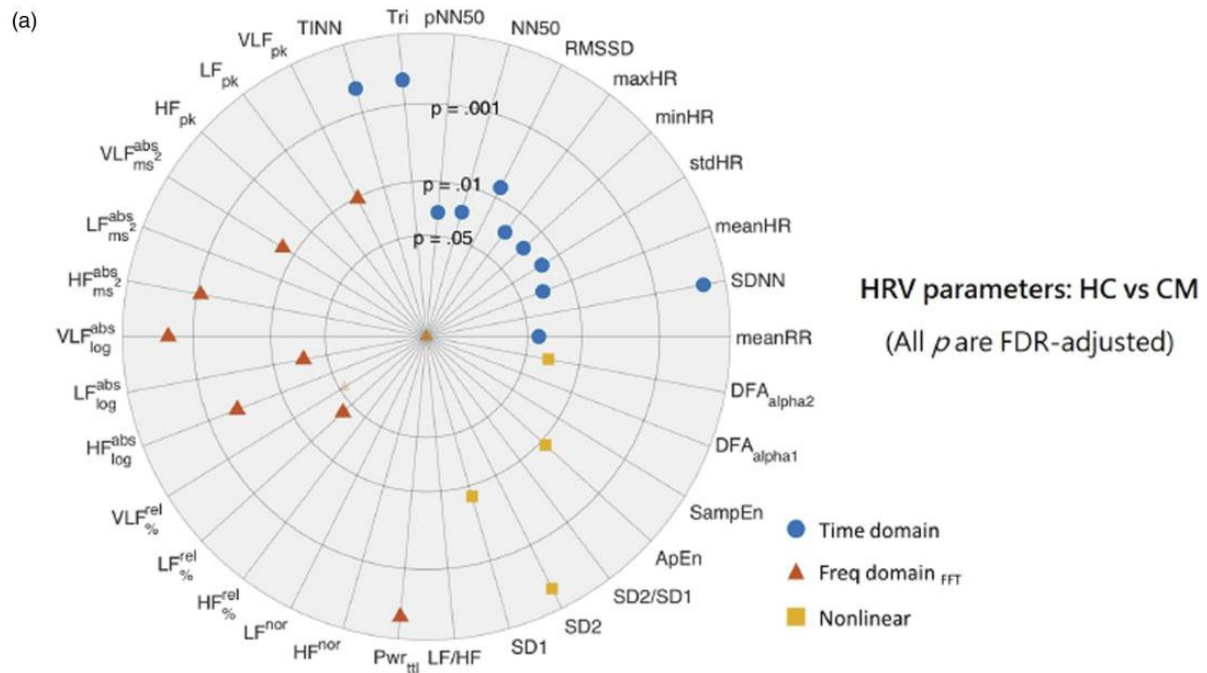
Methods: Patients with newly diagnosed CM were recruited from the Headache Clinic of Taipei Veterans General Hospital. Healthy controls (HC) were also recruited.

A standard 5-minute ECG was recorded from each participant. Off-line HRV analyses were done by Kubios software to yield various time-domain, frequency-domain, and non-linear parameters. Comparison between HC and CM was tested. Subsequently, in CM patients, correlation analyses between clinical headache severity profile (i.e. monthly headache/migraine frequency, migraine disability assessment [MIDAS] score) and parameter(s) that showed significant difference between CM and HC were then carried out.

Results: Forty-eight CM patients (F/M: 45/3, aged 41.4 ± 10.7 years) and 48 age- and gender-matched HC (F/M: 40/8, aged 39.4 ± 8.9 years) were recruited. HRV analysis revealed that CM patients had abnormal ANS parameters in multiple domains, including decreased SDNN, RMSSD, NN50, pNN50, high-frequency power (absolute and log-transformed), total power, Poincare SD1/SD2, and increased low-frequency power (log-transformed) as compared with HC (Figure 1A, 1B, all $p < 0.05$, corrected for false-discovery rate). All these findings suggested CM patients had an impaired parasympathetic modulation as compared with HC. Further correlation analysis between each of these parameters and clinical headache severity profile did not reveal significant results.

Conclusion: Our study showed CM patients had ANS dysfunction, especially parasympathetic modulation ability.

Disclosure of Interest: None Declared



Abstract number: IHC-OR-017

Migraine Acute Therapy

IHC-OR-004

Efficacy, Safety, and Tolerability of Rimegepant 75 mg Orally Dissolving Tablet for the Acute Treatment of Migraine: Results from a Phase 3, Double-Blind, Randomized, Placebo-Controlled Trial, Study 303

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Objective: Rimegepant is a small molecule CGRP receptor antagonist with demonstrated efficacy in the acute treatment of migraine. An ODT formulation with a T_{max} 30 minutes earlier than the previously studied tablet may have a more rapid onset of action. The objective of this study was to compare the efficacy, safety, and tolerability of rimegepant 75 mg ODT with placebo in the acute treatment of migraine.

Methods: This double-blind, randomized, placebo-controlled, multicenter Phase 3 trial (Study 303) included adults ≥ 18 years of age with ≥ 1 -year history of migraine. Subjects randomized to rimegepant 75 mg ODT or placebo treated 1 migraine attack of moderate or severe pain intensity. The coprimary endpoints were 2-hour pain freedom and freedom from the most bothersome symptom (MBS).

Results: Altogether, 1375 subjects were randomized and treated; 1351 were evaluated for efficacy (rimegepant

n = 669, placebo n = 682). Rimegepant ODT was superior to placebo for 2-hour pain freedom (21.2% vs 10.9%, $p < .0001$) and MBS freedom (35.1% vs 26.8%, $p = .0009$). Additionally, rimegepant ODT numerically separated from placebo on pain relief beginning at 15 minutes postdose and was significantly superior to placebo for 60-minute pain relief ($p = .0314$). Significance was also reached on 60-minute functional disability freedom ($p = .0025$); 90-minute pain freedom ($p < .0001$) and MBS freedom ($p = .0128$); 48-hour sustained pain freedom ($p < .0001$), sustained pain relief ($p < .0001$), sustained MBS freedom ($p = .0018$), and sustained functional disability freedom ($p < .0001$). Overall, rimegepant ODT was superior to placebo on 21 prespecified, hierarchically-tested endpoints. The most common adverse events were nausea and urinary tract infection ($\leq 1.6\%$). No serious treatment emergent adverse events were reported.

Conclusion: A single dose of rimegepant ODT met the coprimary endpoints and demonstrated significant clinical benefits within 60 minutes that were sustained through 48 hours. Rimegepant also had placebo-like tolerability in the acute treatment of migraine.

Disclosure of Interests: Richard B. Lipton, MD, serves on the editorial board of *Neurology* and *Cephalalgia* and as senior advisor to Headache but is not paid for his roles on *Neurology* or *Headache*. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's *Headache* (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

Vladimir Coric, MD, David A. Stock, PhD, Micaela Forshaw, MPH, and Robert Croop, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

Ralph Gosden, MSc, is employed by Catalent U.K. Swindon Zydys Limited, Swindon, United Kingdom.

IHC-OR-009

Efficacy and safety of lasmiditan in patients on migraine preventive medications: findings from SAMURAI and SPARTAN Phase 3 trials

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Objective: To study the efficacy and safety of lasmiditan, a novel 5HT_{1F} receptor agonist, for acute treatment of migraine in patients on migraine preventive medications.

Methods: SAMURAI and SPARTAN were similarly designed, double-blind, phase 3, placebo-controlled studies of adult patients with 3–8 migraine attacks per month. Patients were randomized to treat a migraine attack with oral lasmiditan 50 mg (SPARTAN only), 100 mg, 200 mg, or placebo. Migraine preventives were allowed, provided doses were stable during the study and for three months prior to screening. Preventive medications with established and probable efficacy as recommended by the European Headache Federation, American Headache Society, and American Academy of Neurology, plus botulinum toxin type A and candesartan, were included. Lasmiditan and placebo groups were analyzed within the subgroup of patients using preventive therapies for the outcome of pain-free at 2 hours. The subgroups of patients using and not using preventive therapies were compared and interaction p-values were calculated for safety and efficacy outcomes.

Results: In the trials, 698 of 3981 patients (17.5%) used migraine preventive treatment. Among patients using preventives, all lasmiditan doses resulted in significantly more patients being pain-free at 2 hours, compared to placebo ($p < 0.05$). Primary efficacy outcomes (pain-free at 2 h and most bothersome symptom-free at 2 hours) and all other efficacy outcomes were not significantly different between patients using or not using migraine preventives. Treatment-emergent adverse event frequencies were not significantly different between patients using or not using preventive medications (all interaction p-values ≥ 0.1).

Conclusion: Lasmiditan was more effective than placebo for the acute treatment of migraine in patients concurrently using migraine preventive medications. Lasmiditan efficacy and safety measures were similar for patients using and not using preventive medications.

Disclosure of Interests: These studies were sponsored by Eli Lilly and Company, Indianapolis, Indiana, USA.

IHC-OR-015**Ubrogepant is Effective for the Acute Treatment of Migraine in Patients with an Insufficient Response to Triptans**

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Objective: To examine the efficacy of ubrogepant versus placebo in patients based on historical response to triptans.

Methods: Multicenter, double-blind, single-attack, phase 3 trials (ACHIEVE I/NCT02828020; ACHIEVE II/NCT02867709). Adults with a history of migraine, with/without aura, were randomized 1:1:1 to placebo or ubrogepant (50 mg or 100 mg, ACHIEVE I; 25 mg or 50 mg, ACHIEVE II). At baseline, patients were categorized as either a triptan-responder, triptan-insufficient responder (including those contraindicated), or triptan-naïve, based on historical experience. Co-primary efficacy endpoints in both trials were pain freedom and absence of most bothersome migraine-associated symptom (MBS), 2 hours after the initial dose.

Results: At baseline, patients in the mITT population (N = 1327, ACHIEVE I; N = 1355, ACHIEVE II) were categorized as triptan-responder (40%, ACHIEVE I; 35%, ACHIEVE II), triptan-insufficient responder (27%, ACHIEVE I; 23%, ACHIEVE II), and triptan-naïve (32%, ACHIEVE I; 42%, ACHIEVE II). Reasons for categorization as triptan-insufficient responder were insufficient efficacy (78%, ACHIEVE I; 82%, ACHIEVE II), insufficient tolerability (18%, ACHIEVE I; 15%, ACHIEVE II), and contraindications/warnings (3%, ACHIEVE I; 2%, ACHIEVE II). For both 2-hour pain freedom and absence of MBS, response rates were higher for ubrogepant versus placebo, across all triptan subpopulations. Magnitude of efficacy (ubrogepant versus placebo) was not significantly different among the 3 subpopulations for pain freedom (treatment-by-subgroup interaction: $P=0.2561$, ACHIEVE I; $P=0.5011$, ACHIEVE II) or absence of MBS ($P=0.4938$, ACHIEVE I; $P=0.9251$, ACHIEVE II). Placebo response rates were lowest in triptan-insufficient responders and highest in triptan-naïve. Proportion of patients reporting adverse events was comparable across treatment groups; no safety concerns were identified.

Conclusion: Ubrogepant was effective for the acute treatment of migraine in patients categorized as triptan-insufficient responders as well as those who were triptan-responders or triptan-naïve.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland

Author Disclosures:

Andrew M. Blumenfeld, MD has served on advisory boards and/or has consulted for Allergan, Pernix, Teva, Avanir, Depomed, and Supernus, and has received funding for travel, speaking, and/or royalty payments from Allergan.

Peter J. Goadsby, MD, PhD reports personal fees from Allergan, and related grants and personal fees from Amgen and Eli-Lilly and Company, and personal fees from Alder Biopharmaceuticals, Autonomic Technologies Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Novartis, Scion, Teva Pharmaceuticals, and Trigemina Inc., and personal fees from MedicoLegal work, Massachusetts Medical Society, Up-to-Date, Oxford University Press, and Wolters Kluwer; and a patent Magnetic stimulation for headache assigned to eNeura without fee.

David W. Dodick reports: Personal fees: Amgen, Autonomic technologies, Axsome, Aural Analytics, Allergan, Alder, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Neurolief, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, Oppenheimer. CME fees or Royalty payments Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal meeting management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer; Stock options: Aural analytics, Healint, Theranica, Second Opinion/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Consulting without fee: Aural Analytics, Healint, Second Opinion/Mobile Health, Epien; Board of Directors: Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1-1466:vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis without fee. Professional society fees or reimbursement for travel: American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society. Other: Use agreement through employer: Myndshft

Susan Hutchinson, MD has served on advisory boards for Alder, Allergan, Amgen, Avanir, Biohaven, ElectroCore, Eli Lilly, Supernus, and Teva. She is on the speakers bureau for Allergan, Amgen, Avanir, ElectroCore, Eli Lilly, Promius, Supernus, and Teva.

Chengcheng Liu, MPH is a full-time employee and stockholder of Allergan plc.

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Migraine Preventive Therapy

IHC-OR-006

Long-term efficacy and safety of erenumab: Results from 64 weeks of the LIBERTY study

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Objective: The LIBERTY study (NCT03096834) demonstrated efficacy of erenumab 140 mg in episodic migraine patients with 2–4 prior preventive treatment failures.

Abstract number: IHC-OR-006

Table 1. Efficacy outcomes measures at the end of the first year of the OLEP, Observed (Open-Label Analysis Set)

Outcomes	Values at Week 64 (Week 52 of OLEP)		
	Patients on erenumab 140 mg continued on erenumab 140 mg in the OLEP, N = 118	Patients on placebo who initiated erenumab 140 mg in the OLEP, N = 122	Overall population, N = 240
≥50% reduction in MMD	44.3%	50.0%	47.1%
≥75% reduction in MMD	21.4%	25.8%	23.5%
100% reduction in MMD	8.6%	16.7%	12.5%
Change from the DBTP baseline in MMD	−3.8 (3.9)	−3.6 (4.4)	−3.7 (4.1)
Change from the DBTP baseline in HIT-6	−8.5 (7.4)	−9.7 (10.0)	−9.0 (8.7)
Change from the DBTP baseline in MPFID-PI	−5.2 (6.9)	−4.5 (8.4)	−4.8 (7.7)
Change from the DBTP baseline in MPFID-EA	−6.6 (7.7)	−5.1 (9.4)	−5.9 (8.6)

Data are mean (SD) or % of the patients with non-missing value at Week 64; Data for HIT-6 reported at Week 60.

DBTP, double-blind treatment phase; HIT-6, Headache Impact Test; MMD, monthly migraine days; MPFID-EA; Migraine Physical Function Impact Diary-everyday activities MPFID-PI, Migraine Physical Function Impact Diary-physical impairment; N, number of subjects included in the analysis set; OLEP, open-label extension phase; SD, standard deviation.

The aim of this analysis was to assess efficacy and safety of erenumab at Week 64 of the LIBERTY study.

Methods: Patients completing the 12-week double-blind treatment phase (DBTP) of the LIBERTY study (N=240) initially randomised to placebo and erenumab 140 mg subcutaneous injections were enrolled into the open-label extension phase (OLEP) to receive open-label treatment with monthly erenumab 140 mg for 3 years. The efficacy outcomes included ≥50%/≥75%/100% reduction from the DBTP baseline in monthly migraine days (MMD) (responder rates), change from the DBTP baseline in MMD, Headache Impact Test total score, and Migraine Physical Function Impact Diary (Everyday Activities and Physical Impairment) scores in the overall population, patients on continuous erenumab and patients from placebo group who initiated erenumab. The outcomes were assessed throughout the first 52 weeks in OLEP (total 64 weeks from DBTP baseline).

Results: Overall, 204/240 (85.0%) patients completed the Week 52 visit of the OLEP. Results for the outcomes measured are presented in Table 1. On all efficacy outcomes assessed, patients on continuous erenumab showed sustained efficacy, while those who initiated erenumab in the OLEP showed sustained improvement from Week 13 onwards. Nearly 80.8% (overall group), 76.3% (continuing erenumab) and 85.2% (initiating erenumab) of patients reported adverse events (AEs). The corresponding incidences for serious AEs were 6.7%, 5.9%, and 7.4%. No deaths were reported.

Conclusion: Efficacy of erenumab was sustained throughout 64 weeks in a difficult-to-treat patient population with multiple prior preventive treatment failures in both continuous erenumab and those initiating erenumab treatment

groups. Safety of erenumab was in line with previously reported clinical trials.

Disclosure of Interests: The study was supported by Novartis Pharma AG, Basel, Switzerland. Erenumab is codeveloped by Novartis and Amgen. The abstract has been accepted as an e poster presentation at EHF 2019.

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Chrystel Fernandes — employee: Novartis. Michel Ferrari — consultancy from Medtronic, Electrocore, Amgen, Lilly, Teva, and Novartis, and independent support from the European Community, NWO, NIH and the Dutch Heart Foundation and grants, trial support from Medtronic, Electrocore, Amgen, Lilly, Teva, and Novartis, and independent support from the European Community, NWO, NIH and the Dutch Heart Foundation.

IHC-OR-012

Very early onset of action of fremanezumab in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive treatments: results of the international, multicentre, randomised, placebo-controlled FOCUS study

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Objective: Preventive treatments for episodic and chronic migraine (EM and CM) have been associated with slow onset of action. Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for preventive migraine treatment in adults. The FOCUS study of fremanezumab was the first and largest study of a migraine preventive treatment in adults with both CM and EM and documented inadequate response to 2–4 classes of migraine preventive medications. This post hoc analysis evaluated efficacy within the first week of study treatment.

Methods: Patients were randomised (1:1:1) to quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), monthly fremanezumab (Month 1: CM, 675 mg; EM, 225 mg; Months 2 and 3: 225 mg), or matched monthly placebo for 12 weeks. Proportions of patients with migraine days during the first 7 days of treatment were evaluated in the overall population and patients with CM.

Results: 838 patients were randomised. Significantly fewer patients in the overall population had a migraine day with fremanezumab (quarterly, 32%; monthly, 36%) vs placebo (46%) on Day 2 and on each day through Day 7 (all $P \leq 0.011$). In patients with CM ($n = 509$), significantly fewer patients had a migraine day with fremanezumab (quarterly, 41%; monthly, 43%) vs placebo (57%) on Day 2 and on each day through Day 7 (all $P < 0.05$).

Conclusion: Fremanezumab demonstrated very early onset of action, with a larger proportion of patients reporting no migraine attacks within 24 hours and daily through Day 7 vs placebo. Fremanezumab showed very early onset of action in patients with EM and CM and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: J. Brandes has served on speaker's bureaus/advisory boards for Amgen, Teva, Lilly, Promius, Supernus, Novartis, Alder, Valeant, and

electroCore and has received research support from Amgen, Teva, Lilly/Colucid, Biohaven, Allergan, Clinvest, and Alder. V. Ramirez-Campos, R. Yang, J. M. Cohen, M. Galic, and X. Ning are employees of Teva Pharmaceuticals. C. Treppendahl has received honoraria as a speaker for Allergan, American Academy of NPs, Amgen, Avanir Pharmaceuticals, Depomed, Inc., Iroko Pharmaceuticals, National Headache Foundation, Nautilus Neurosciences, Inc., Novartis, Pernix Therapeutics Holdings, Inc., Promius Pharma, Southern Headache Society, Supernus Pharmaceutical, Teva Pharmaceutical Industries, Inc., and Zogenix, Inc. C. Treppendahl has served on advisory boards and/or as a consultant for Amgen, Electrocore, Ely Lilly, National Headache Foundation, Pernix, Promius Pharma, Supernus Pharmaceutical, and Teva Pharmaceutical Industries, Inc.

IHC-OR-018

HIT-6 Responder Rates after 1 and 3 Months of Eptinezumab Treatment

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Objective: Migraine has been linked to a variety of negative health-related outcomes that broadly impact patients' lives. An effective preventative migraine treatment should lessen the impact of migraine on everyday life. The 6-item Headache Impact Test (HIT-6) is a tool for quantifying the negative impact of headache on daily activities and can be used to assess treatment response. The current analyses aimed to evaluate the effect of eptinezumab on reported HIT-6 total score and on individual items in patients with chronic migraine (CM).

Methods: These post hoc analyses used data from the randomized, double-blind, placebo-controlled PROMISE-2 trial (NCT02974153). Responder rates for the HIT-6 total (decrease of ≥ 6 points) and item scores (improvements of 1 category on items 1–3 or 2 categories on items 4–6) at Months 1 and 3 were analyzed using logistic regression models.

Results: Scores from 1062 patients with CM were included in the analyses (eptinezumab 100 mg, n = 352; eptinezumab 300 mg, n = 347; placebo, n = 363). Enrolled patients were predominantly white (91%) and female (88%), with an average age of 40.6 years. After controlling for randomization factors and baseline HIT-6 scores, eptinezumab treatment was associated with increased odds of HIT-6 response at Months 1 and 3 for total scores and all

individual items. At Month 1, eptinezumab 100 mg had increased odds of response on the HIT-6 total score (odds ratio [OR] 1.7, p = 0.0009) and five of the HIT-6 items vs placebo; at Month 3, eptinezumab 100 mg had increased odds of response on the HIT-6 total score (OR 1.6, p = 0.0019) and four of the HIT-6 items vs placebo. At both Months 1 and 3, eptinezumab 300 mg had significantly higher odds of response on the HIT-6 total score (OR 2.4, p < 0.0001 and 2.2, p < 0.0001, respectively) and all six HIT-6 items vs placebo.

Conclusion: In patients with CM, eptinezumab 100 mg and 300 mg provided meaningful reduction of headache impact at early and later time points compared with placebo, suggesting that preventive benefits of eptinezumab treatment are rapid and impact daily life and activities.

Disclosure of Interests: Richard B. Lipton: Serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta.

eNeura, Biohaven – Received compensation, that could include stock, stock options or expense compensation for serving on a board of directors for a commercial entity (for-profit business)

Biohaven – Within the past year, Dr. Lipton or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value in a company sponsoring research with which he was involved as an investigator.

Biohaven – Within the past year, Dr. Lipton or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value (which ever dollar value is lowest) in a company whose medical equipment or other materials related to the practice of medicine.

Within the past year received research support from the Migraine Research Foundation, the National Headache Foundation and Amgen.

James S. McGinley:

Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

Joe Hirman: Received compensation from Alder BioPharmaceuticals.

Rj Wirth:

Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

Carrie R. Houts:

Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

Roger Cady: Full time employee of Alder Biopharmaceuticals.

Neuromodulation for Headaches

IHC-OR-003

Effects of Single pulse transcranial magnetic stimulation on the propagation of cortical spreading depression

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Objective: Cortical Spreading Depression (CSD), the physiological correlate of migraine aura, is a self-propagating wave associated with blood flow changes, neuronal depolarization and glial activation. [A1] Single pulse transcranial magnetic stimulation (sTMS) is a non-invasive neuromodulation technique shown to be effective as an acute and preventative treatment for migraine, when applied at the occipital cortex. We have previously shown that sTMS increases the electrical threshold required for the induction of CSD. Here we aimed to investigate the actions of sTMS on the propagation of CSD.

Methods: All procedures were performed under a UK Home Office licence in accordance with the 1986 Animal (Scientific Procedures) Act in Snap25-2A-GCaMP6s-D mice (Jackson Labs). A custom made sTMS coil with diameter 11 mm, with stimulating parameters that mimic the sTMS treatment in migraine patients, was used to apply two subsequent sTMS pulses. The effect of sTMS (0T sham control group or 1.1T active sTMS group) on CSD propagation was assessed using genetically encoded calcium indicators. Cortical signal of murine GCaMP expressing neurons were recorded through an intact skull using laser-assisted fluorescence microscopy. A small opening was drilled in posterior of the viewing window to allow of CSD by pinprick.

Results: Application of two pulses of 1.1T sTMS significantly reduced the fluorescence peak of the CSD wave ($t(14)=3.508$, $p<0.01$) and the decay of the of the wave was quicker ($t(14)=3.168$, $p<0.01$) compared to the control sham group. The total area under the calcium uptake curve (integration of the signal) of the wave was significantly reduced in the active stimulation group

($t(14)=3.075$, $p<0.01$). sTMS treatment had no significant impact on the rise speed of the CSD wave compared to the control group ($t(13)=1.098$, $p=0.29$).

Conclusion: As well as increasing the threshold required to generate the CSD wave, sTMS affects the propagation of the wave once it has been generated, potentially through molecular changes that interfere with calcium uptake.

Disclosure of Interests: eNeura:equipment grant, lecturer fees, sponsorship. novartis sponsorship, allergan sponsorship, lecturer fees, consultation fees

Other Secondary Headache Disorders

IHC-OR-013

Inflammation as a risk factor for development of idiopathic intracranial hypertension

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Objective: The etiology of idiopathic intracranial hypertension (IIH) is not fully understood. It is proposed that an inflammatory response may be associated with IIH. We aimed to investigate whether IIH patients are more exposed to conditions causing inflammatory activation (infections and inflammatory disorders) prior to diagnosis.

Methods: Using data from the Swedish health registers and predefined algorithms we identified incident IIH patients between 2000–2016 and compared them with matched comparators (five healthy + five obese randomly selected individuals matched for age, sex, region and vital status). The Swedish National Patient Register and Prescribed Drug Register provided information on diagnosis and treatment of infectious and inflammatory disorders. Logistic regression with robust standard errors was used to estimate odds ratios (OR) and 95% confidence intervals (CI).

Results: We identified 902 IIH patients whose diagnosis was correct according to our algorithms. IIH patients had fourfold increased odds of having a specific viral or bacterial infection (ICD-10 A + B codes) the year before first IIH diagnosis compared to healthy comparators (OR = 4.4, CI 3.2–6.0). Increased odds were also seen for upper respiratory infections (OR = 5.5, CI 3.3–9.2) and influenza/lower respiratory infections (OR = 6.7, CI 2.8–16.1). An increased OR was seen for systemic inflammatory disorders (OR = 14.1, CI 6.2–31.8), and asthma (OR = 4.0, CI 2.2–7.1). IIH patients also differed significantly to obese comparators. Sub-analyses on exposure to

anti-infectious and anti-inflammatory drugs confirmed the increased odds for IHH patients; anti-infectious drugs (OR = 2.1, CI 1.8–2.5), non-steroidal anti-inflammatory drugs (OR = 3.9, CI 3.2–4.7), and corticosteroids (OR = 5.4, CI 4.0–7.1) all showed increased use among IHH patients relative to comparators in the year preceding diagnosis.

Conclusion: Inflammatory conditions were significantly more common in patients with IHH the year preceding first diagnosis of IHH compared to comparators. It suggests that a major inflammatory activation could trigger IHH development in predisposed individuals.

Disclosure of Interest: None Declared

Headache Science Excellence Tournament

IHC-OR-019

Alterations in functional connectivity during nitroglycerin (NTG)-triggered premonitory symptoms and migraine headache assessed using blood oxygen level dependant (BOLD) functional magnetic resonance imaging (fMRI)

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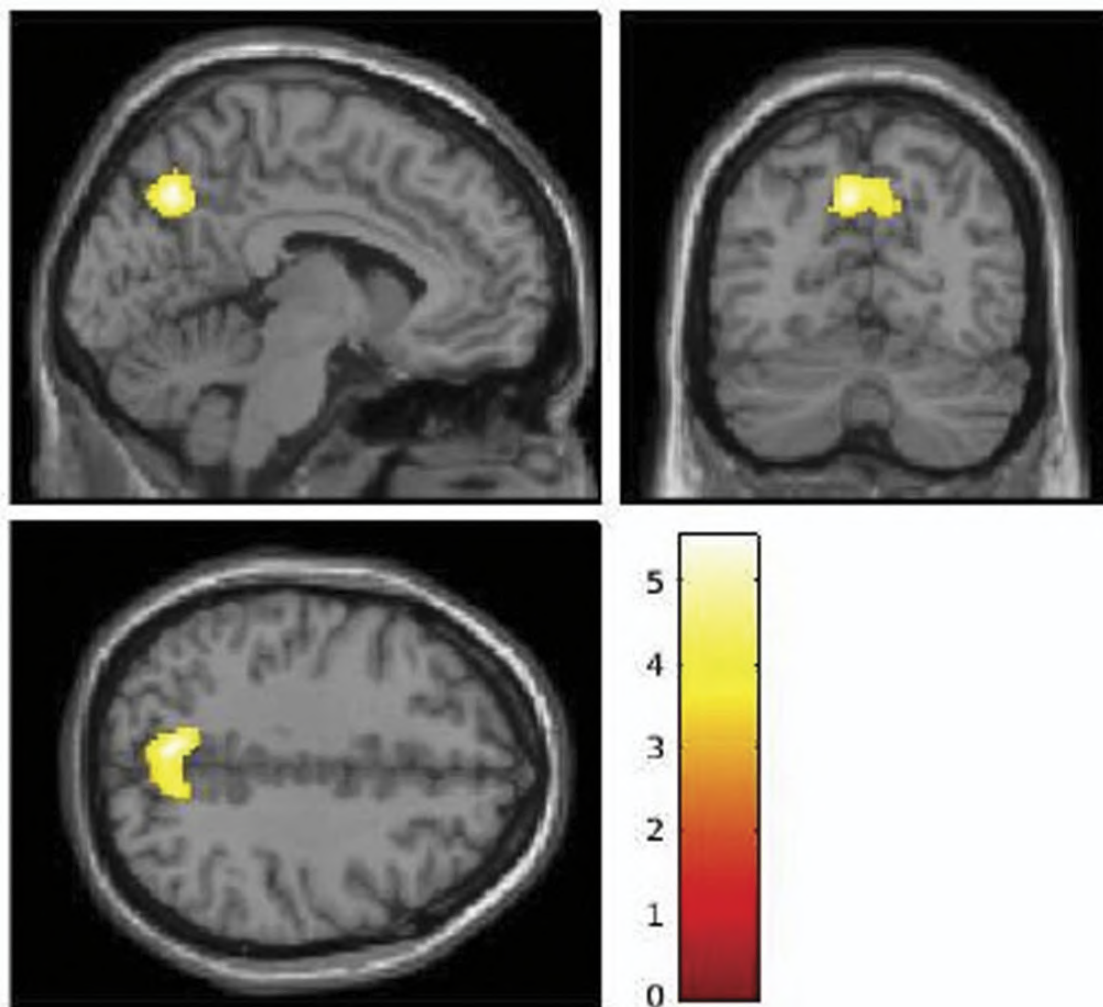
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Objective: Human functional imaging offers insights into the neurobiology of migraine. We aimed to study the



imaging characteristics of the premonitory and headache phases of migraine using NTG-triggered attacks.

Methods: Subjects ($n=25$) were screened, consented and recruited and randomised to either a 0.5 mcg/kg/min NTG infusion over 20 minutes or placebo, in a double-blind crossover study design. Following the infusion, the timeline and phenotype of symptom development was documented.

Structural T1, T2 and FLAIR imaging and resting state blood oxygen level dependant contrast (rsBOLD) time series, using a multiecho EPI sequence, was conducted at baseline and during premonitory symptoms and migraine headache on a 3T General Electric MR750 MRI scanner. Imaging was conducted at the same times following placebo infusion in the absence of symptoms.

Imaging was analysed using SPM 12 (www.fil.ion.ac.uk/SPM). Whole brain, voxel-wise analysis, in repeated measures ANOVA models using time and trigger substance as factors, was performed.

Results: Significant positive functional coupling was found between the thalami and the right precuneus and cuneus during the premonitory phase ($T=3.23$, peak connectivity change at $[-6, -68, 40]$ for left thalamus, $p=0.012$ and $[-4, -68, 40]$ for right thalamus, $p=0.019$). The premonitory phase was associated with a change in the direction of connectivity from positive to negative between the pons and the limbic lobe ($T=3.47$, peak connectivity change at $[2, 8, 50]$, $p<0.001$). The headache phase was associated with ongoing negative functional coupling between the pons and the cingulate and frontal cortices, and positive functional coupling between the pons and the cerebellar tonsils and medulla ($T=3.47$, peak connectivity change at $[-8, -52, -58]$, $p=0.007$).

Conclusion: The premonitory and headache phases of the migraine attack are associated with alterations in functional connectivity between subcortical and cortical brain areas, including areas of sensory processing and integration.

Disclosure of Interest: None Declared

IHC-OR-020

Opening of ATP sensitive potassium channels causes migraine attacks: a new target for the treatment of migraine

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Objective: Background: Migraine is one of the most disabling and prevalent of all disorders. To improve understanding of migraine mechanisms and to suggest new therapeutic target, we investigated whether opening of

ATP sensitive potassium channels (K_{ATP}) would cause migraine attacks.

Methods: Methods: In this randomized, double-blind, placebo-controlled, cross-over study, 16 patients aged 18–49 years with one to five migraine attacks a month were randomly allocated to receive an infusion of 0.05 mg/min K_{ATP} channel opener levcromakalim and placebo on two different days. The primary end-points were the difference in incidence of migraine attacks, headaches and the difference in area under the curve (AUC) for headache intensity scores (0–12 hours) and for middle cerebral artery blood flow velocity (V_{MCA}) (0–2 hours) between levcromakalim and placebo.

Results: Findings: 16 patients (100%) developed migraine attacks after levcromakalim compared with one patient (6%) after placebo ($P=0.0001$); the difference of incidence is 94% (95% CI 78% to 100%). The incidence of headache over the 12 hours observation period was higher but not significant after levcromakalim day ($n=16$) than after placebo ($n=7$) ($P=0.016$) (95% CI 16% to 71%). The AUC for headache intensity was significantly larger after levcromakalim compared to placebo ($AUC_{0-12\text{ hours}}$, $P<0.0001$). There was no change in mean V_{MCA} after levcromakalim compared to placebo ($AUC_{0-2\text{ hours}}$, $P=0.46$).

Conclusion: Interpretation: Opening of K_{ATP} channels caused migraine attacks in all patients. This suggests a crucial role of these channels in migraine pathophysiology and that K_{ATP} channel blockers are potential targets for novel drugs for migraine.

Disclosure of Interest: None Declared

IHC-OR-021

Investigating macrophage-mediated inflammation in migraine using ultrasmall superparamagnetic iron oxide-enhanced 3T magnetic resonance imaging

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Objective: Initiating mechanisms of migraine headache remain poorly understood. Inflammation pertaining to cerebral artery walls and brain parenchyma has been suggested to play a role in migraine pathophysiology. We conducted the first experimental human study to investigate macrophage-mediated inflammation as a biomarker of migraine.

Methods: Using ultrasmall superparamagnetic iron oxide (USPIO)-enhanced 3T MRI, we investigated the presence of macrophages in cerebral artery walls and in brain parenchyma of patients with migraine without aura. We used cilostazol as an experimental migraine trigger, and investigated both patients who received sumatriptan treatment, and patients who did not. To validate our use of

USPIO-MRI, we conducted a preclinical model with subcutaneous capsaicin injection in the trigeminal area.

Results: Twenty-eight patients with migraine without aura underwent the complete MRI protocol including a post-USPIO scan >24 hours after administration of USPIO. Twelve patients treated their attack with sumatriptan, 16 patients received no migraine-specific rescue medication. The preclinical model confirmed that USPIO-MRI detects macrophage-mediated inflammation. In patients, however, migraine attacks were not associated with increased USPIO signal on the pain side of the head compared to the non-pain side.

Conclusion: Migraine without aura is not associated with macrophage-mediated inflammation specific to the head pain side.

Disclosure of Interests: SK has acted as invited speaker for Novartis.

FMA reports travel grant from Allergan. FMA has acted as invited speaker for Teva, Novartis, and Eli Lilly. FMA acts on the advisory boards of Novartis and Eli Lilly.

MA reports personal fees from Allergan, Amgen, Alder, Eli Lilly, Novartis and Teva. MA participated in clinical trials as the principal investigator for Alder ALD403-CLIN-011 (Phase 3b), Amgen 20120178 (Phase 2), 20120295 (Phase 2), 20130255 (OLE), 20120297 (Phase 3), GM-11 gamma-Core-R trials, Novartis CAMG334a2301 (Phase 3b), Amgen PAC1 20150308 (Phase 2a), Teva TV48125-CNS-30068 (Phase 3). MA has no ownership interest and does not own stocks of any pharmaceutical company. MA serves as associated editor of *Cephalalgia*, co-editor of the *Journal of Headache and Pain*. MA is President-elect of the International Headache Society and General Secretary of the European Headache Federation.

IHC-OR-022

Differential Effects of Mu and Delta Opioid Receptor Agonists in Models of Chronic Migraine-Associated Pain and Aura

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Objective: μ -opioid receptor agonists such as morphine and oxycodone are commonly prescribed for migraine. Use of μ agonist can result in detrimental effects including medication overuse headache/opioid induced hyperalgesia (OIH). Comparatively δ opioid receptor agonists in pre-clinical models have been effective in reducing migraine correlates of allodynia and aura, with limited opioid

induced hyperalgesia. The aim of this study was to develop mouse models that reflect the exacerbation of migraine related symptoms by μ agonists and investigate the effects of the novel δ agonist, KNT-127, in models of migraine

Methods: C57BL6/J mice were used. The effect of morphine on migraine aura was assessed by a well-established model of OIH, morphine or vehicle (VEH) was injected twice daily for 4 days (20 mg/kg for days 1–3, 40 mg/kg day 4, SC). On day 5, cortical spreading depression (CSD) was induced by dripping 1M KCl on the dura. To model the exacerbating effects of μ opioids on migraine-associated pain, mice were administered morphine (20 mg/kg, SC)/VEH daily for 11 days and received low dose of the human migraine trigger nitroglycerin (NTG; 0.1 mg/kg, IP)/VEH every other day for the last 9 days. To test the effects of the δ agonist, KNT-127, a separate cohort of mice were injected with high-dose NTG (10 mg/kg, IP)/VEH every other day for 9 days; and tested 24 h after final injection with KNT-127 (50 mg/kg SC)/VEH. The effect of KNT-127 was also examined in the CSD model

Results: Chronic morphine treatment significantly increased the number of CSD events relative to control. Chronic morphine also exacerbated the effects of low-dose NTG, and mice that received both morphine and NTG showed a sustained and severe allodynia, that was not observed in mice treated with morphine or NTG alone. In contrast, the novel δ agonist KNT-127 inhibited CSD events and reversed established NTG-induced pain

Conclusion: These results indicate the differential effect of μ and δ opioid receptor agonists on migraine. We can model the exacerbation of migraine-associated symptoms by μ agonists. Comparatively, we show that a novel δ agonist relieves migraine-related symptoms, further supporting the development of this target for this disorder

Disclosure of Interest: None Declared

IHC-OR-023

Cannabinoids induce latent sensitization in a preclinical model of medication overuse headache

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Objective: We evaluated the effects of cannabinoid receptor agonists, WIN55,212-2 and Delta-9-tetrahydrocannabinol (Δ -9-THC) in eliciting latent sensitization of female rats to bright light stress (BLS) suggestive of risk to development of medication overuse headache (MOH).

Methods: Female, Sprague Dawley rats received graded intraperitoneal (i.p.) doses of WIN55,212-2 or Δ -9-THC. Antinociception (tail-flick test), catalepsy and hypomotility

(open field test) and impairment of motor function (rotarod test) were assessed to establish effective dosing. Rats were then treated twice-daily with equianalgesic doses of i.p. WIN55,212-2 or Δ -9-THC or vehicle for 7 days and cutaneous tactile sensory thresholds were evaluated at different time points. Three weeks after the discontinuation of the drugs, rats received a one-hour period of bright light stress (BLS) exposure for two consecutive days and tactile sensory thresholds were re-assessed.

Results: WIN55,212-2 and Δ -9-THC produced dose- and time-related antinociception as well as hypomotility, catalepsy and motor impairment, confirming cannabinoid receptor engagement. Repeated administration of WIN55,212-2 and Δ -9-THC induced generalized periorbital and hindpaw allodynia that resolved within 3 weeks after discontinuation of drug. Two episodes of BLS produced a delayed and long-lasting periorbital and hindpaw allodynia selectively in rats previously treated with WIN55,212, and Δ -9-THC.

Conclusion: Cannabinoids are perceived to be analgesic in migraine but risks of overuse of medications containing Δ -9-THC or other components of marijuana remain uncertain. We demonstrated that cannabinoid receptor agonists, including Δ -9-THC, produce a state of latent sensitization characterized by increased sensitivity to stress, a commonly accepted migraine trigger. Overuse of cannabinoids, including cannabis, may promote medication overuse headache in vulnerable individuals.

Disclosure of Interest: None Declared

IHC-OR-024

Central sites controlling CGRP-induced light-aversive behavior

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Objective: A hallmark of migraine is photophobia. This photophobia in patients with PTH or migraine can be debilitating and treatments are lacking. The neuropeptide CGRP is a key player in migraine and induces photophobia-like behavior in mice. Although we know that CGRP is a player in migraine, it is still not known where it acts centrally to induce migraine-like phenotypes. In this study, we have focused on central sites of potential CGRP action that could act as sensory integration centers such as the posterior thalamic area (PTA) and the cerebellum. We therefore tested the hypothesis that CGRP could act in these areas to induce light-aversive behavior in mice.

Methods: We used two targeted approaches. First, we injected CGRP into either the PTA or the cerebellum and

then tested light sensitivity via the light dark assay. Second, we used optogenetics to determine the role the neurons in these locations play in light-aversive behavior. For both paradigms, anxiogenic responses were assessed using the open field assay.

Results: Injection of CGRP into the PTA sent wildtype mice into the dark, even with dim light, and without increased anxiety behavior in an open field assay. A similar phenotype was elicited by optogenetic activation of glutamatergic PTA neurons. In addition to the PTA, the injection of CGRP in the deep cerebellar nuclei induced significant light-aversive behavior, but with anxiety-like behavior as well. As a control, neither CGRP or optical stimulation of the hippocampus affected light aversion or open field behaviors.

Conclusion: The PTA is likely to be a key integrator of light aversive signals that are modulated by CGRP in migraine. The cerebellum may also contribute to light-aversive behaviors but further testing is needed to tease out its exact role.

Disclosure of Interest: None Declared

Cluster Headache and Other Trigeminal Autonomic Cephalalgias

IHC-DP-001

Gender differences in cluster headache in Sweden

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Objective: Cluster headache is considered a male-dominated disorder, but we have previously suggested that woman may display a more severe phenotype. In order to understand better how the disease is manifested in the two sex groups, we analyzed our large Swedish cluster headache cohort with respect to treatment, rhythmicity, heritability and impact on everyday life in relation to gender.

Methods: Our cluster headache cohort consists of >750 patients with a validated diagnosis according to ICHD-3. We performed a statistical analysis and compared collected clinical data and lifestyle factors from female (33%) and male (67%) patients using Student's t-test for continuous variables and Fisher's exact test or Chi-squared test for categorical variables in GraphPad Prism 5 (San Diego, California USA).

Results: According to the ICHD-3 about 10–15% of the cluster headache patients suffer from the chronic subtype and in our cohort we could see a clear difference for women (17.4%) and men (7.9%, $p = 0.0002$). More women (33.2%) than men (25.7%) used oxygen as abortive medication ($p = 0.0331$) and in addition, female patients (58.9%) were generally more reliant on prophylactic treatment than male patients (47.4%, $p = 0.0027$). Women with cluster headache have longer cluster periods than men ($p = 0.0029$) and are generally more prone to exhibit diurnal rhythmicity in their attack pattern (76.3% women vs 65.1% men, $p = 0.0018$). Regarding heritability, female patients (18.2%) were more likely to have a first-, second-, or third-degree relative also diagnosed with cluster headache than male patients (7.7%, $p < 0.0001$). Alcohol as a headache trigger occurs less often in women (49.2%) than in men (56.9%, $p = 0.0487$) and, interestingly, female patients are more often sleep deprived (<5 hours/night) than male patients ($p = 0.0195$).

Conclusion: This study demonstrates that female and male cluster headache patients are affected differently by the disorder with regard to need of prophylactic treatment, bout and attack patterns, heritability and lifestyle factors. These intriguing new findings have to be taken into consideration by clinicians when diagnosing and treating cluster headache patients.

Disclosure of Interest: None Declared

IHC-DP-005

Circadian rhythm gene expression in cluster headache

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Objective: Cluster headache is a devastating neurovascular disorder characterized by a striking circadian and circannual attack pattern. Previous genetic studies suggest an association between cluster headache and the *CLOCK* gene, which has a critical role in the generation of circadian rhythms. In this study, we wanted to characterize general circadian rhythm in cluster headache by comparing gene expression in biological tissue from patients and controls.

Methods: We analyzed gene expression with focus on circadian rhythm using a predesigned PrimePCR assay from BioRad, Neurophysiological process-Circadian rhythm H96, to identify possible gene expression differences in 43 of the key genes regulating circadian rhythm. Genes differentially expressed in patients and controls will be validated with qRT-PCR using highly specific primers and

SYBR green chemistry in a relative quantification setting. We investigated primary fibroblast cell cultures, since human fibroblasts show circadian oscillations in expression of “clock genes”. These fibroblasts were obtained from skin biopsies from 11 cluster headache patients and 9 controls, exposed to a serum shock in order to reset the biological clock and harvested at zeitgeber time (ZT) + 6 h.

Results: When comparing gene expression levels from the preliminary screening between cluster headache patients and controls at ZT + 6 h, the relative *ARNTL* (aryl hydrocarbon receptor nuclear translocator like) gene expression was significantly lower in cluster headache patients compared to controls ($p = 0.001$). *ARNTL* is part of a heterodimer with *CLOCK* which upregulates the transcription and translation of key players in molecular circadian rhythmicity. In addition the *NR1D1* (nuclear receptor subfamily 1, group D, member 1) expression was increased in cluster headache compared to controls ($p = 0.03$). *NR1D1* is an important circadian regulator and has previously been implicated in cluster headache.

Conclusion: Decreased *ARNTL* expression and increased *NR1D1* expression may contribute the periodically reoccurring cluster headache attacks in a yet unknown manner. Although a lot more research needs to be done, this study points to a role of the clock genes in the pathophysiology of cluster headache.

Disclosure of Interest: None Declared

IHC-DP-006

Clock Gene expression in Cluster Headache

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Objective: One of the most striking features of Cluster Headache(CH) is its circannual and circadian patterns. The bouts have seasonal incidence in the spring and autumn and attacks a daily clockwise regularity. The *CLOCK* gene is a core gene that regulates the molecular mechanism of the circadian clock and polymorphisms rs12649507 have been associated with CH in a Swedish sample. Our objective is to measure the expression of *CLOCK* over one year in a population of CH patients and matched controls.

Methods: CH patients were sampled 2 to 4 times over one year, in or outside bouts, 7 to 9 days after each solstice an equinox. We quantified the expression of *CLOCK*

in the peripheral blood by isolating RNA from PBMCs that was later measured by quantitative RT-PCR. Relative expression levels were calculated using the internal control GAPDH and then normalized to the average of the control population.

Results: Twenty-nine patients (24, 83% males, age 47 years) of which 24 (83%) were episodic CH and 23 controls were included in the first year. Each patient had three or four samples collected in a total of 107 (19 in December solstice, 29 in March equinox, 33 in June solstice, 26 in September equinox); of these, 27 (25.2%) coincided with CH bouts. The differences in CLOCK expression in patients compared to controls were: -33.2% in December solstice; 11.3% in March equinox; 21.0% in June solstice; and 36.4% in September equinox. Twenty-seven (25%) of samples were collected within an active bout. The expression of CLOCK was not significantly different between bout samples (1.14 average relative expression) and non-bout samples (1.12 average relative expression). The mixed effects model was applied to these samples and the p value calculated between bout and non-bout groups was 0.3028.

Conclusion: Preliminary results show that CLOCK expression in CH patients varies along the seasons being lower in the December solstice and higher in the September equinox. Bout activity does not seem to influence CLOCK expression. Additional data is needed to confirm these results.

Disclosure of Interest: None Declared

IHC-DP-007

Diagnostic delay of cluster headache: A cohort study from the Danish Cluster Headache Survey

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Objective: To investigate the influence of clinical and demographic features on diagnostic delay (in cluster headache (CH) patients, in order to discuss diagnostic pitfalls and raise disease awareness.

Methods: A large study of a well-characterized cohort of 400 CH patients from the Danish CH survey, diagnosed according to ICHD-II. ANOVA was applied to investigate differences in diagnostic delay between groups. Selected independent variables were assessed in relation to diagnostic delay using a gamma regression model.

Results: Diagnostic delay was significantly reduced for each decade of CH onset from 1950–2010 ($P < 0.001$). Debut after 1990 was associated with shorter diagnostic delay (OR = 0.28 $P < 0.001$), whereas attack duration > 180 minutes (OR = 1.62, $P < 0.034$), migraine-like features (OR = 1.30, $P < 0.043$) and nocturnal attacks (OR = 1.39, $P < 0.021$) were associated with prolonged diagnostic delay. Further, diagnostic delay decreased with age of onset (age < 20: 13.8 years, age 20–40: 5.4 years and age > 40: 2.1 years, $P < 0.001$).

Conclusion: Diagnostic delay was reduced for every decade investigated, whereas some atypical CH features were associated with prolonged diagnostic delay. Interestingly, nocturnal attacks were associated with prolonged diagnostic delay even though this feature is well-known among CH patients. Furthermore, debut of CH at a higher age decreases diagnostic delay significantly whereas patients with debut when < 20 years have the longest diagnostic delay. Better medical education and more disease awareness are needed to prevent misdiagnosis and prolonged diagnostic delay especially among patients who present atypical CH features.

Disclosure of Interest: None Declared

IHC-DP-018

More precise phenotyping of cluster headache using prospective attack reports

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Objective: The clinical characteristics of cluster headache (CH) are based mainly on retrospective attack descriptions of “usual” attacks, but whether these reports are reliable is uncertain. We aimed to compare retrospective and prospective attack descriptions and describe the within- and between patient variability of attacks.

Methods: Fifty-seven CH patients underwent a semi-structured interview obtaining a retrospective account of usual CH attacks. Patients thereafter prospectively recorded the clinical characteristics of up to 10 attacks/patient in a headache diary. We investigated four different attack characteristics; i) severity, ii) duration, iii) number of autonomic- and iv) number of migrainous symptoms. Retrospective and prospective data was compared. Within- and between patient variability of attacks was assessed.

Results: Retrospective attacks descriptions ($n = 57$) were significantly longer ($p = 0.046$) and more severe ($p < 0.0001$) for untreated attacks compared with prospective reports ($n = 500$). The number of autonomic

symptoms was significantly higher in the retrospective reports compared to the prospective reports ($p < 0.0001$). Within-patient variability for attack duration, pain severity, number of autonomic and migrainous symptoms was low. Compared to men, more women reported longer ($p = 0.026$) and more severe ($p = 0.028$) attacks with more migrainous symptoms ($p = 0.033$).

Conclusion: We found important differences between prospectively and retrospectively reported attacks with duration and severity of untreated attacks overestimated in retrospective attack descriptions. CH attacks display low within-patient variability, but the presentation of CH attacks varies between patients.

The high prevalence of symptoms typically associated with migraine should raise more diagnostic awareness for CH, especially in women who are more often misdiagnosed as having migraine.

Disclosure of Interest: None Declared

Comorbidity of Primary Headaches

IHC-DP-002

Comorbidity with Fibromyalgia Predicted a Poorer Outcome in Patients with Chronic Migraine on Flunarizine: A 16-week Study

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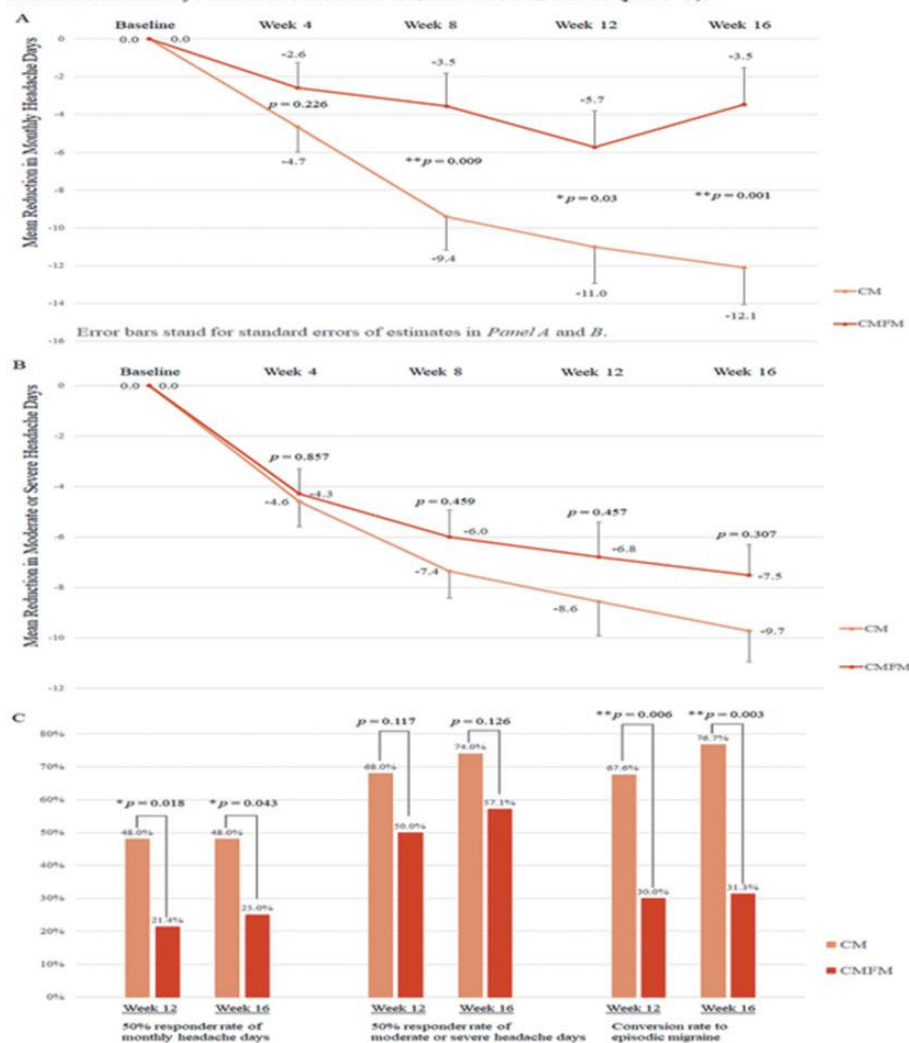
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Objective: Fibromyalgia is a common comorbidity (35.6%) in chronic migraine (CM) with an unknown impact on treatment. This study aimed to investigate

Fig. 1. The mean reductions in MHDs (panel A) and MS-HDs (panel B), and the 50% responder rate of headache days and conversion rate to EM at week 12 and 16 (panel C).



whether the outcome differed between CM patients with and without fibromyalgia (CMFM vs. CM).

Methods: We prospectively recruited CM patients with or without fibromyalgia at the Headache Clinic of Taipei Veterans General Hospital. Patients with major depressive disorders were excluded. The study consisted of a 4-week baseline observation and a 16-week treatment period. During the observation, only acute analgesic medications were allowed. Flunarizine (5–10 mg/day) was administered to all patients. Pregabalin was given to CMFM patients. All patients were asked to keep a headache diary throughout the study. Monthly headache days (MHDs) and moderate or severe headache days (MS-HDs) were compared between CM and CMFM patients every 4 weeks after adjusting the baseline headache frequency. We also calculated 50% responder rate and the rate of conversion to episodic migraine (EM).

Results: Of the 87 recruited CM patients (81F/6M, mean age 40.9), 30 had comorbid fibromyalgia (CMFM). There were no differences in sex or age between CM and CMFM patients. The baseline MS-HDs were higher in CMFM patients (16.8 ± 8.6 vs. 11.7 ± 7.0 , $p = 0.004$). Compared to CMFM patients, the mean reduction in MHDs was greater in CM patients at week 8 (9.4 vs. 3.5, $p = 0.009$), week 12 (11.0 vs. 5.7, $p = 0.03$), and week 16 (12.1 vs. 3.5, $p = 0.001$). However, the reduction of MS-HDs was comparable between CM and CMFM patients. CM patients had higher 50% responder rate of MHDs (week 12: 48 vs. 21.4%, $p = 0.018$; week 16: 48.0 vs. 25%, $p = 0.043$) and the rate of conversion to EM (week 12: 67.0 vs. 30.0%, $p = 0.006$; week 16: 76.7 vs. 31.3%, $p = 0.003$) at week 12 and 16.

Conclusion: CMFM patients were associated with poorer treatment outcomes to flunarizine than CM patients despite simultaneously treated with fibromyalgia medication. It suggests that comorbid fibromyalgia makes CM patients more intractable to migraine treatments.

Disclosure of Interest: None Declared

Genetics and Biomarkers of Headache Disorders

IHC-DP-014

Migraine polygenic risk score associates with efficacy of migraine-specific drugs

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Objective: The objective is to assess the association of the polygenic risk scores (PRS) for migraine with patient's response to migraine treatment.

Methods: At the Danish Headache Centre, 2,219 migraine patients were interviewed using a semi-structured interview to assess headache diagnose and acute and prophylactic drug response. All participants were unrelated and whole genome genotyped. Using the LDpred algorithm and the summary statistics from the most recent migraine genome-wide association study ($n = 375,000$), the PRS was calculated for each participant. Using unrelated Danish controls ($n = 929$), the PRS-score was normalized, so that one unit resembles a two-fold increase in the risk of migraine. We used logistic regression to assess the association of the PRS and treatment response, and subsequently the area under the curve (AUC) to estimate the predictive power.

Results: For acute treatment, an increase in migraine risk was associated with a positive response to migraine-specific treatment (OR = 1.25 [95% CI = 1.05–1.49]). The same was observed when analysing the PRS-score in deciles, here patients in the highest decile were more likely to respond to treatment (OR = 1.65 [95% CI = 1.07–2.56]) in comparison with the remaining 90%. No association was seen with prophylactic treatment.

Conclusion: The additive genetic risk for migraine captured by PRS was significantly associated with a positive response to migraine-specific treatment and provide an important piece in our understanding of migraine pharmacogenetics.

Disclosure of Interest: None Declared

Headache Epidemiology, Outcomes and Burdens

IHC-DP-012

Reduction in Healthcare Resource Utilisation in Patients Treated With OnabotulinumtoxinA for Chronic Migraine: Results From the REPOSE Study

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Objective: To assess healthcare resource utilisation (HRU) in patients treated with onabotulinumtoxinA for chronic migraine (CM) in a European sample, with a focus on German patients.

Methods: REPOSE is a 2-year, multicentre (78 sites, 7 European countries), prospective, noninterventional, open-label study that describes the real-world use of onabotulinumtoxinA in adults with CM. Enrolled patients received onabotulinumtoxinA for CM approximately every 12 weeks according to the physician's discretion and guided by the Summary of Product Characteristics. HRU data, including visits to a healthcare professional (HCP; any reason), accident and emergency (A&E) visits (any reason), and hospital admittance for headache, were collected at baseline and at each treatment session. All variables were summarized descriptively as mean (SD) or counts (percentages).

Results: A total of 641 patients were enrolled; 633 received at least 1 dose of onabotulinumtoxinA for CM. Mean age was 45 years, 85% were female, and 60% (n = 377) were from Germany. At baseline, 45.8%, 6.3%, and 6.0% of all patients reported HCP visits, A&E visits, and hospital admittance for headache, respectively. Reductions from baseline were reported at each follow-up session for HCP visits (range: 12.5%–20.8%), A&E visits (range: 1.0%–2.4%), and hospital admittance for headache (range: 0.4%–1.7%). Within the German subgroup, 35.8%, 2.1%, and 4.2% reported HCP visits, A&E visits, and hospital admittance for headache at baseline, respectively. At each follow-up session, decreases were recorded in HCP visits (range: 7.4%–13.4%), A&E visits (range: 0.0%–0.8%), and hospital admittance for headache (range: 0.7%–2.1%).

Conclusion: Real-world findings from REPOSE demonstrate that onabotulinumtoxinA treatment for CM is associated with a reduction in HRU, including HCP visits (any reason), A&E visits (any reason), and hospital admittance (headache). Similar trends in HRU reductions were observed between the total sample and the German subgroup. Combined, these data support the long-term benefits associated with the use of onabotulinumtoxinA for CM in clinical practice.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland

Katja Kollwe, MD, has received travel grants and honoraria for lectures from Allergan plc, Ipsen, Merz, and Biogen. Angela Antonakakis, MD, has nothing to disclose. Michael Kiszka, MD, has received travel grants from Bayer and Merck. Katherine Sommer, MRes, PhD, is an employee of Allergan plc and receives stock or stock options from the company. Justin Yu, MS, PharmD, is an employee of Allergan plc and receives stock or stock options from the company.

Katja Kollwe, MD, has received travel grants and honoraria for lectures from Allergan plc, Ipsen, Merz, and Biogen.

Angela Antonakakis, MD, has nothing to disclose.

Michael Kiszka, MD, has received travel grants from Bayer and Merck.

Katherine Sommer, MRes, PhD, is an employee of Allergan plc and receives stock or stock options from the company. Justin Yu, MS, PharmD, is an employee of Allergan plc and receives stock or stock options from the company.

IHC-DP-029

Work-related disability caused by headache disorders among workers in Japan – A survey at an Information Technology company, with technical support from WHO-WPRO –

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Objective: The purpose of this study is to determine the prevalence of and disability caused by headache disorders among employees at an information technology (IT) company in Japan.

Methods: The survey assessed prevalence, characteristics, and disability of headache disorders among full-time IT employees. The study utilized intranet through mobile devices. This study was supported by WHO-Western Pacific Region Office (WPRO) and International Headache Society. The protocol was approved by the IRB of National Institute of Public Health of Japan and WHO-WPRO.

Results: 2,458 (1,963 men, 495 women) out of 2494 (99%) responded to the survey that utilized ICHD-3 beta criteria. Headache type(s) and proportions were classified as: migraine and tension type headache (M/TTH, 4%; 61 male/27 female), migraine (M, 13%; 205 male/123 female), tension type headache (TTH, 53%; 61 male/27 female), other headache, 15%; 265 male/95 female) and no headache (NHA, 15%; 339 male/43 female). In the past 3 months, the average number of headache days were significantly higher in M/TTH and M compared to TTH.

The number of days when productivity at work was reduced by half or more because of headache was significantly higher in M/TTH and M compared to TTH, and the cost of productivity loss due to M/TTH and M is estimated at 360 US\$/year/person. SF12 and WPAI also revealed significant impairment in quality of life (QOL) and work productivity estimated at 2200 US\$/year/person in M/TTH and

M. Estimated cost of productivity loss by presenteeism and absenteeism using the productivity scores was calculated 8.9 billion US\$/year.

Conclusion: This study revealed that within a Japanese IT company, employees with migraine miss significantly more time from work and are significantly less productive when at work compared to those with other headache disorders and those without headache. These results support the development and implementation of workplace programs to improve migraine-related QOL and reduce the workplace burden and costs associated with lost workplace productivity.

Disclosure of Interest: None Declared

Headache Pathophysiology – Basic Science

IHC-DP-022

Central CGRP receptor occupancy following oral dosing of a CGRP receptor antagonist utilizing a humanized RAMP1 expressing mouse

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Objective: Recent advances in migraine treatment and prevention have focused on the calcitonin gene related peptide (CGRP) pathway, which has been shown to play a key pathophysiological role in the disorder. Telcagepant, a small molecule antagonist of the CGRP receptor (CGRP_r) that has been effective in patients with migraine, displays a species-specific binding affinity difference which complicates the results of preclinical studies. The difference in affinity is due to variance in the accessory protein RAMP1, which forms a heterodimer with the calcitonin receptor-like receptor (CLR) to compose the CGRP_r. A human RAMP1 expressing mouse line was developed to explore the amount of central receptor occupancy obtained by oral dosing of a CGRP receptor antagonist.

Methods: Partially humanized CGRP_r mice were generated by creating a knockout of native mouse Ramp1 by CRISPR/Cas9 methodology followed by introduction of human RAMP1 utilizing a modified BAC construct. The humanized hRAMP-mCLR receptor distribution in the brain was determined with autoradiographic analysis using ¹²⁵I-CGRP in sections from fresh frozen brain from the transgenic line and compared to wild type mice. To assess the central receptor occupancy, an ex vivo autoradiographic binding assay was conducted following oral dosing of telcagepant at a dose range of 10–500 mg/kg.

Results: The hRamp-mCLR receptor distribution in the brain was essentially equivalent to the wildtype mouse CGRP receptor. In both males and females, the receptor density was found to be higher than in wildtype mice, particularly in the cerebellum, lateral septum and amygdala. Tissue homogenate binding from the cerebellum of the partially humanized mice confirmed the affinity of telcagepant at the hRAMP1-mCLR receptor is similar to the fully human receptor. The ex vivo autoradiography demonstrated that oral telcagepant was able to dose dependently occupy the central hRAMP1-mCLR receptor.

Conclusion: Creation of a hRAMP1-mCLR transgenic mouse line enables preclinical assessment of pharmacodynamic measures of human CGRP_r preferring antagonists.

Disclosure of Interests: M. Morin is an employee of Eli Lilly and Company.

B. Li is an employee of Eli Lilly and Company.

A. Mogg is an employee of Eli Lilly and Company.

M. Johnson is an employee of Eli Lilly and Company.

K. Johnson is an employee of Eli Lilly and Company.

IHC-DP-023

CGRP outflow from the meninges into blood and cerebrospinal fluid

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Objective: Calcitonin gene-related peptide (CGRP) has frequently been detected in the blood of the jugular vein at increased concentrations during migraine and cluster headache. Few CGRP measurements have been reported in peripheral blood and cerebrospinal fluid (CSF). Perivascular trigeminal, particularly meningeal afferents are considered as the source of CGRP. In an animal model we aimed to understand the pathways of CGRP outflow into the circulation.

Methods: In adult anaesthetized Wistar rats, a catheter was introduced into the right external jugular vein in caudal direction. Blood was collected from the jugular vein or the femoral artery and CSF from the cisterna magna. The exposed parietal dura mater was stimulated electrically or with 60 mM potassium chloride (KCl). Changes in CGRP content of jugular venous blood and CSF samples after stimulation or application of 10 μM CGRP onto the exposed dura mater were measured with an ELISA.

Results: Electrical stimulation of the dura mater with C-fibre strength or application of depolarizing KCl was followed by a moderate increase in CGRP in the blood

of the jugular vein at the branching point of the external and the internal jugular vein 5 min after stimulation. The CGRP concentration was comparable to that collected from the right femoral artery. In contrast, significant increases in CGRP concentrations were measured in CSF. Direct application of CGRP onto the dura mater was followed by a minimal increase in CGRP in the jugular vein and a significant but delayed increase in the CSF.

Conclusion: CGRP released in the dura mater is mainly taken up from venous vessels and flowing out via the jugular veins. However, the collection of CGRP from the branching point of external and internal jugular vein is insufficient, because in rat the internal jugular vein conducts very little venous blood. The increasing concentration of CGRP in the CSF may be due to the release from medullary sources during stimulation and slow diffusion from the dura mater into the subarachnoid space.

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Disclosure of Interest: None Declared

IHC-DP-024

Delta opioid receptor activation regulates migraine-associated pain by inhibiting CGRP signaling in the trigeminovascular complex

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Objective: We have previously identified the delta opioid receptor (DOR) as a novel therapeutic target for headache disorders. DOR agonists effectively reduce cephalic allodynia in models of chronic migraine, post-traumatic headache, and triptan or opioid-induced medication overuse headache. Further, activation of DOR reduces cortical spreading depression. The mechanism by which DORs regulate migraine is currently unclear. The aim of this study was to determine the expression of the DOR in the trigeminovascular complex, and investigate its association with the pro-migraine neuropeptide, calcitonin gene related peptide (CGRP) and its receptor.

Methods: Male and female C57BL/6J and DOR-eGFP knockin mice were used throughout this study. To induce chronic migraine-associated pain mice were treated every other day for 9 days with the known human migraine trigger, nitroglycerin (NTG, 10 mg/kg IP) or vehicle. To determine the effect of DOR activation on the development of chronic cephalic allodynia, mice were also injected with the delta agonist SNC80 (10 mg/kg IP) or vehicle. Immunohistochemistry was performed to identify DOR, CGRP, and RAMP1. We used RNAScope in situ hybridization to examine the co-expression between DOR and calcitonin receptor like receptor (CRLR).

Results: Chronic NTG resulted in severe chronic cephalic allodynia which was prevented with the co-treatment of SNC80. Chronic NTG produced a corresponding increase in CGRP expression in the trigeminal nucleus caudalis (TNC) and trigeminal ganglia (TG); which was inhibited by treatment with SNC80. Chronic NTG also produced an upregulation of DOR in the TNC and TG. However, DOR was not co-expressed with CGRP but with components of the CGRP receptor, CRLR and RAMP1.

Conclusion: These results indicate that activation of DOR inhibits the upregulation of CGRP associated with chronic migraine-related pain. In addition, DORs are upregulated in response to chronic allodynia, and could serve as a protective measure. Finally, DORs are co-expressed with CGRP receptor. As DOR activation has an inhibitory effect on the cell, it likely prevents the propagation of CGRP receptor signaling.

Disclosure of Interest: None Declared

IHC-DP-025

Direct disruption of the molecular clock increases migraine-like phenotypes in a genetic mouse model with circadian dysfunction

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Objective: Migraine is strongly linked to disruptions in circadian rhythms. A mutation in the molecular clock regulatory kinase, casein kinase 1δ (CK1δ), is known to be comorbid for the rare circadian disorder Familial Advanced Sleep Phase (FASP) and an increased prevalence of migraine with aura. However, it is unclear if this effect on migraine is through direct disruption of the molecular clock, or if CK1δ is having other downstream effects. To answer this question, we are exploiting a second mutation affecting the clock specific protein Period 2, which is directly regulated by CK1. This mutation is known to cause FASP, but has yet to be linked to migraine. By directly comparing migraine-like phenotypes in transgenic mice harbouring these two human mutations, we hope to identify if clock disruption alone is sufficient to increase migraine-like susceptibility in pre-clinical models.

Methods: Migraine-like phenotypes, including cortical spreading depression (CSD) and nitroglycerin-induced periorbital allodynia, were assessed in CK1δ-T44A (*n* = 24), Per2-S662G (*n* = 25) transgenic mice and matched WT littermates (*n* = 47). CSD was induced in

anaesthetized mice using constant stimulus potassium chloride (1 M) and recorded for 1 hr. Periorbital allodynia was assessed via measurement of mechanical sensitivity using the von Frey assay at baseline and again 2 hrs post nitroglycerin treatment (5 mg/kg i.p.).

Results: Both transgenic lines showed a significant increase in the number of CSD events compared to WT controls. (WT = 7, CK1d-T44A = 10; $U = 12$, $p < 0.0001$) (WT = 6, Per2-S662G = 7; $U = 30$, $p < 0.05$). Transgenic mice also showed an increase in mechanical sensitivity post nitroglycerin treatment (WT vs CK1d-T44A: $F_{1,22} = 41.61$; $p < 0.0001$; WT vs Per2-S662G: $F_{1,22} = 32.13$; $p < 0.0001$) indicating a sensitization of trigeminal pain processing as compared to WT.

Conclusion: These results confirm that disruption to the clock protein Period 2 is, at least in part, sufficient to induce increased susceptibility to migraine-like phenotypes, which for the first time, implicates a purely circadian gene in migraine pathophysiology. From here, we aim to dissect out the underlying mechanisms in order to identify new therapeutic targets for migraine.

Disclosure of Interest: None Declared

Headache Pathophysiology – Imaging and Neurophysiology

IHC-DP-003

Aberrant pain network connectivity in chronic migraine: a resting-state MEG study

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Objective: Episodic migraine may evolve into disabling chronic migraine with unknown mechanism. Previous MRI studies have shown altered resting-state functional connectivity of the pain-related brain network in episodic migraine. This study investigated the connectivity change of the pain network in migraine through direct neural signals to explore the embedded spectrotemporal features and the link to migraine chronification.

Methods: We enrolled patients with episodic (EM) and chronic migraine (CM) and healthy controls to record the closed-eyes resting-state cortical activities by using magnetoencephalography (MEG). The functional connectivity within the pain-related cortical network (including 10 regions of interest: bilateral insula, medial frontal, anterior cingulate, primary and secondary somatosensory cortices) at 1–40 Hz were analyzed by depth-weighted minimum norm estimates with imaginary coherence analysis.

Results: Patients with EM ($n = 74$, interictal phase), CM ($n = 87$, interictal phase) and healthy controls ($n = 65$) did not differ in demographics but the EM and CM groups had higher scores in the Hospital Anxiety and Depression Scale (vs. controls, both $p < 0.010$). Overall, the total node strength (the sum of region-to-region connectivity strength for each region of interest) within the pain-related cortical network differed between the EM, CM and control groups at the beta (13–25 Hz, $p < 0.001$) but not at other frequency bands. The beta connectivity was decreased in EM (vs. controls) at the left primary somatosensory and the right anterior cingulate cortices (both $p < 0.005$) and in CM (vs. controls) at all regions of interest (all $p < 0.005$). These findings did not change after adjustment of depression and anxiety. The connectivity measurements did not differ between EM and CM; however, the node strength at the left anterior cingulate cortex was negatively correlated with the headache frequency in all patients with migraine ($r = -0.263$, $p = 0.002$).

Conclusion: Brain connectivity of the pain network is decreased at the beta band in migraine and linked to migraine chronification. The finding provides new insights into the mechanism of migraine chronification. Further studies must elucidate if resting-state MEG connectivity can be used as a brain signature monitoring migraine progression.

Disclosure of Interest: None Declared

IHC-DP-004

Investigation of distinct molecular pathways in migraine induction using calcitonin gene-related peptide and sildenafil

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Objective: Migraine displays clinical heterogeneity of attack features and attack triggers. The question is whether this heterogeneity is explained by distinct intracellular signaling pathways leading to attacks with distinct clinical features. One well-known migraine-inducing pathway is mediated by cyclic adenosine monophosphate (cAMP) and another by cyclic guanosine monophosphate (cGMP). Calcitonin gene-related peptide (CGRP) triggers migraine via the cAMP pathway and sildenafil via the cGMP pathway. To date, no studies have examined whether migraine induction mediated via the cAMP and cGMP pathways yield similar attacks within the same patients.

Methods: Patients were subjected to migraine induction on two separate days using CGRP (1.5 mg/min for 20 minutes) and sildenafil (100 mg) in a double-blind, randomized,

double-dummy, cross-over design. Data on headache intensity, characteristics and accompanying symptoms were collected until 24 hours after drug administration.

Results: Twenty-seven patients completed both study days. Seventeen patients developed migraine after both study drugs (63%; 95% CI: 42–81). Headache laterality, nausea, photophobia and phonophobia were similar between drugs in 82%, 65%, 100%, and 94%, respectively, of the 17 patients who developed attacks both days.

Conclusion: A majority of patients developed migraine after both CGRP and sildenafil. This suggests that the cAMP and cGMP intracellular signaling pathways in migraine induction converge in a common cellular determinant, which ultimately triggers the same attacks.

Disclosure of Interests: The authors report no conflicts of interests pertaining to this work.

Disclosure of Interest: None Declared

IHC-DP-015

Is there an imaging biomarker to discriminate migraine and cluster headache patients?

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Objective: Similar alterations in brain regions involved in multisensory processing have been shown in migraine and cluster headache. The aim of this study was to identify magnetic resonance imaging (MRI) biomarkers to discriminate migraine, cluster headache patients and controls.

Methods: Functional and structural MR modalities were acquired from 20 migraineurs, 20 cluster headache patients and 15 controls. Patterns of MRI metric changes across subjects were identified using probabilistic spatial independent components analysis. Support vector machine algorithms and stepwise removal research were used to obtain the best accuracy rates for discrimination between patients and controls, and between patients.

Results: The overall accuracy for classifying migraine and cluster headache patients from controls ranged from 80% to 83%. The best accuracy for distinguishing cluster headache patients from migraineurs was 73%. The right thalamic resting state functional connectivity (RS FC) was the most useful distinctive feature between headache and

control groups. The right hypothalamic RS FC and the left pontine RS FC were most important when classifying migraineurs from controls. The right hypothalamic RS FC was also the most important MRI feature in migraine and cluster headache classification.

Conclusion: Among the different brain networks involved in primary headaches, there are a few subcortical regions that play a central role in migraine and cluster headache pathophysiology: thalamic activation seems to be related to both types of primary headaches; the dorsal pons contributes to the migraine attack generation and different hypothalamic activity might drive a migraine or a cluster headache attack.

Disclosure of Interests: The authors have no potential conflicts of interest related to this study

Disclosure of Interest: None Declared

IHC-DP-020

Descending and centrifugal spread of bodily pain in migraine chronification

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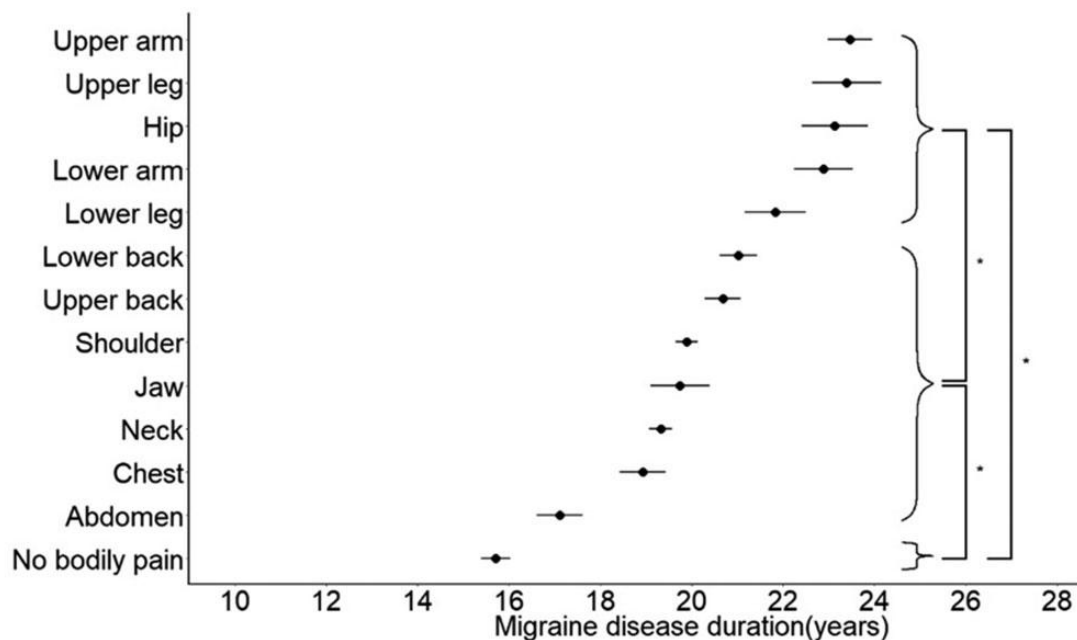
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Objective: Pain in migraine can spread to extracephalic regions as a consequence of central sensitization, particularly in the ictal stage. However, data regarding the distribution of constitutional bodily pain in migraineurs have rarely been discussed upon.

Methods: Patients newly diagnosed as migraine with and without aura were enrolled consecutively. Questionnaire-based face-to-face interviews were carried out by neurologists to collect clinical profiles, including headache patterns, Migraine Disability Assessment (MIDAS), Hospital Anxiety and Depression Scale (HADS), and Pittsburgh Sleep Quality Index (PSQI). Distribution of bodily pain was assessed by the Widespread Pain Index. Migraine disease durations were compared between those with and without bodily pain with the Student's t-test. The patients were grouped according the disease durations, and comparisons among groups were made by one-way analysis of variance followed by post-hoc least significant difference analysis.

Results: During the study period (March 2010 to December 2018), 4,875 migraineurs (1,013 M/3,862 F, mean age 38.6 ± 12.7 years) were recruited, including 3,375 patients with episodic migraine (765 M/2,610 F, mean age 37.1 ± 11.9 years) and 1,500 with chronic migraine (CM) (248 M/1,252 F, mean age 42.1 ± 13.8 years). The mean migraine disease durations were longer in



All $p < 0.0001$ when comparing pain in each body parts with no bodily pain

* $p < 0.0001$ between groups

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	No pain (n = 1,164)	Axial pain (n = 2,519)	Limb pain (n = 1,192)	p value
Age (Y)	35.1 ± 12.6	38.0 ± 12.2	43.5 ± 12.7	<0.001
CM (%)	208 (17.9%)	810 (32.2%)	482 (40.4%)	<0.001*
Disease duration (Y)	15.7 ± 10.9	17.8 ± 11.1	22.0 ± 12.0	<0.001
Headache freq (d/mon)	8.0 ± 8.1	11.2 ± 9.0	13.1 ± 9.9	<0.001
MIDAS	20.2 ± 30.2	29.4 ± 39.6	36.3 ± 53.5	<0.001
HADS	10.7 ± 6.9	14.1 ± 7.4	15.6 ± 7.7	<0.001
PSQI	7.4 ± 3.7	9.4 ± 4.1	10.5 ± 4.2	<0.001

All $p < 0.001$ between each two groups by post-hoc analysis (LSD).

*Chi square for linear trend.

migraineurs with bodily pain as compared to those without (all $p < 0.001$) (figure). The patients were further categorized as “no pain”, “axial pain”, and “limb pain”. There was a gradual increase in the proportions of CM (17.9% in “no pain”, 32.2% in “axial pain”, and 40.0% in “limb pain”, $p < 0.001$), as well as the scores in HADS (10.7 ± 6.9 vs 14.1 ± 7.4 vs 15.6 ± 7.7 , $p < 0.001$) and PSQI (7.4 ± 3.7 vs 9.4 ± 4.1 vs 10.5 ± 4.2 , $p < 0.001$) (table).

Conclusion: The differences in the disease durations could imply a descending and centrifugal spread of bodily pain, i.e. from trunk to limbs, in the process of migraine chronification. Whether this could indicate the process of progressive central sensitization warrants further explorations.

Disclosure of Interest: None Declared

IHC-DP-027

Altered Ventral Diencephalon Structural Co-variance in Migraine and Cluster Headache: An MRI Study

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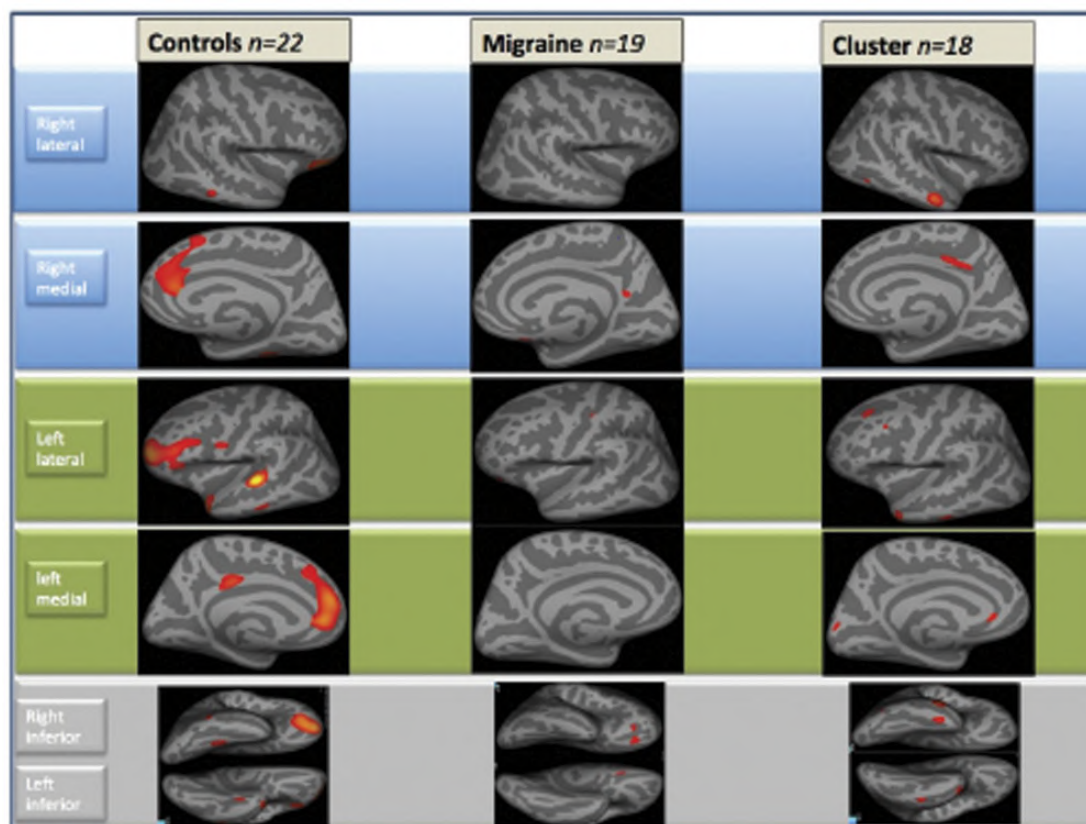


Figure 1. Ventral diencephalon volume (vDC) to vertex-by-vertex cortical thickness correlations shown for controls, migraineurs and cluster headache patients for the right and left hemispheres separately. The color red indicates positive correlations ($p < 0.001$) between the right vDC and right hemisphere thickness and between the left vDC and left hemisphere thickness.

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Table 1. Subject characteristics (age and sex), ventral Diencephalon (vDC) and total grey matter (GMV) volume (mm^3)

	Cluster (CH) n = 18	Migraine (Mig) n = 19	p-value CH vs Mig	Controls (HC) n = 22	p-value CHvs HC	p-value Mig vs HC
Age, mean (SD)	43.78 (12.45)	40.1 (12.2)	.36	39.1 (8.2)	.14	.75
Sex (f/m)	1/17	1/18	.97	2/20	.86	.89
Right vDC	4375.80 (656.3)	4379.24 (358.1)	.88	4250.18 (363.4)	.43	.24
Left vDC	4425.46 (851.7)	4394.68 (376.8)	.98	4293.53 (383.5)	.51	.38
Total GMV	674330.94 (57471.6)	679419.23 (71344.1)	.82	670391.61 (57696.7)	.83	.64

Objective: The hypothalamus, which is part of the ventral diencephalon, is believed to play a key role in both migraine and cluster headache (CH). As brain region-to-region structural correlations are believed to reflect structural and functional brain connectivity patterns, we assessed the structural co-variance patterns between ventral diencephalon volume (vDC) and vertex-by-

vertex measurements of cortical thickness in patients with migraine and in those with CH relative to healthy controls (HC).

Methods: T1-weighted images were acquired for a total of 59 subjects including 18 patients with CH 19 with migraine and 22 HCs. Imaging was collected during the interictal (migraineurs) and out-of-bout (CH) phases.

Data were post-processed using FreeSurfer version 6.0 and correlations between vDC volume with cortical thickness were explored using a whole-brain vertex-wise linear model approach. Partial correlations between vDC volume and vertex-by-vertex measurements of cortical thickness were corrected for age, sex, and total brain volume.

Results: There were no significant between-group differences for age, sex, total brain volume or vDC volume. Within each group, there were significant positive correlations ($p < 0.001$) between right and left vDC volume and cortical thickness measurements. HC had significant positive correlations between vDC volume and cortical thickness over large portions of the superior and rostral medial frontal cortex and smaller clusters in the superior and middle temporal cortex. For migraine, there was a positive correlation between vDC volume and orbitofrontal thickness and for CH there were significant correlations between vDC volume and cortical thickness over the middle and inferior temporal cortex, anterior and posterior cingulate, and isolated areas in the middle frontal area.

Conclusion: In contrast to HC, both migraineurs and CH patients show weakened covariance between the vDC and frontal regions. Recent evidence suggests connectivity between frontal and hypothalamic regions to be relevant for regulating pain perception. Thus, the diminished structural co-variance in migraineurs and CH between the vDC and frontal regions might suggest abnormal functioning of the pain control circuitry and contribute to mechanisms underlying central sensitization or chronification of pain.

Disclosure of Interest: None Declared

Migraine Acute Therapy

IHC-DP-011

Characterization of the Effects of the Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists, Atogepant and Ubrogapant, on Isolated Human Coronary, Cerebral, and Middle Meningeal Arteries

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Objective: To examine effects of 2 novel calcitonin gene-related peptide (CGRP) receptor antagonists, ubrogapant and atogepant, on relaxation induced by α -CGRP in isolated human coronary, cerebral, and middle meningeal arteries. Also, contractile per se responses to atogepant and ubrogapant were compared with responses to zolmitriptan.

Methods: Human coronary arteries were obtained from 4 donor hearts. Human cerebral (cortex) arteries and middle meningeal arteries were removed peri-operatively from patients undergoing neurosurgery. Relaxant effects of human α -CGRP were examined by cumulative application of increasing concentrations (1 pM–100 nM) of the peptide to KCl (30 mM)-precontracted arterial segments in the absence/presence of ubrogapant or atogepant. For each segment, the maximum vasodilator effect (E_{max}) was calculated. Per se contractile responses to atogepant, ubrogapant, and vehicle (dimethyl sulfoxide) were compared with the responses to zolmitriptan.

Results: Both ubrogapant and atogepant had no vasoconstrictor effect at any concentration, whereas zolmitriptan elicited concentration-dependent contractions of all vessels. In distal coronary arteries, both CGRP antagonists competitively antagonized α -CGRP, with a parallel shift of the concentration-response curve without affecting the maximum response (E_{max}) of α -CGRP. In cranial arteries, a parallel shift in the concentration-response curve at low gepant concentrations indicated competitive antagonism. At higher concentrations, a depressed E_{max} and minor shift of the CGRP-induced relaxation curve were observed, suggesting reversible, noncompetitive antagonism. Also, both gepants antagonized CGRP-induced relaxation more potently in middle meningeal and cerebral than in coronary arteries; atogepant showed higher potency.

Conclusion: Ubrogapant and atogepant were devoid of vasoconstrictive properties at concentrations studied; the anti-CGRP effects of both were more robust in cranial arteries.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland

Author Disclosures:

Eloísa Rubio-Beltrán reports no conflicts of interest.

Ka Yi Chan reports no conflicts of interest.

Antoon van den Bogaerd reports no conflicts of interest.

Ad J.J.C. Bogers reports no conflicts of interest.

A.H. Jan Danser reports no conflicts of interest.

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IHC-DP-019**Validation of K(ATP) channel antagonism as a new target for migraine treatment**

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Objective: ATP-sensitive potassium (K_{ATP}) channels couple cellular metabolism to membrane potential and excitability. Recently, infusion of the K_{ATP} channel agonist levcromakalim provoked a migraine attack in 100% of migraine patients, a far higher incidence than any previously tested provocation agents such as GTN or CGRP. It follows that K_{ATP} antagonism might therefore be effective therapy, but histamine also causes migraine while antihistamines are ineffective. Effect of antagonism in validated animal models would greatly strengthen the case.

Methods: Cutaneous sensitivity to hindpaw, and periorbital mechanical stimulation were used as surrogate markers of activation of relevant pain pathways in two validated migraines models: (i) a mouse model of glyceryl trinitrate (GTN) provoked migraine-like pain and (ii) a spontaneous rat model (STA rats) of migraine-like pain.

Results: The K_{ATP} channel antagonist glibenclamide (1 mg/kg, i.p.) attenuated cutaneous hyperalgesia in GTN-injected mice and in rats with spontaneous trigeminal allodynia (STA). Cephalic pain in STA rats was also diminished by the K_{ATP} channel blocker gliquidone (10 mg/kg, i.p.). In addition, mice injected repeatedly with levcromakalim over 10 days developed a progressive basal hyperalgesia like that mediated by GTN. Target engagement was confirmed in levcromakalim-sensitized mice in which the hyperalgesia was completely blocked by glibenclamide.

Conclusion: Strong migraine provocation combined with the present demonstration of effect of K_{ATP} antagonism in validated animal models strongly suggest that K_{ATP} channel blockers could prove to be extremely effective drugs in the treatment of migraine.

Disclosure of Interests: The authors have nothing to disclose.

IHC-DP-021**Rimegepant 75 mg Exposure, Safety, and Tolerability are Similar in Elderly and Nonelderly Adults: a Phase I, Open-Label, Parallel-Group, Single-Dose Study**

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Objective: Treatment of elderly persons with migraine can be challenging due to comorbid conditions and a greater probability of adverse events (AEs). The objective of this study was to evaluate the pharmacokinetics (PK), safety, and tolerability of a single-dose of rimegepant, a small molecule calcitonin gene-related peptide receptor antagonist with efficacy in migraine, in elderly and nonelderly male and female subjects.

Methods: This was a single center, Phase I, open-label, two-group, single-dose, parallel PK study in elderly and nonelderly healthy volunteers. Elderly subjects with stable chronic illness (same medication for ≥ 3 months; no dosage change within 14 days predose) were eligible. Adult nonsmokers aged ≥ 18 and ≤ 45 years (non-elderly) or ≥ 65 years of age (elderly), with BMI ≥ 18.5 and ≤ 30.0 kg/m²; weight ≥ 50.0 kg (males) and ≥ 45.0 kg (females); and a score of 0 on the Sheehan Suicidality Tracking Scale (S-STs) were given a single 75 mg tablet of rimegepant on Day 1 under fasting conditions.

Results: Forty-two healthy elderly or nonelderly adults were enrolled, and 28 subjects (14 elderly, 14 non-elderly) were treated, completed the study, and analyzed for safety and PK. Compared with nonelderly subjects, elderly subjects had small ($< 5\%$) and nonsignificant increases in AUC and decreases in C_{max} . There were no serious adverse events (SAEs) or AEs leading to discontinuation reported during the study. Eight (28.6%) subjects (4 elderly, 4 non-elderly) experienced at least 1 TEAE. The only event TEAE reported in more than 1 subject was headache, which was reported in 2 (7.1%) subjects (1 elderly, 1 non-elderly). All TEAEs were mild in intensity; no clinically meaningful changes from baseline in laboratory values, vital signs, ECGs, or the S-STs were identified.

Conclusion: Exposure, safety, and tolerability following a single 75 mg dose of rimegepant was similar in elderly and nonelderly subjects.

Disclosure of Interests: Robert Croop, MD, Joseph Stringfellow, MS, Andrea Ivans, MHS, and Vladimir Coric, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

IHC-DP-030**Ubrogepant for the Acute Treatment of Migraine: Pooled Safety and Tolerability from ACHIEVE I and ACHIEVE II Phase 3 Studies**

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Objective: To evaluate pooled safety and tolerability of the oral CGRP receptor antagonist, ubrogepant, for acute treatment of migraine.

Methods: ACHIEVE I and II (NCT02828020; NCT02867709) were multicenter, double-blind, single-attack, phase 3 trials in adults with migraine randomized 1:1:1 to placebo or ubrogepant (50 mg or 100 mg, ACHIEVE I; 25 mg or 50 mg, ACHIEVE II). Adverse events (AEs) were evaluated within 48 hours of dosing and within 30 days of any dose. This analysis pooled data from ubrogepant 50 mg and placebo treatment groups from the 2 trials.

Results: The entire pooled safety population included 2901 participants (ubrogepant 50 mg [n = 954]; placebo [n = 984]). Average age was 41 years. The majority were female (89% placebo, 90% ubrogepant 50 mg) and white (82% both groups). Within 48 hours of dosing, 113 placebo participants (11.5%) and 107 (11.2%) on ubrogepant 50 mg reported ≥ 1 treatment-emergent AE (TEAE); most common TEAE was nausea (placebo, 1.8%; ubrogepant 50 mg, 1.9%). Of those, 71 participants (7.2%) on placebo and 69 (7.2%) on ubrogepant 50 mg reported AEs that were considered treatment-related. No serious AEs (SAEs) were reported within 48 hours of dosing. Within 30 days of any dose, 225 participants (22.9%) on placebo and 259 (27.1%) on ubrogepant 50 mg reported ≥ 1 TEAE; most common was nausea (2.2%, both groups). Of those, 88 participants (8.9%) on placebo and 90 (9.4%) on ubrogepant 50 mg reported AEs considered treatment-related. Three (0.3%) SAEs in the ubrogepant 50 mg group (pericardial effusion, appendicitis, spontaneous abortion) were not deemed treatment-related. Seven cases of ALT/AST ≥ 3 x the upper limit of normal were reported (2 placebo, 5 ubrogepant 50 mg) and adjudicated by treatment-blinded liver experts. Five of 7 (ubrogepant) were judged unlikely to be related to study medication based on plausible alternatives. Two of 7 (both placebo) were judged possibly related.

Conclusion: Overall, ubrogepant 50 mg was well tolerated, with no new safety concerns identified from the pooled ACHIEVE I and II phase 3 studies.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland

Author Disclosures:

Susan Hutchinson, MD has served on advisory boards for Alder, Allergan, Amgen, Avanir, Biohaven, ElectroCore, Eli Lilly, Supernus, and Teva. She is on the speakers bureau for Allergan, Amgen, Avanir, ElectroCore, Eli Lilly, Promius, Supernus, and Teva.

David W. Dodick reports: Personal fees: Amgen, Autonomic technologies, Axsome, Aural Analytics, Allergan, Alder, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Neurolief, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, Oppenheimer. CME fees or Royalty payments Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal meeting management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer; Stock options: Aural analytics, Healint, Theranica, Second Opinion/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Consulting without fee: Aural Analytics, Healint, Second Opinion/Mobile Health, Epien; Board of Directors: Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1-1466:vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis without fee. Professional society fees or reimbursement for travel: American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society. Other: Use agreement through employer: Myndshft

Christina Treppendahl served on advisory boards for Amgen, Electrocore, Ely Lilly, National Headache Foundation, Pernix, Promius Pharma, Supernus Pharmaceuticals, Teva Pharmaceuticals, consulted for Pernix, Promius Pharma, Supernus, and received speaker honoraria from Allergan, American Academy of Nurse Practitioners, Amgen, Avanir, Depomed, Inc., Iroko Pharmaceuticals, National Headache Foundation, Nautilus Neurosciences, Inc., Novartis, Pernix Therapeutic Holding, Inc., Promius Pharma, Southern Headache Society, Supernus Pharmaceuticals, Teva Pharmaceutical Industries, Inc., and Zogenix, Inc.

Nate Bennett reports no conflicts of interest.

Sung Yun Yu is a full-time employee of Allergan plc and owns stock in the company.

Hua Guo is a full-time employee of Allergan plc and owns stock in the company.

Joel M. Trugman is a full-time employee of Allergan plc and owns stock in the company.

IHC-DP-031**Long-term Safety Evaluation of Ubrogepant for the Acute Treatment of Migraine Attacks**

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Objective: To evaluate the long-term safety and tolerability of ubrogepant for the acute treatment of migraine.

Methods: Phase 3, multicenter, randomized, open-label, 52-week extension trial. Adults with migraine with or without aura were randomized 1:1 in a blinded fashion to ubrogepant 50 mg or 100 mg. Safety and tolerability were assessed.

Results: In total, 837 participants were randomized to ubrogepant; 813 composed the safety population. Mean age was 42 years for ubrogepant 50 mg and 41 for ubrogepant 100 mg; 91% were female, 84% white; mean BMI was 30 mg/kg². Throughout the study, 22,454 migraine attacks were treated with 31,968 doses of ubrogepant. Treatment-emergent adverse events (AEs) reported: ubrogepant 50 mg, 268/404 (66%); ubrogepant 100 mg, 297/409 (73%); most common was upper respiratory tract infection (82/813, 11%), with a similar incidence observed across treatments. Treatment-related AEs: ubrogepant 50 mg, 42/404 (10%); ubrogepant 100 mg, 43/409 (10%). Serious AEs: ubrogepant 50 mg, 9/404 (2%); ubrogepant 100 mg, 12/409 (3%); 1 considered related by the investigator (ubrogepant 50 mg; sinus tachycardia). 16 cases of ALT/AST $\geq 3 \times$ ULN were reported and adjudicated by an independent panel of liver experts blinded to treatment. 13 of 16 cases (ubrogepant 50 mg, 3; ubrogepant 100 mg, 10) were adjudicated as unlikely to be related based on plausible alternative etiology/confounding factor(s). Two cases (both ubrogepant 50 mg) were adjudicated as possibly related to study medication and 1 case (ubrogepant 100 mg) as probably related; however, confounding factors were noted. All cases were asymptomatic, with no concurrent bilirubin elevation. ALT/AST elevations resolved in those who continued dosing.

Conclusion: Intermittent use of ubrogepant for the acute treatment of migraine over 1 year was well tolerated, with no safety concerns identified.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland

Author Disclosures:

Jessica Ailani, MD is a speaker for Alder, Amgen, Avanir, Allergan, Eli Lilly and Company, Electrocore, Promius, and Teva. She has served as consultant to or advisory board member of Alder, Amgen, Allergan, Eli Lilly and Company, Electrocore, Impel, Promius, Teva, Miller Communications, and Alpha Sites Consulting. She is also a section editor for Current Pain and Headache.

Susan Hutchinson, MD has served on advisory boards for Alder, Allergan, Amgen, Avanir, Biohaven, ElectroCore, Eli Lilly, Supernus, and Teva. She is on the speakers bureau for Allergan, Amgen, Avanir, ElectroCore, Eli Lilly, Promius, Supernus, and Teva.

Richard B. Lipton, MD serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS; serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache, 8th Edition (Oxford University Press, 2009), and Informa. He holds stock options in eNeura Therapeutics and Biohaven.

Kerry Kniewel, DO has consulted for Allergan, Lilly, Biohaven and Amgen and spoken for Allergan and Amgen. Kaifeng Lu, PhD is a full-time employee and stockholder of Allergan plc.

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IHC-DP-033**Absence of Clinically Significant Drug Interactions With Co-administration of Atogepant and an Ethinyl Estradiol–Levonorgestrel Oral Contraceptive in Healthy Female Subjects: A Phase I Pharmacokinetic Analysis**

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Objective: To assess the drug-interaction potential of atogepant and the combination oral contraceptive, Nordette[®]-28 (ethinyl estradiol [EE]/levonorgestrel [LNG]).

Methods: This phase I, open-label, single-center, 2-period, fixed-sequence study examined the effect of multiple-dose atogepant (60 mg) on single-dose PK of EE 0.03 mg/LNG 0.15 mg in healthy postmenopausal or oophorectomized adult females. In period 1, subjects received a single dose of EE/LNG followed by a 7-day washout. In period 2, they received atogepant once daily on days 1–17; an oral dose of EE/LNG was coadministered with atogepant on day 14. Plasma PK parameters included AUC_{0-inf} and C_{max} of EE and LNG calculated as geometric mean ratios (GMRs; with/without atogepant). Lack of an effect of atogepant on EE/LNG PK values was confirmed if all GMR 90% CIs were within (0.80, 1.25). Safety and tolerability were assessed.

Results: Of 26 subjects aged 45–64 years, 1 discontinued due to moderate pneumonia and ligament sprain unrelated to study drugs; 2 discontinued for personal reasons. The 90% CIs for the GMRs were within (0.80, 1.25) for the AUC_{0-inf} and C_{max} of EE and the C_{max} of LNG, but not the AUC_{0-inf} of LNG (GMR: 1.19; 90% CI: 1.13, 1.26). Adverse events were mild to moderate and resolved by study end.

Conclusion: Coadministration of multiple doses of atogepant and a single dose of EE/LNG did not substantially alter the PK of EE; the ~19% increase in plasma AUC_{0-inf} of LNG is not anticipated to be clinically significant. Coadministration of atogepant and EE/LNG was safe and generally well tolerated.

Disclosure of Interests: Support: Study funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. (Kenilworth, NJ), and editorial support by Allergan plc (Dublin, Ireland).

Author Disclosures:

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Ramesh Boinpally, PhD is an employee and shareholder of Allergan plc.

K. Chris Min, MD, PhD was an employee and shareholder of Merck & Co, Inc. at the time of this study.

IHC-DP-036**Comparison of Early Plasma Exposure to DHE by Nasal, Oral Inhalation, or Intravenous Administration**

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Objective: To compare plasma exposure in the first two hours following administration of INP104 (dihydroergotamine mesylate [DHE] by Precision Olfactory Delivery [POD[®]]), Migranal[®] Nasal Spray, D.H.E. 45[®] (IV) or MAP0004 (oral inhalation) using data obtained from the STOP 101 study and literature reports. IV DHE is a reliable and effective treatment for migraine approved in the US since 1946. DHE plasma exposure in the first 2 hours is critical to migraine pain relief, justifying an emphasis on AUC_{0-2hr} when assessing novel DHE products. Although C_{max} is also important for efficacy, research suggests that the high C_{max} of IV administration may predict a higher rate of adverse events. INP104, a novel drug-device combination product in Phase 3 clinical development, targets delivery of a liquid DHE formulation to the upper nasal cavity using the POD device.

Methods: PK results from STOP 101, a Phase I, single dose, safety, tolerability, and bioavailability study in healthy subjects who received INP104 (1.45 mg), Migranal (2 mg), or D.H.E. 45 (IV) (1 mg) in a 3-way, 3-period crossover were compared. Trends of DHE PK, efficacy, and adverse events related to AUC_{0-2hr} and C_{max} reported in the literature were reviewed and are described.

Results: AUC_{0-2hr} following administration of INP104, Migranal, and D.H.E. 45 (IV) was 1,603, 387.5, and 3,022 hr*pg/mL, respectively, in the STOP 101 trial. C_{max} values were highest following IV DHE (14,190 pg/mL), then INP104 (1,301 pg/mL) and Migranal (299.6 pg/mL). A literature report of MAP0004 (1 mg), clinically developed but never marketed due to CMC challenges, states an AUC_{0-2hr} value of 1,447 hr*pg/mL. Another MAP0004 literature report describes onset of pain relief in migraineurs as early as 10 minutes and only 1 incidence of nausea. Lastly, a

review of the literature suggests that the probability of nausea is <2% when plasma DHE C_{max} is $\leq 5,000$ pg/mL, whereas at 13,400 pg/mL, the probability of nausea is $\geq 50\%$.

Conclusion: INP104 administration results in high plasma exposure to DHE in the first 2 hours, a goal for acute migraine products to enable rapid and sustained pain relief, as validated by the MAP0004 clinical program. Further, the significant reduction in C_{max} of DHE following INP104 treatment, relative to IV, may lead to more favorable tolerability of INP104.

Disclosure of Interests: K. Satterly, S. Shrewsbury and J. Hoekman are employees of Impel NeuroPharma.

Migraine Preventive Therapy

IHC-DP-008

The effect of erenumab on vasoactive compounds other than CGRP in human isolated coronary arteries

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Objective: Calcitonin gene-related peptide (CGRP) is an important neuropeptide in migraine pathophysiology and is a target for antimigraine treatment. Erenumab, a monoclonal antibody against the CGRP receptor, is effective for migraine prophylaxis and is approved for use in the clinic. So far, no major cardiovascular side effects have been observed with erenumab, but as migraine patients have an increased cardiovascular risk and CGRP may be cardioprotective in case of ischemia, it is important to further assess its cardiovascular safety. While we have previously demonstrated that erenumab does not have contractile properties per se and does not affect human isolated coronary artery (HCA) contractions to sumatriptan[1], here we set out to investigate whether erenumab affects responses to other vasoactive compounds.

Methods: HCA segments (n = 6–7/group) were mounted in Mulvany myographs and incubated with and without 1 μ M erenumab for 30 min. Isometric tension measurements were performed during a concentration response curve to the vasoconstrictor dihydroergotamine (DHE), to

the endothelium-dependent vasodilators substance P and bradykinin, as well as the endothelium-independent vasodilators nicardipine and sodium nitroprusside.

Results: Contractile responses to DHE were similar with (pEC₅₀: 8.70 \pm 0.3, E_{max}: 26% \pm 21) and without (pEC₅₀: 7.47 \pm 0.9, E_{max}: 11% \pm 7) erenumab. Erenumab did not affect endothelium-dependent vasodilation to substance P (pEC₅₀: 8.04 \pm 0.4, E_{max}: 54% \pm 13 and pEC₅₀: 8.34 \pm 0.3, E_{max}: 45% \pm 11, with and without erenumab, respectively) and bradykinin (pEC₅₀: 7.09 \pm 0.2, E_{max}: 36% \pm 7 and pEC₅₀: 7.40 \pm 0.3, E_{max}: 44% \pm 12, resp.). The endothelium-independent vasodilators nicardipine (pEC₅₀: 7.85 \pm 0.4, E_{max}: 96% \pm 3 and pEC₅₀: 8.01 \pm 0.3, E_{max}: 99% \pm 3, resp.) and sodium nitroprusside (pEC₅₀: 7.34 \pm 0.1, E_{max}: 94% \pm 4 and pEC₅₀: 7.50 \pm 0.1, E_{max}: 95% \pm 4, resp.) were also not affected by erenumab.

Conclusion: While the safety of blocking CGRP in HCA still needs to be confirmed, our results indicate that erenumab does not affect the contractile response of HCA to DHE, nor the relaxant response to multiple vasodilators with known mechanisms of action.

Disclosure of Interests: Received a grant from Novartis

Reference

1. Rubio-Beltran, E. et al. (2016) Effects of AMG 334 on HCA. *Cephalalgia* 36(S):41

IHC-DP-010

Do color tinted glasses ameliorate pain intensity in patients with migraine?

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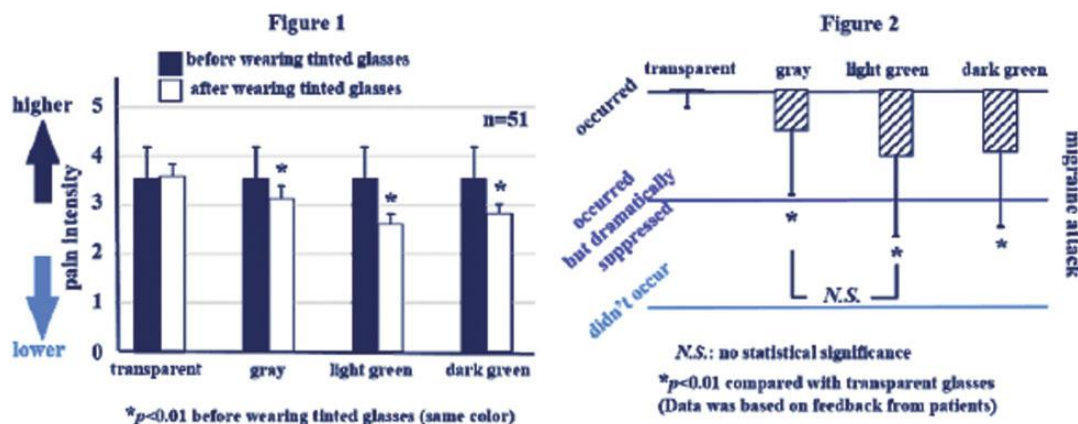
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Objective: Previously we reported blue, red and white ambient lights exacerbated migraine attacks, while green light ameliorated migraine regardless of photophobia. In the present study, we investigated the effect of tinted glasses instead of ambient light color on migraine-aversiveness and pain intensity during interictal, prodromal or aura, and ictal phases.

Methods: The study included 51 patients (ages 15–61) with migraine (ICHD-3). We prepared four types of tinted glasses, three of which were colored (gray, light green and dark green), and one transparent as control. The colored glasses block 50% of luminous transmittance, but the rate of light blocking for S-cone stimulation was 59% by gray, 86% by light green and 68% by dark green. The specialized glasses were made by Tokai Co., Ltd. in Aichi. We studied degree of discomfort and pain intensity



Abstract number: IHC-DP-010

before and after wearing the tinted glasses during all phases. When the degree of discomfort or pain intensity was aggravated while wearing tinted glasses, observations were stopped. Furthermore, we also evaluated whether migraine attacks occur or not after wearing tinted glasses during the prodromal or aura phase. To evaluate the degree of discomfort and pain intensity after wearing tinted glasses, patients were asked to choose from six levels for each color.

Results: All colored glasses, predominantly light green, reduced discomfort during prodromal or aura, and ictal phases and pain intensity during ictal phase (Fig. 1). All colored glasses, both greens especially, were able to prevent migraine attacks while wearing them in prodromal or aura phase (Fig. 2).

Conclusion: Our results might be caused by differences in S-cone and melanopsin stimulations, because melanopsin stimulation was suppressed by all tinted glasses by approximately half, when compared to transparent glasses. According to S-cone stimulation, migraine attacks will be decreased by light green, dark green and gray glasses in order of efficacy. The effectiveness of tinted glasses was similar to the effect of ambient light colors', but delayed by 5 minutes. Since tinted glasses can be worn whenever needed, appropriately tinted glasses could potentially become an important preventive method for patients with migraine, without the use of medication.

Disclosure of Interest: None Declared

IHC-DP-013

Dual ENKephalinase Inhibitor (DENKI) PL37: A possible new class of migraine therapeutics

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Objective: Migraine is a chronic neurovascular disorder characterized by recurrent headache attacks accompanied by various neurological disorders including cephalic cutaneous mechanical allodynia (MA). Among the different opioidergic systems, the enkephalinergic is primarily recruited via activation of delta opioid receptor (DOR) in chronic pain. PL37 belongs to a new pharmacological class of analgesics, the Dual ENKephalinase Inhibitors (DENKI), small molecules protecting enkephalins from their rapid degradation by the metalloenzymes neutral endopeptidase and aminopeptidase N, thereby increasing the duration and intensity of their analgesic effects. Its efficacy was demonstrated in a wide range of rodent pain models. This study tested the antimigraine therapeutic and prophylactic potential of PL37 in an animal model of migraine.

Methods: Experiments were performed on male Sprague-Dawley CD rats according to ethical guidelines. The effects of PL37 (50 mg/kg or 100 mg/kg, p.o.) administration were tested on cephalic cutaneous mechanical sensitivity triggered by the acute or chronic dose of a nitric oxide donor, isosorbide dinitrate (ISDN), a known migraine trigger. The corresponding mechanical sensitivity was assessed using von Frey filaments.

Results: Acute ISDN injection induced a cephalic MA in vehicle-treated rats that peaked at 1 h and lasted less than 2 h. Conversely, PL37-treated rats did not develop such cephalic MA with significant effect at 30 min after ISDN

administration lasting at least 2 h. Single oral administration of PL37 (50 or 100 mg/kg) has no effect on persistent cephalic MA induced by recurrent administration of ISDN. Repeated systemic ISDN induced a strong, persistent cephalic MA in vehicle-treated rats. Interestingly, daily oral administration of PL37 prevent repeated ISDN-induced persistent cephalic MA.

Conclusion: This study shows that protecting enkephalins from degradation using the PL37 DENKI, has pain-alleviating effects in migraine. These results suggest that PL37 may represent a novel class of therapeutics for migraine as both an acute treatment of migraine attacks and a prophylactic treatment for migraine.

Disclosure of Interests: HP, TO, MW are employees from Pharmaleads

IHC-DP-026

Effects of Vitamin D on migraine: A meta-analysis

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Objective: To evaluate the difference in mean serum 25-OH vitamin D concentration between migraineurs and non-migraineurs, the association of hypovitaminosis D with the incidence of migraine, and the effects of oral vitamin D supplementation on migraine-frequency, duration, and severity.

Methods: Relevant databases were searched for observational and interventional studies which evaluated the difference in mean serum 25(OH) vitamin D level between migraineurs and non-migraineurs, the association of hypovitaminosis D with migraine, and the effects of vitamin D supplementation on migraine-frequency, duration, and severity. Pooled standardized mean difference and odds ratio were calculated using a random effects model (MetaXL version 5.3) (PROSPERO ID: CRD42018116984).

Results: Ten observational studies and 3 interventional trials were included in the analyses. There was a significantly lower concentration of serum 25-OH vitamin D in the migraineurs [mean difference: -5.60 ng/mL (95% CI: $-8.72, -2.49$)] than in the non-migraineurs (low-GRADE evidence). There was a trend of association between hypovitaminosis D and the incidence of migraine, although it did not reach a statistical significance [odds ratio: 1.16 (95% CI: 0.99, 1.36)] (low-GRADE evidence). Oral vitamin D supplementation significantly improved migraine-frequency [mean difference: -1.55 (95% CI: $-2.09, -1.00$)], although

it did not improve migraine-duration [mean difference: -16.00 h (95% CI: $-42.77, 10.76$)] and severity [mean difference: -0.37 (95% CI: $-1.33, 0.59$)] within the treatment period (moderate-GRADE evidence).

Conclusion: Serum 25-OH vitamin D was significantly lower in the migraineurs than in the non-migraineurs. A trend of association between hypovitaminosis D and the incidence of migraine was found. Oral vitamin D supplementation improved migraine-frequency, but not migraine-duration and severity.

Disclosure of Interest: None Declared

IHC-DP-028

Long-term efficacy of fremanezumab in chronic and episodic migraine patients who failed at least one prior migraine preventive medication: results of a 1-year study

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Objective: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), is approved in the US and the EU for the preventive treatment of migraine in adults. We evaluated the long-term efficacy of fremanezumab in migraine patients who failed ≥ 1 prior migraine preventive medication.

Methods: In this 12-month, multicenter, randomized, double-blind, parallel-group study, patients with chronic (CM) or episodic migraine (EM) received subcutaneous fremanezumab quarterly (675 mg every 3 months) or monthly (225 mg every month; CM patients received a 675 mg starting dose). This *post hoc* analysis was limited to patients who had failed (defined as lack of efficacy or intolerability) ≥ 1 prior migraine preventive medication. We measured the mean change from baseline in the monthly average number of migraine days and in headache days of at least moderate severity at Months 6 and 12.

Results: This analysis included 490 CM patients (quarterly: $n=247$; monthly: $n=243$) and 206 EM patients (quarterly: $n=105$; monthly: $n=101$) who had failed ≥ 1 prior migraine preventive medication. In CM patients, the monthly average number of migraine days decreased from baseline at Month 6 (quarterly: -5.2 days, monthly: -7.0 days) and 12 (quarterly: -6.4 days; monthly: -7.1 days). EM patients also reported a reduction in the monthly average number of migraine days at Months 6 (quarterly: -4.9 days; monthly: -4.6 days) and 12 (quarterly: -5.1 days; monthly: -5.2 days). Reductions in the monthly average number of

headache days of at least moderate severity were also observed for both dosing regimens in both CM and EM patients at Months 6 (CM: quarterly, -5.0 days; monthly, -6.8 days and EM: quarterly, -4.3 days; monthly: -3.8 days) and 12 (CM: quarterly, -6.1 days; monthly, -6.9 days and EM: quarterly, -4.5 days; monthly: -4.3 days).

Conclusion: Patients who have failed ≥ 1 prior migraine preventive medication may be challenging to treat. These data suggest that fremanezumab demonstrates long-term efficacy for the reduction of migraine days and headache days of at least moderate severity in this population.

Disclosure of Interests: Paul K. Winner: Investigator in clinical trials sponsored by Teva, Amgen, Genentech, Novartis, Allergan, AstraZeneca, Biogen Idec, Ipsen, and Lilly; has participated in advisory boards for Teva Pharmaceuticals, Amgen, Avanir, Novartis, Allergan, Supernus, and Lilly; and has been on a speaker's bureau for Allergan, Amgen, Avanir, Lilly, Promius, Novartis, and Supernus.

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Joshua M. Cohen: Employee of Teva Pharmaceuticals.

Ronghua Yang: Employee of Teva Pharmaceuticals.

Xiaoping Ning: Employee of Teva Pharmaceuticals.

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IHC-DP-032

Population Pharmacokinetics of Eptinezumab for the Preventive Treatment of Migraine

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Objective: Eptinezumab is a humanized IgG1 anti-CGRP monoclonal antibody that selectively inhibits the CGRP ligand. Here, we present population pharmacokinetics (PPK) and exposure-response (ER) analysis across clinical trials that evaluated eptinezumab in healthy subjects and/or patients with episodic (EM) or chronic migraine (CM).

Methods: PPK was analyzed for the intravenous (IV) administration of eptinezumab (over ~30 min to 1 h) at single doses of 10 to 1000 mg in healthy subjects and in patients with EM and CM (8 studies [N = 2123]). The primary endpoint for the ER analysis included change from baseline in mean monthly migraine days (MMDs) over Weeks 1–12 and was based on a subset of 3 placebo-controlled studies at single doses of 10 to 300 mg (N = 2543).

Results: Eptinezumab following IV dosing demonstrated linear PK and was adequately characterized by a 2-compartmental model. The population estimates of CL and Vc for eptinezumab were 0.00621 L/h (0.15 L/d) and 3.72 L, respectively. The elimination half-life was 27 d, and the median time to maximal concentration (T_{max}) occurred at the end of 30-min or 1-h infusion. None of the covariates associated with PK variability warranted dose adjustments for adults. In the ER analysis, treatment benefit was pronounced at doses of ≥ 100 mg. A saturable inhibitory E_{max} model described the relationship between the PK parameters of eptinezumab and change in MMDs over Weeks 1–12. An AUC_{0-12wk} of $\geq 15,000$ h \cdot μ g/mL (≥ 100 mg) tended to produce a sustained decrease in MMDs compared with baseline. Eptinezumab 100 mg and 300 mg provided exposure (AUC_{0-12wk} , C_{max} , C_{avg} , C_{trough}) that exceeded estimates for achieving 90% of the maximum efficacy (EC90) in patients with EM or CM.

Conclusion: Eptinezumab administered via IV infusion demonstrated linear PK, with C_{max} achieved at the end of infusion, and a long half-life (27 d), supporting infrequent (every 3 months) dosing. The ER analysis demonstrated maximal reductions in MMDs over Weeks 1–12 for eptinezumab 100 mg or 300 mg. All exposure metrics for eptinezumab 100 mg and 300 mg exceeded EC90 efficacy estimates for CM or EM patients.

Disclosure of Interests: Brian Baker: Full time employee of Alder Biopharmaceuticals.

Barbara Schaeffler: Nothing to disclose.

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Susan Pederson: Full time employee of Alder Biopharmaceuticals.

MyMy Trinh: Nothing to disclose.

Jeff Smith: Received compensation from Alder Biopharmaceuticals.

Within the past year, Dr. Smith or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value in Alder Biopharmaceuticals.

John Latham: Full time employee of Alder Biopharmaceuticals.

IHC-DP-034**Long-term efficacy of fremanezumab in migraine patients with and without concomitant oral preventive medication use: results of a 1-year study**

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Objective: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), is approved in the US and the EU for the preventive treatment of migraine in adults. The impact of using fremanezumab with additional migraine preventive medications deserves greater attention. Here we evaluate the long-term efficacy of fremanezumab in patients with chronic (CM) and episodic migraine (EM) concomitantly using oral migraine preventive medication.

Methods: In this 12-month, randomized, double-blind, parallel-group study, CM and EM patients were assigned to either fremanezumab quarterly (675 mg every 3 months) or monthly (225 mg monthly; CM: starting dose of 675 mg). Use of ≤2 concomitant oral migraine preventive medications was allowed provided that dosing was stable for ≥2 consecutive months prior to study entry. We measured mean change from baseline in monthly average number of headache days of at least moderate severity and in migraine days at Months 6 and 12 in patients with or without concomitant oral preventive medication use.

Results: This *post hoc* analysis included 449 patients with concomitant oral preventive medication use (CM: n = 268; EM: n = 181) and 1429 patients without (CM: n = 835; EM: n = 594) concomitant medication use. The mean monthly number of headache days of at least moderate severity decreased from baseline to Month 12 in CM and EM patients with (CM: quarterly -5.9 days, monthly -6.1 days; EM: quarterly -3.9 days, monthly -4.0 days) and without (CM: quarterly -6.5 days, monthly -7.1 days; EM: quarterly -4.6 days, monthly -4.3 days) concomitant oral preventive medication use. The mean number of monthly migraine days was also reduced from baseline to Month 12 in CM and EM patients with (CM: quarterly -6.9 days, monthly -6.8 days; EM: quarterly -4.2 days, monthly -4.8 days) and without (CM: quarterly -7.4 days, monthly -8.5 days; EM: quarterly -5.5 days, monthly -5.2 days) concomitant oral preventive medication use.

Conclusion: Fremanezumab demonstrated efficacy over 12 months in CM and EM patients regardless of concomitant use of additional oral migraine preventive medication.

Disclosure of Interests: Peter J. Goadsby: Reports grants and personal fees from Amgen and Eli Lilly and Company, and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Biohaven Pharmaceuticals Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Novartis, Teva Pharmaceuticals, Trigemina Inc., medicolegal work, Massachusetts Medical Society, UpToDate, Oxford University Press, and Wolters Kluwer; he holds a patent for magnetic stimulation for headache assigned to eNeura without fee.

Stephen D. Silberstein: Provides consultation to Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Curelater Inc., Depomed, Dr. Reddy's Laboratories, Ensured Inc., ElectroCore Medical LLC, eNeura Therapeutics, INSYS Therapeutics, Lilly USA LLC, Supernus Pharmaceuticals Inc., Teva Pharmaceuticals, Theranica, and Trigemina Inc.

David W. Dodick: Reports the following conflicts from within the past 48 months: Personal fees and expense reimbursement: Amgen, Autonomic technologies, Axsome, Allergan, Alder, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Neuroief, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, Oppenheimer. CME fees and/or royalty payments and/or expense reimbursement: Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal meeting management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer. Stock options: Aural analytics, Healint, Theranica, Second Opinion/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Board of Directors: Aural analytics, Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1-1466:v Title: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis. Professional society fees or reimbursement for travel: American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society. Other: Use agreement through employer: Neuroassessment systems, Myndshft.

Joshua M. Cohen: Employee of Teva Pharmaceuticals.

Ronghua Yang: Employee of Teva Pharmaceuticals.

Xiaoping Ning: Employee of Teva Pharmaceuticals.

Karen Carr: Employee of Teva Pharmaceuticals.

IHC-DP-035

Long-term response rates in chronic and episodic migraine patients with concomitant preventive medication use: results of a 1-year study

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Objective: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), is approved in the US and the EU for the preventive treatment of migraine in adults. Here we evaluated response rates after treatment with fremanezumab in chronic (CM) and episodic migraine (EM) patients who used concomitant migraine preventive medications.

Methods: In this 12-month, multicenter, randomized, double-blind, parallel-group study, CM and EM patients were assigned to fremanezumab quarterly (675 mg every 3 months) or monthly (225 mg monthly; CM: starting dose of 675 mg) dosing. Use of ≤2 concomitant oral migraine preventive medications was allowed, provided that dosing was stable for ≥2 consecutive months prior to study entry. *Post hoc* analyses measured the proportion of CM and EM patients who used oral concomitant preventive medication and had a ≥50%, ≥75%, and 100% reduction in the monthly average number of migraine days and in headache days of at least moderate severity at Month 12.

Results: This analysis included 268 CM patients (quarterly: n = 128; monthly: n = 140) and 181 EM patients (quarterly: n = 89; monthly: n = 92) who used oral concomitant preventive medications. At Month 12, the ≥50%, ≥75%, and 100% response rates for monthly average number of migraine days were: CM quarterly: 53%, 20%, and 3% respectively; CM monthly: 48%, 24%, and 7%, respectively; EM quarterly: 58%, 27%, and 9% respectively; EM monthly: 63%, 41%, and 18%, respectively. A ≥50%, ≥75%, and 100% reduction in the monthly number of headache days of at least moderate severity at Month 12 were reported in CM (quarterly: 51%, 23%, and 8%, respectively; monthly: 51%, 25%, and 10%, respectively) and EM patients (quarterly: 63%, 30%, and 17%, respectively; monthly: 61%, 42%, and 22%, respectively).

Conclusion: Long-term fremanezumab treatment led to clinically meaningful reductions, which increased over time, in the monthly number of migraine days and headache days of at least moderate severity in CM and EM patients receiving concomitant oral migraine preventive medications.

Disclosure of Interests: Peter J. Goadsby: Reports grants and personal fees from Amgen and Eli Lilly and Company, and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Biohaven Pharmaceuticals Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Novartis, Teva Pharmaceuticals, Trigemina Inc., medicolegal work, Massachusetts Medical Society, UpToDate, Oxford University Press, and Wolters Kluwer; he holds a patent for magnetic stimulation for headache assigned to eNeura without fee.

Stephen D. Silberstein: Provides consultation to Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Curelater Inc., Depomed, Dr. Reddy's Laboratories, Ensured Inc., ElectroCore Medical LLC, eNeura Therapeutics, INSYS Therapeutics, Lilly USA LLC, Supernus Pharmaceuticals Inc., Teva Pharmaceuticals, Theranica, and Trigemina Inc.

David W. Dodick: Reports the following conflicts from within the past 48 months: Personal fees and expense reimbursement: Amgen, Autonomic technologies, Axsome, Allergan, Alder, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Neuroief, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva Pharmaceuticals, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, Oppenheimer. CME fees and/or royalty payments and/or expense reimbursement: Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal meeting management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer. Stock options: Aural analytics, Healint, Theranica, Second Opinion/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Board of Directors: Aural analytics, Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1-1466:v Title: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis. Professional society fees or reimbursement for travel: American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society. Other: Use agreement through employer: Neuroassessment systems, Myndshft.

Joshua M. Cohen: Employee of Teva Pharmaceuticals.

Ronghua Yang: Employee of Teva Pharmaceuticals.

Xiaoping Ning: Employee of Teva Pharmaceuticals.

Shawn Elms: Employee of Teva Pharmaceuticals.

Neuromodulation for Headaches

IHC-DP-016

Does tDCS modulate visual cortical excitability—a proof of concept study for migraine prevention

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Objective: Previous studies have attempted to normalize the aberrant visual cortical excitability of migraine using transcranial direct current stimulation (tDCS). Current understanding of tDCS mechanism mainly depends on electrophysiological evidence of the motor cortex, with limited and discrepant results supporting the modulating effects of tDCS on the visual cortex. In this proof of

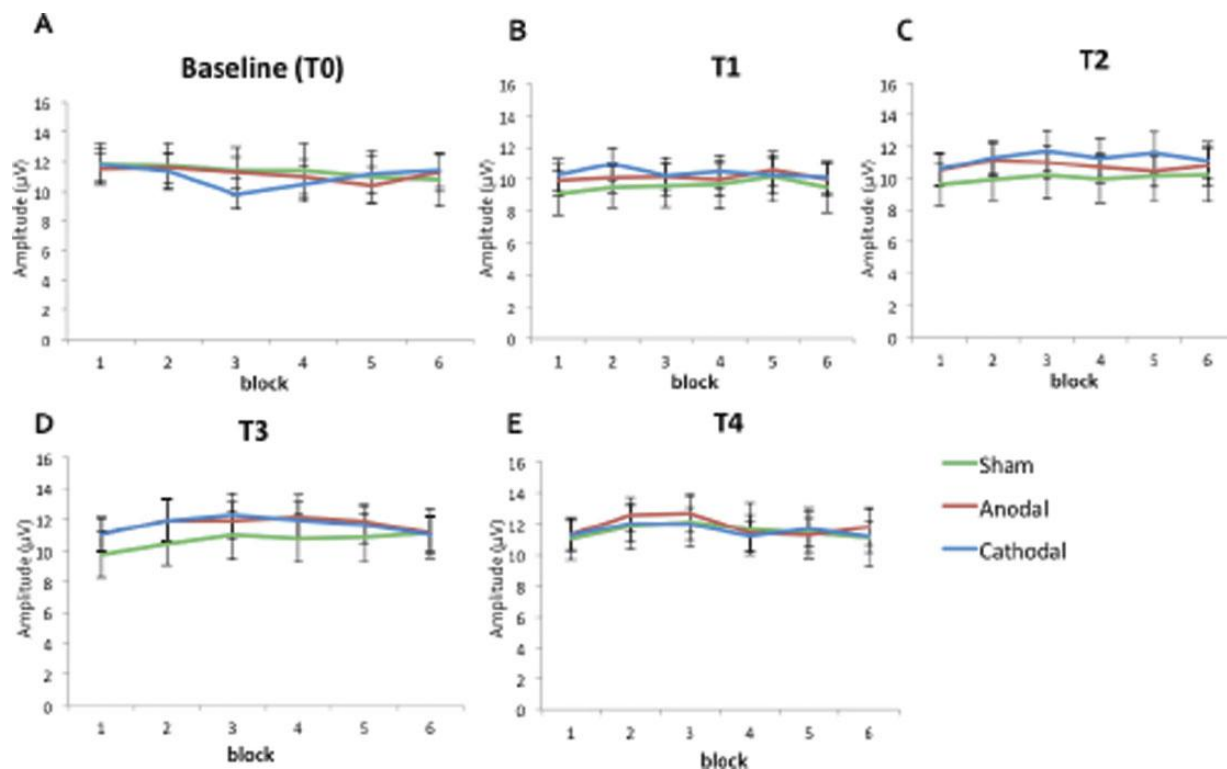
concept study, we aimed to explore the single-session tDCS effects over the visual cortex.

Methods: In a counterbalanced within-subject crossover design, 20 healthy subjects each completed three sessions of anodal, cathodal and sham tDCS (2mA for 20 min) applied over the visual cortex. Pattern-reversal VEPs (6 blocks of 100 sweeps, each for 1 min) were recorded at five time-points, i.e. before (T0), immediately after (T1), and every 15 minutes (T2, T3, T4) after tDCS intervention. We measured and compared the VEP NI-PI amplitudes and habituation (slope of the linear regression line of amplitude changes from the 1st to 6th block of 100 sweeps) between the three tDCS conditions (figure).

Results: Comparing the effects of three tDCS conditions on VEP NI-PI amplitudes across successive blocks and at various time-points, a three-way ANOVA revealed a significant main effect of time ($F(4,76) = 9.46$, $p < 0.001$) and interaction between time and block ($F(20,380) = 2.836$, $p < 0.001$). There was no significant effect of stimulation.

Conclusion: Our findings revealed no modulation of VEP responses with anodal or cathodal tDCS over the visual cortex. Our results do not support the hypothesis of rectifying visual cortical excitability with tDCS as a possible migraine intervention.

Disclosure of Interest: None Declared



Abstract number: IHC-DP-016

Other

IHC-DP-009

Use of automated facial pain detection to explore the role of CGRP and amylin in a preclinical mouse model of migraine

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Objective: Calcitonin gene-related peptide (CGRP) is a neuropeptide that is elevated during migraine. Recently, the FDA has approved the use of monoclonal antibodies targeting CGRP or its receptor for the treatment of migraine headache. However, these treatments are not universally effective, and new targets are still needed. We decided to investigate a related member of the CGRP family, amylin. CGRP and amylin are the most closely related peptides in terms of amino acid sequence and CGRP can activate both the canonical CGRP receptor and amylin AMY₁ receptor equally. We hypothesized that our mice would exhibit increased pain expression after amylin administration, similar to CGRP.

Methods: After acclimation, mice were recorded in both restraint and free moving conditions using multiple cameras. Mice were then given an intraperitoneal injection of either vehicle, CGRP, or amylin and underwent the same conditions. Using our automated facial detection software, facial pain expression was quantified via squint.

Results: The automated facial detection software was able to identify the face of both C57BL/6J and CDI mice. Automated measurements of eye diameter made with restrained mice closely matched our previous manual measurements with CGRP. Eye diameter changes were also detected in free moving mice. In both conditions, the automated software detected CGRP-induced facial changes. The effects of amylin are currently under investigation.

Conclusion: An automated facial recognition and tracking software system is capable of detecting signs of grimace that are consistent with an increased pain state caused by CGRP. This new tool will allow us to quantitatively compare CGRP and amylin effects and treatments in potentially translatable mouse models of migraine.

Disclosure of Interest: None Declared

Post-Traumatic Headache

IHC-DP-017

Targeted Next Generation Sequencing identifies a genetic spectrum of FHM mutations

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Objective: Hemiplegic migraine in both familial (FHM) and sporadic (SHM) forms is a rare subtype of migraine with aura that can involve mutations in the *CACNA1A*, *ATP1A2* and *SCN1A* genes. It is characterised by severe attacks of typical migraine accompanied by hemiparesis, as well as episodes of complex aura that vary significantly between individuals.

Methods: Using a targeted next generation sequencing multi-gene panel, we have sequenced the genomic DNA of 172 diagnostically referred FHM cases, in whom no mutation had previously been found by Sanger sequencing of selected exons in FHM genes.

Results: Mutational screening identified 29 potentially causative mutations, 17 of which were novel, in 35 cases in the three FHM genes (*CACNA1A*, *ATP1A2*, and *SCN1A*). Unexpectedly, the most frequently mutated gene was *ATP1A2* with 20 mutations. *CACNA1A* ranked the second gene most likely to cause FHM in this cohort, with 5 mutations identified, while 4 mutations were identified in *SCN1A*. Analysis of clinical characteristics revealed an over-representation of mild traumatic brain injury triggered concussion in the *ATP1A2* mutation positive group compared to the rest of the cohort (33.3%). [NMI] All detected mutations were confirmed by Sanger sequencing and were absent in 100 non-migraine healthy control individuals. Targeted NGS gene-panel increased the diagnostic yield by four-fold compared to iterative Sanger sequencing (SS) of likely exons in this cohort.

Conclusion: From this study, it is clear that in this Australian and New Zealand cohort the *ATP1A2* gene was the most commonly mutated gene in FHM cases. Our results also show a link between *ATP1A2* mutations and increased susceptibility to concussion, with 35% of *ATP1A2* mutation carriers showing concussion related symptoms after trivial head trauma. Work following up the connection to concussion and searching for currently unknown FHM genes is currently underway using whole exome sequencing.

Disclosure of Interest: None Declared

Big Data**IHC-PO-001****Network Analysis of the International Classification of Headache Disorders, 3rd Edition**Zhang Pengfei^{1,*} and Thomas Berk²¹Neurology, Rutgers Robert Wood Johnson Medical School, New Brunswick²Neurology, NYU Langone Health, New York, United States

Objective: Network analysis is the utilization of mathematical techniques to analyze the relationships of information within a network. We conducted a network analysis of the International Classification of Headache Disorders, 3rd Edition (ICHD3). Our goal is to better understand individual disease entity based on the interconnectedness inherent in the ICHD3 hierarchy.

Methods: A network is defined by a set of objects, called “nodes”, and the connections between them. If two nodes are connected, an “edge” exists between them.

We define a node as a headache diagnosis identified by at least one ICHD3 diagnosis criterium. An edge between two headache disorders exists if one disorder is mentioned explicitly by the other in the “notes” or “comments” section of the ICHD3.

We identify key nodes in a network by measuring mathematically a node’s interconnectedness in three ways: degree centrality, between-ness centrality, and closeness centrality.

To examine how hierarchy affects classification, we developed two models for the ICHD3, a non-hierarchical model and a hierarchical model. In the non-hierarchical model, only cross-references in the subsections qualify as edges. In the hierarchical model, the structure of the ICHD3 is taken into account by establishing additional edges between sections and their subsections.

Results: There are 396 nodes in both of our models. In the non-hierarchical model, there are 718 edges with average degree of separation of 3.63. In the hierarchical model, there are 1385 edges with average degree of 6.99.

In both models, migraine and medication-overuse headache (MOH) are in the top 10 diagnoses according to the three centrality measurements. The choice of non-hierarchical or hierarchical model affects which diagnoses occupy the top 10 centrality nodes; specifically, there are more secondary headache diagnoses in the top 10 position in the hierarchy model compared to the non-hierarchical model.

Conclusion: Migraine and MOH are the most well connected nodes in ICHD3. Diagnostic hierarchy allows for unification of secondary headaches that would otherwise be considered isolated diagnoses. Once connected in a

hierarchical fashion, secondary headache diagnoses form a majority of the most well-connected nodes in our field.

Disclosure of Interests: Pengfei Zhang: Consultant for BoardVitals Inc., Consultant for Fieve Clinical Research. Thomas Berk: Membership on Advisory Committees or Review Panel for Biohaven, Medlink Neurology

IHC-PO-002**Treatment Patterns and Health Care Expenditures in Patients with Migraine: Results from China Health Insurance Research Association (CHIRA) database**Shengyuan Yu^{1,*}, Yanlei Zhang², Yuan Yao², Haijun Cao², Ning Yu³ and Qingjing Liu³¹Department of Neurology, Chinese PLA General Hospital, Beijing²Lilly Suzhou Pharmaceutical Co., Ltd. Shanghai Branch, Shanghai³Beijing Brainpower Pharma Consulting Co., Ltd, Beijing, China

Objective: To understand treatment patterns and health care expenditures among patients with migraine in China.

Methods: We retrospectively analyzed data from China Health Insurance Research Association (CHIRA) database, which was collected from 87 sampling cities and over 19 million insured patients in the calendar year of 2016 and 2017. Patients aged ≥ 18 years old, having at least one migraine diagnosis (ICD-10 code G43 supplemented by physician’s Chinese characters description), without cluster headache, cancer, schizophrenia, stroke, and hemodialysis or peritoneal dialysis were included for analysis. Descriptive analyses were used to evaluate demographics, comorbidities, and prescription medication usage in patients with migraine. To understand the annual health care expenditures, patients with migraine who visit outpatient department between 1–31 Jan of each year, with at least 11 months follow-up were analyzed as subgroup.

Results: Of 90,948 headache population, 10,652 (11.7%) patients had a migraine diagnosis. The mean (SD) age was 51.4(15.8) years and 55.4% were female. The most common comorbidities were major depressive disorder (4.1%) and anxiety (2.3%). Among migraine patients, 2,813 (26.4%) of patients had at least one prescription for acute medication, while 1,602 (15.0%) received preventive medication, and 2,611(24.5%) received traditional Chinese medication. Of the patients with any acute medication, the majority of patients had a prescription for NSAIDs (75.5%), 7.1% had opioids and 6.1% had ergot derivative. Only 3.3% of patients were prescribed with triptans. Of the patients with preventive medication, flunarizine was the most commonly used (87.6%). The average annual outpatient costs per patients were USD

46.4 ± 80.8 (median = 20.6) with 1.8 ± 2.0 (median = 1.0) number of visits.

Conclusion: NSAIDs were commonly used as acute migraine medications, while the use of triptans and preventive medications were insufficient in China. The management of migraine could focus on appropriate use of migraine acute and preventive medications.

Disclosure of Interest: None Declared

IHC-PO-003

Using longitudinal real-world electronic healthcare records to study long-term outcomes in headache sufferers.

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Objective: The long term outcomes for headache patients are poorly understood. We used a real-world dataset to study long term patterns of health behaviour, including healthcare encounters, analgesic prescription patterns, comorbidities and real world efficacy of commonly used migraine preventatives.

Methods: This longitudinal study uses the 2018 Clinical Practice Research Datalink (CPRD) database. Headache codes were used to extract 523,556 patient electronic healthcare records (EHR) with at least one code between 18–65 years of age from 2000–2016. Of those patients, 325,670 were linked with deprivation scores and 178,613 had at least three headache events. Whilst controlling for covariates, patterns in headache occurrence were recorded to ascertain periods at which patients were most at risk of headache. Headache burden was derived using mean cumulative function and Cox regression was used to calculate the efficacy of headache therapeutics.

Results: Patients typically experienced headache events for a median duration of 238 days although some individuals in this cohort could experience headaches for 15 years+. We found headache burden was associated with socio-economic status. One in every nine patients were referred to a neurologist. The commonest migraine-specific abortive used was sumatriptan, although opiate analgesic use was ubiquitous. Amitriptyline was the most common preventative prescribed but topiramate was the most often prescribed in subjects with the greatest burden of headaches. Cox regression demonstrated changes to the duration of headache persistence when patients were prescribed headache preventatives. Triptans were only associated with a

change in headache outcome when combined with preventatives. We also identified depression, hypertension and bipolar disorder as significant comorbidities.

Conclusion: We have been able to describe patterns of headache persistence and treatment using real-world EHR. Our preliminary results reveal a change in headache burden depending on socio-economics, comorbidities, and a change in headache outcome associated with migraine preventatives.

Disclosure of Interest: None Declared

IHC-PO-241

Migraine comorbidity and phenotypic disease networks in occupational health care

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Objective: Migraine is related to significant burden with respect to health care visits and sick leave days compared to a control population [1]. The objective was to examine the ICD-10 coded diseases for migraine patients.

Methods: Data were collected through the follow-up period from 1st January 2012 to 31st December 2017. Electronic medical records of 17 623 patients with migraine (G43) were included in the retrospective analyses. An age and gender matched control population was created for comparison. The pairwise fii correlations between the diagnosis codes were calculated as previously described, and used to draw phenotypic disease networks (PDN) to visually assess the morbidity [2]. An automatic subnetwork detection algorithm was used to group comorbid diagnoses.

Results: Migraine patients had 1.7-fold increase in the mean number of diagnoses compared to controls. Altogether, 1337 ICD-10 codes were detected but only 10% (n = 136) were present in more than 2% of the migraine patients. Among these, over 2-fold increase in the frequency of ICD-10 codes was detected in migraine patients compared to controls for headache and related syndromes (R51, G44), visual and ear disturbances (H53, H81), nausea and vomiting (R11), dizziness (R42), viral and other intestinal infections (A08), dorsopathies (M50, M53) as well as for injuries (S30, S33, S06, S13). The network analysis showed ICD-10 codes pertaining to etiologically related diseases appearing close to each other in the network. Expected clusters of diagnosis codes were found in the PDNs, including a cluster of mental health and sleep related (F32, F41, F43 and F51) as well as a cluster of injury related diagnosis codes (multiple M- and S- codes).

Conclusion: Migraine patients showed increased morbidity detected by the frequencies of ICD-10 codes when compared to controls. Diagnoses of etiologically related diseases appeared close to each other in network analyses. Comparing the PDNs drawn for the migraine patients and the control population showed further evidence for migraine-specific propensity to a wide array of diseases.

Disclosure of Interests: MAK, JS and TP are employed by Novartis.

References

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2. Hidalgo et al. *PLoS Comput Biol*. 2009 Apr 5(4):e1000353.

IHC-PO-242

Migrebot – interactive chat-based headache diary

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Objective: Headache diary is the best way of objective assessment of the patients' headache. Various headache diaries are widely used for correct diagnosis and for effective management of migraine and other headaches. Paper-based diaries are less valid because of suboptimal patient compliance to diary completion. Our aim was to create the interactive chat-based headache diary with high patient adherence and easy to use.

Methods: Unlike other electronic diaries on the market which need to be installed on the smartphone, we used the platform of commonly used messenger Telegram. Another important difference is that we used interactive method of data capturing. The whole process of headache diary completion is based on chatting in messenger like chatting with the friend. For example, the start of the day session is: «Hi, it's me! Did you have a headache today?»

Results: To raise the adherence of patients to diary completion we created two dialogue scenarios. The short version captures only the frequency of headaches (and / or auras) and the use of acute medications. This information is the most important for monitoring headache chronification and for assessment of preventive treatment efficacy. Also this short version is perfect for the patients tired of long questionnaires. If the patient is willing to tell more about his attack, he could continue telling more about his headache with the long version of diary. The long version include the assessment of different characteristics of the attack (triggers, intensity, quality of pain, accompanying symptoms, abortive medication used etc.). The statistics of headache could be exported from the Migrebot database to the user email in Excel file format. Migrebot

interactive chat-based headache diary was successfully launched on January 2019.



Abstract number: IHC-PO-242

Conclusion: Interactive chat-based electronic headache diary offers several advantages over paper-based and other e-diaries. These include the alarms to remind patients to complete diary, minimization of missing data since the bot programmed to prevent the skipping or exclusion of diary items and convenient chatting format of data entry.

Disclosure of Interest: None Declared

IHC-PO-243

Headache and Rhinitis: A 15-Year Long Trend in Search Engine Query Data

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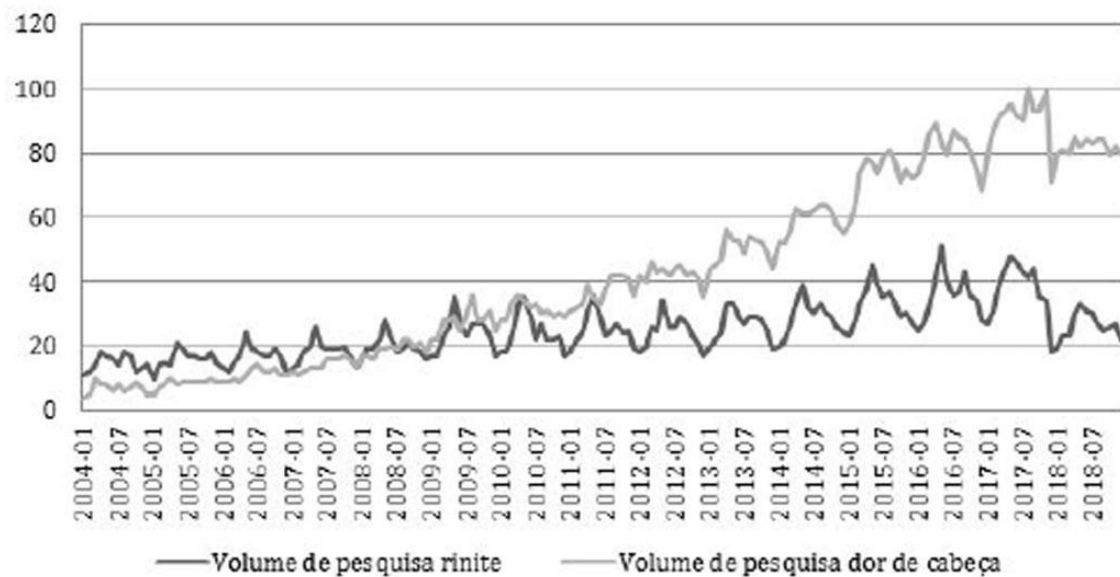
Objective: Headaches and sinus disorders have been linked in several ways. Rhinitis and chronic headaches are both highly common conditions that coexist in the general world population. In order to shed light into the mechanisms between headache and rhinitis, using a digital epidemiology methodology, we aimed to investigate the correlation between the two terms and their temporal pattern in a search engine database.

Methods: On January 8th, 2019, we queried the Google Trends website for the terms 'rinite' and 'dor de cabeça,' limiting the search region to Brazil and other Portuguese-speaking countries. Data was obtained for every month from January 2004 to December 2018. After the descriptive analysis by dispersion diagrams, the Pearson test was performed to evaluate the correlation between the volume of research on rhinitis, headache and Alzheimer's disease, which was included as a control group. A linear regression model was used to predict the volume of searches for the term headache from the term rhinitis, with a 95% confidence interval. Finally, we analyzed the seasonality of rhinitis research volume.

Results: We found that the Pearson coefficient for rhinitis and headache was 0.80 indicating a strong correlation in the time interval analyzed. On the other hand, the test result for Alzheimer's and headache and rhinitis was respectively -0.17 and 0.19 , indicating a very low correlation. The regression model showed that the increase in rhinitis volume increased by 2.69 the volume of headache. In addition we note seasonality in the volume of research of the term rhinitis, we noticed that the peaks of research volume tend to concentrate in the month of May, with the smaller volumes of research concentrating during the months of spring and early summer, and in the autumn this volume of research increases. Finally, we note an increase in the research volume of the term headache, which may suggest an increase in the burden of this pathology.

Conclusion: Headaches and rhinitis were significantly correlated in 15 years of Google Search query data,

Headaches and Rhinitis relation



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where a circannual variation could be observed with both conditions. Further studies using digital search engine query data may be useful for better understanding of comorbidity in headache disorders and possible treatments.

Disclosure of Interest: None Declared

Cluster Headache and Other Trigeminal Autonomic Cephalalgias

IHC-PO-004

Phase 3 Randomized Trial of Galcanezumab in Chronic Cluster Headache: Double-Blind Treatment

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Objective: To evaluate efficacy and safety of galcanezumab (GMB) for attack prevention in adults with chronic cluster headache (CH).

Methods: This was a Phase 3 randomized, double-blind, placebo-controlled trial in adults (18–65 years) with chronic CH defined by ICHD-3 beta (NCT02438826). Eligibility criteria included an attack frequency of ≥ 1 every other day and ≤ 8 /day during a 2-week baseline period. Up to six prespecified preventive treatments were allowed if patients were on a stable dose for 2 months prior to baseline and remained on a stable dose. Patients were randomized (1:1) to monthly subcutaneous GMB 300 mg or placebo (PBO) for 12 weeks during the double-blind treatment period. The primary endpoint was overall mean change from baseline in weekly attack frequency across Weeks 1–12. Gated secondary endpoints were mean proportion of patients with $\geq 50\%$ reduction from baseline in weekly attack frequency (Weeks 1–12) and proportion of patients meeting sustained response through Week 12.

Results: Patients ($n = 237$) were randomized and treated (120 PBO, 117 GMB): 84% white, 73% male, and mean age 45 years. During the baseline period, 63% used ≥ 1 preventive drug (1 [72%], 2 [24%], 3 [3%], and 4 preventives

[1%]); 50% used verapamil. The primary endpoint was not met (change in weekly attacks: -4.6 PBO vs -5.4 GMB; $p = .334$) nor were key secondary endpoints. Treatment-emergent adverse events (AEs) were experienced by 63% of PBO- and 72% of GMB-treated patients; the most common were injection site pain (9% PBO, 11% GMB) and nasopharyngitis (13% PBO, 10% GMB). Injection site erythema was reported by significantly more GMB-treated patients (7% vs 1%, $p = .018$). Five serious AEs (3 PBO, 2 GMB) were reported; 1 was considered treatment-related by the investigator (constipation in GMB arm).

Conclusion: GMB 300 mg did not achieve its primary and key secondary endpoints in this chronic CH prevention trial. The safety profile is consistent with that observed in patients with episodic cluster headache and migraine.

Disclosure of Interests: D. Dodick reports: Personal fees from Amgen, Autonomic technologies, Axsome, Allergan, Alder, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly and Company, eNeura, Neuroliif, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, and Oppenheimer. CME fees or Royalty payments from Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal Meeting Management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, and Wolters Kluwer. Equity (stock options) from Aural analytics, Healint, Theranica, Second Opinon/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Board of Directors of Aural analytics, Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1-1466.vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis. Professional society fees or reimbursement for travel from American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, and Canadian Headache Society. Other: Use agreement through employer: Myndshft.

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C. Lucas reports: consulting fee/honoraria for advisory board membership or speaking: Novartis, TEVA, Sanofi,

Grunenthal, Eli Lilly and Company, Biogen, and Ethypharm, and conducting clinical trials for Novartis and Eli Lilly and Company.

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J. Bardos, J. Martinez, C. Zhou, S. Aurora, J. Yang, R. Conley, and T. Oakes are full-time employees and minor stock holders of Eli Lilly and Company.

IHC-PO-005

Clinical features of Familial Cluster Headache

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Objective: Cases of concordance in monozygotic twins and previously reported genetic associations with variants in candidate genes, imply a genetic component in the aetiology of Cluster Headache (CH). The aim of this study was to estimate the occurrence of a family history in CH patients and to identify the likely mode of inheritance in these families. Furthermore, to delineate the differing clinical parameters between patients with familial CH compared to those with the sporadic form.

Methods: A retrospective study conducted on patients with CH between 2007 and 2017 in a tertiary referral headache clinic. All patients were diagnosed by a neurologist in concordance with the ICHD3b criteria. Those reporting a family history were interviewed over the phone to confirm the pedigree and diagnosis of affected family members.

Results: Overall, 532 individuals were recruited. Approximately 10% (n = 54) of patients reported a family history of CH. A review of pedigrees implied an autosomal dominant mode of inheritance with variable penetrance in the majority of families. In contrast to previous studies, the gender and age of onset were similar in cases and controls. However, familial cases presented with more severe autonomic features. They were also more likely to have a co-existing TAC such as SUNCT and SUNA (O.R 3.22, p = 0.035319) and to respond poorly to acute treatment (p = 0.00000205, O.R 9.47).

Conclusion: A family history in 10% of our cohort further supports a genetic role in the pathophysiology of CH. We also identified differing clinical features and a lower response rate to acute treatment in patients with familial CH compared to those with sporadic CH. These findings

suggest that genetic variation may influence phenotype and response to current acute treatments. Further studies investigating the genetic architecture of CH are required to understand the genotype – phenotype correlation and its impact on therapeutic intervention.

Disclosure of Interest: None Declared

IHC-PO-006

A literature review of screening tools for the detection of cluster headache

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Objective: To identify, appraise and synthesise clinical studies that developed and validated screening tools for the detection of cluster headache.

Methods: A review of the English literature was conducted by searching PubMed for studies that tested screening tools for the detection of cluster headache. We entered [cluster headache] and [screening tool] in Pubmed and 25 articles were obtained. Articles were then included according to their relevance to the topic. Reference lists of relevant articles were hand searched.

Results: Seven unique studies were included in the review. The studies included 1530 patients (310 patients with cluster headache and 1220 controls). According to the studies included in the review, the best discriminatory items between cluster headache and other primary headaches are: untreated attack duration <180 minutes, restlessness during the attacks, strictly unilateral pain, ipsilateral conjunctival injection and/or lacrimation, attacks free period and the male gender.

Conclusion: The review showed that the screening tools could be an useful aid in the detection of cluster headache.

Disclosure of Interest: None Declared

IHC-PO-007**Access to healthcare for Cluster Headache (ch) patients in the European Union: A survey of the European and Migraine Headache Alliance (EMHA)**

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Objective: The objective of this survey was to identify potential challenges in the area of access to healthcare for CH patients in the European Union and to inform policy-making and ensure that future advocacy actions are developed with consideration of the special needs of CH patients

Methods: Access to healthcare has been defined accordingly with European Patient Forum as a multidimensional concept. This definition is based on 5 As – Adequate, Accessible, Affordable, Appropriate, and Available – as the defining aspects of access.

Results: The study was carried out online in February 2018 and had very high participation (2057 responses from 10 countries). The highest number of surveys were completed by CH patients from Germany (n=611), France (n=455), Italy (n=298) and UK (257). All the responders were from members states who joined the EU before 2004. 50.4% of the respondents reported having being diagnosed with episodic CH and 41.3% were chronic CH. 31% of the CH patients rated as difficult or very difficult to obtain the healthcare services they need. 43% of the CH patients experience financial difficulties as the result of spending on healthcare. Almost half of the respondents reported delays in accessing key services such as headache specialists (47%) and medicines (43%). The majority of CH patients (76%, 85% in the chronic CH group) reported they experienced discrimination for their CH (Table 1).

Abstract number: IHC-PO-007

Table 1. Appropriateness of the access to healthcare as indicated by the ability to avoid patients' discrimination. Patients were asked: "have you ever been stigmatized or discriminated against because of your cluster headache? What kind of discrimination have you experienced"? Percentages of CH patients answering yes to the different options

	ALL	Belgium	France	Germany	Italy	NL	Spain	UK
I have never been stigmatized	23	13	25	20	28	37	17	22
Lack of recognition of CH related disability	57	56	50	65	54	45	53	61
Treated as having a trivial disorder	59	69	67	58	62	41	35	67
Prejudices/negative attitudes in family	26	27	34	24	15	17	22	31
Prejudices/negative attitudes in working life	48	55	42	59	34	36	57	43
Prejudices/negative attitudes in society	40	54	42	49	23	43	50	33

Conclusion: The survey demonstrated that the quality of healthcare for CH in Europe is not perceived as optimal and aspects of patient-centred care are not implemented. The survey's results point to fundamental challenges to tackle and key areas of action for decision makers at EU and national level to address in order to ensure patients with Cluster Headache have access to high quality, affordable healthcare across the European Union.

Disclosure of Interest: None Declared

IHC-PO-008**Temporal changes of circadian rhythmicity in cluster headache**

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Objective: To investigate the temporal change of the circadian rhythmicity according to the disease course in patients with cluster headache (CH).

Methods: In this multicenter study, 193 CH patients were recruited between September 2016 and August 2018. Patients in their active within-bout period were included in this study. We evaluated patients regarding circadian rhythmicity in the current bout and any change in circadian rhythmicity between bouts. We analyzed patterns of circadian rhythmicity according to disease progression. The number of total lifetime bouts was divided into 10 groups (deciles) and used as a marker of disease progression.

Results: Among 175 CH patients in the within-bout period included in this study, 86 (49.1%) patients had a circadian rhythmicity in the current bout. The prevalence of circadian rhythmicity was similar throughout the 1st – 9th deciles, although it decreased to 28.6% in patients of 10th decile (>20 lifetime bouts). Sixty-six (46.3%) out of 136 patients with ≥ 2 bouts reported bout-to-bout changes in circadian rhythmicity. In patients with circadian rhythmicity, patients in earlier disease course showed a relatively even distribution of the time of most frequent occurrence, whereas it showed a temporal trend toward dichotomy into hypnic and midday occurrence in patients with advanced disease (p for homogeneity of variance = 0.037). When the time of most frequent occurrence was grouped into night and daytime, daytime predominance increased as the disease progresses (up to seventh deciles), while night predilection was predominant at earliest and later disease spectrum (p for non-linear fit = $p = 0.013$).

Conclusion: Circadian rhythmicity changes over time in patients with CH. Its dynamic changes may represent an evolution of hypothalamic activity during CH courses.

Disclosure of Interests: None declared.

IHC-PO-009

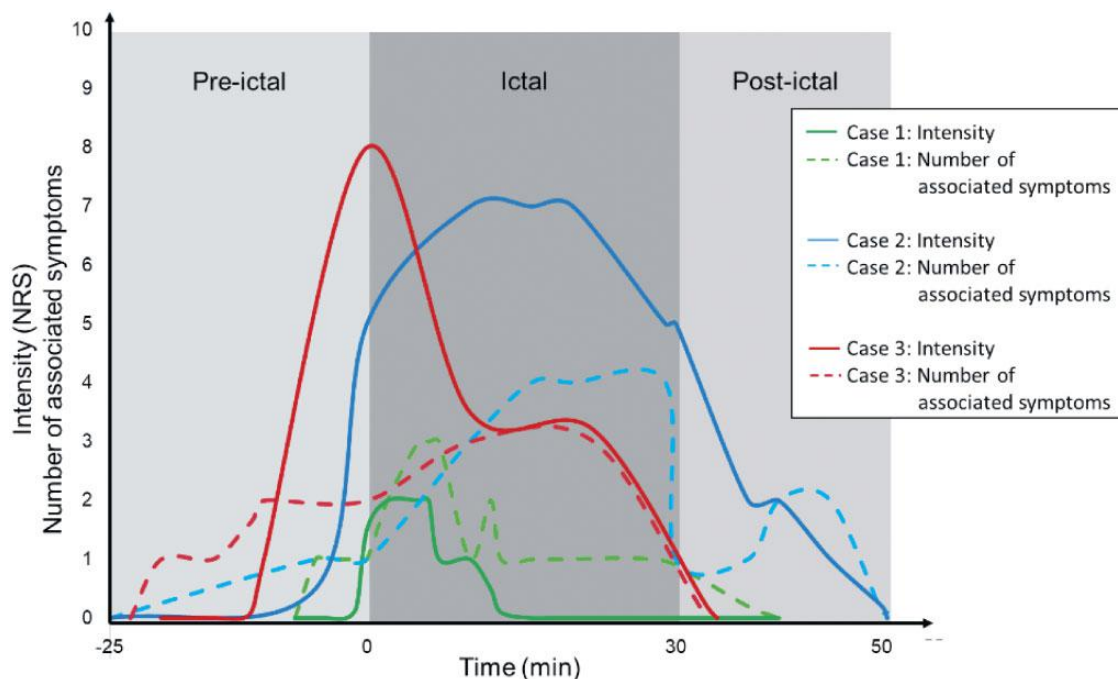
Autonomic disturbances precede the pain of cluster headache: Insights from spontaneous cluster headache attacks.

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Objective: Cluster Headache (CH) attacks are short-lived, pathological phenomena with severe pain. Investigations during spontaneous attacks are complicated and time consuming. Therefore, the literature on observed spontaneous attacks are sparse. Our group has recently proposed a three-phase model of CH attacks in which pre- and postictal symptoms of attacks enclose the headache phase. We aimed to characterize all phases of spontaneous CH attacks both clinically and paraclinically.



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Methods: We recorded headache characteristics, cephalic autonomic symptoms (CAS), heart rate variability, plasma levels of pituitary adenylate cyclase-activating peptide-38 (PACAP38) and vasoactive intestinal peptide (VIP) during spontaneous CH attacks in the clinic.

Results: Three chronic CH patients were observed during all phases of a CH attack. In all three patients, the headache was preceded by painless CAS (lacrimation or rhinorrhea) and/or restlessness lasting 7 to 25 minutes. Two patients received abortive treatment with SPG stimulation and high flow oxygen and here the CAS stopped at the same time as the pain, however, in the patient who did not receive acute therapy the lacrimation continued 15 minutes after cessation of pain. Heart rate variability recordings revealed a high RMSSD (Root-mean square differences of successive R-R intervals, a measure of parasympathetic activity) around ten minutes before the headache debut in two out of three cases and a possible activity spike in the third case. No differences were found in PACAP38 or VIP plasma concentrations during attacks. There was no apparent change in blood pressure and pulse.

Conclusion: Increased local and systemic parasympathetic outflow preceded the pain of spontaneous CH-attacks. These data suggest that CAS and restlessness are of central origin and not a result of extreme pain. Further investigations of the pre-ictal phase of a CH-attack is crucial for understanding the CH pathophysiology.

Disclosure of Interest: None Declared

IHC-PO-010

Efficacy and safety of oral prednisone as add-on therapy for the initial prophylactic treatment of episodic cluster headache: a multicenter, randomised placebo-controlled, parallel study – PredCH-Study

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Objective: To investigate the efficacy and safety of 100 mg oral prednisone over five days in the early treatment of episodic CH as add-on therapy for prophylactic therapy with verapamil.

Methods: Multicenter, randomized, placebo-controlled, clinical trial.

Results: A total of 117 patients were included. 107 patients were available for the intention-to-treat analysis (55 placebo, 52 prednisone). Prednisone showed a significant reduction in CH attacks within the first 7 days of treatment compared to placebo (prednisone 7 vs. placebo 9.5 attacks, $p=0.0125$). Relevant side effects were not observed during this time.

Conclusion: Prednisone reduces the CH attack rate at the beginning of an episodic CH bout and therefore can be recommended for the use as initial short-term prophylaxis.

Disclosure of Interests: Supported by the Federal Ministry for Education and Research (BMBF)

IHC-PO-011

Episodic Cluster Headache: Impact of length of episode on pain free periods for patients in the United Kingdom, Germany and Spain

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Objective: To explore the influence of length of episode on pain free periods for episodic cluster headache patients.

Methods: The Ipsos Healthcare Cluster Headache Therapy Monitor: Physicians involved in the treatment management of both episodic (ECH) and chronic (CCH) cluster headache patients provided demographic, disease and treatment data on the last cluster headache patients aged over 18 seen in their practice. Data were collected online in EU3 [United Kingdom (UK): $n=458$; Germany (DE): $n=450$; Spain (ES): $n=524$]. This abstract will focus on episodic cluster headache patients in the EU3 – UK: $n=241$; DE: $n=285$; ES: $n=340$). Episodic cluster

headache patients are defined as those patients who experience periods of attacks lasting seven days to one year, separated by pain free periods lasting one month or longer.

Results: The length of time ECH patients experience an

Table 1.

	A 7 days	B 8–31 days	C Over 31 days
Number of patients	79	319	194
Average pain free period (in days)	99.54 Days	176.63 Days	263.09 Days
Standard Deviation	77.17	141.62	300.75

episode of cluster headache was analysed to see if there is a potential effect on the average length of these patients' pain free periods.

The results showed that those with shorter episodes experienced shorter pain free periods on average. Inversely, those patients with longer episodes experienced a longer duration of pain free periods on average.

Those patients in the 8–31 day episode grouping (B) had a significantly longer pain free period than those in the 7 day episode grouping (A). Those patients with episodes over 31 days (C) had a significantly longer pain free period than those in the 8–31 day episode grouping (B) and the 7 day episode grouping (A).

Conclusion: Results show that there is a potential link between the length of an episode and the duration of a pain free period for patients with episodic cluster headache. This relationship should be examined in subsequent years and potentially in different sub groups of the patient population to identify potential variations to this analysis.

Disclosure of Interest: None Declared

IHC-PO-012

Dynamic Mechanical Hypersensitivity in the Trigeminal Area in Episodic Cluster Headache

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Objective: Hypersensitivity to pressure pain is a common manifestation of sensitization of the central nervous system. Most studies used a mechanical algometer for evaluating PPTs, which represents a static assessment. A new method for assessing dynamic hyperalgesia has been developed (dynamic pressure algometry set, Aalborg University©, Denmark) and used in patients with tension type headache and migraine. We aimed to investigate differences in dynamic pressure pain sensitivity between patients with episodic Cluster Headache (CH) and headache-free controls

Methods: Forty men with episodic CH and 40 matched headache-free healthy controls were included. Static PPTs were bilaterally assessed with a pressure algometer (Somedic©, Sweden) over the centre of the muscle belly of the temporalis. Dynamic pressure pain hyperalgesia was assessed with a dynamic pressure algometry set (Aalborg University©, Denmark) consisting of 8 rollers with the following fixed levels (500 g, 700 g, 850 g, 1350g, 1550g, 2200g, 3850g, 5300g). Each roller was moved at a speed of 0.5 cm/sec over a diagonal line covering the temporalis muscle from an anterior to posterior direction. The dynamic pain threshold (DPT – load level of the first painful roller) and pain elicited during DPT (roller evoked pain) were determined in both groups by an assessor blinded to the subject's condition. Patients with CH were assessed in a remission phase

Results: Side-to-side consistency between DPT ($r_s = 0.781$, $P < .001$) and roller evoked pain ($r_s = 0.586$, $P < .001$) was found for patients with cluster headache. Men with episodic cluster headache showed bilateral lower (all, $P < .001$) DPT (mean: 1005g) and higher roller evoked pain (mean: 3/10 on a NPRS) than headache-free healthy controls (DPT: 2035g; roller evoked pain: 1.5/10).

Conclusion: This study observed that men with episodic cluster headache exhibit dynamic pressure pain hyperalgesia in the trigeminal region as compared with matched headache-free controls.

Disclosure of Interest: None Declared

IHC-PO-013

SI00B and NSE in cluster headache -evidence for glial cell activation?

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Objective: Neuronal specific enolase (NSE) and protein S100B have gained considerable interest as markers of CNS injury, glial cell activation and/or blood brain barrier (BBB) disruption. No studies have investigated NSE and S100B in cluster headache (CH), but these biomarkers could contribute to understanding of CH.

Methods: Patients with episodic CH in bout (eCHa)-, in remission (eCHr) and chronic CH (cCH) were included in this randomized, double-blind, placebo-controlled, two-way cross-over provocation study during which we measured NSE and S100B at baseline, and in response to CGRP and placebo infusion. Baseline findings were compared to historical data on migraine patients and healthy controls.

Results: Nine eCHa, 9 eCHr and 13 cCH patients completed the study and blood samples from 11 CGRP-induced CH attacks were obtained. At baseline we saw no differences in NSE levels between CH groups, but CH patients in active bout had higher levels compared with migraine patients ($p < 0.0001$) and healthy controls ($p = 0.0065$). CGRP-infusion caused no NSE changes and only a trend towards an increase was seen in patients who reported a CGRP-induced CH attack ($p = 0.0611$). At baseline S100B levels in eCHa patients were higher compared to cCH patients ($p = 0.0176$) but otherwise no other variations were noted. S100B was unaffected in relation to CGRP infusion or CGRP-induced CH attacks.

Conclusion: Of CH-patients in an active disease phase we found higher S100B levels in eCHa patients and a trend towards an NSE increase in response to CGRP induced CH attack. Our findings suggest that glial cells are activated in CH and that the resulting inflammatory response may pose a role in CH pathophysiology.

Disclosure of Interest: None Declared

IHC-PO-014

Diagnostic delay in cluster headache

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Objective: Cluster headache (CH) is a rare severe primary headache disorders with remission periods. Diagnostic delay is frequent and problematic in proper management of patients with CH.

Methods: During September 2016 to June 2018, consecutive patients with CH based on the third edition of the ICHD were prospectively recruited from 16 hospitals in Republic of Korea. Duration before the diagnosis was assessed the time interval between the year of onset of cluster headache and the year diagnosed as CH by physician. The duration of CH before diagnosis was divided into quartiles, more than median was diagnosis delay, and more than three quartiles were classified as serious diagnosis delay.

Results: Diagnosis was delayed about 5.5 ± 7.2 (0–36) years in 191 patients. Duration before the diagnostic was 0.3 ± 0.8 year in first-onset CH, 7.4 ± 7.8 years in episodic CH, 2.1 ± 2.5 years in chronic CH, and 3.5 years in probable CH. The CH patients with serious delayed diagnosis (8 or more years after their onset) had younger onset, higher total cluster bouts, and more frequently episodic CH than those without. Headache impact, depression, anxiety parameters were not different between two groups. According to the onset year, diagnostic delay (3 or more years after their onset) was reported in 88% of

the patients between 1979–1998, 77% of the patients between 1999–2010, and in 47% of the patients between 2011–2015. Diagnostic delay (3 or more years after their onset) did not differ by the visit year (41.7% in 2016, 56.1% in 2017, and 45.9% in 2018).

Conclusion: Diagnosis of CH was frequently delayed, especially in episodic CH. Diagnostic delays are still common, so public awareness of CH and proper transfer to neurologist is required.

Disclosure of Interest: None Declared

IHC-PO-015

Dynamic Mechanical Sensitivity in the Trigeminal Area is Associated with Widespread Pressure Pain Sensitivity in Cluster Headache

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Objective: Previous studies observed that primary headaches as migraine, tension type headache and cluster headache exhibit widespread pressure pain hyperalgesia as a clinical manifestation of central sensitization. A method for assessing dynamic hyperalgesia has been recently developed and used in patients with tension type headache and migraine. We aimed to investigate the association between dynamic sensitivity to pressure pain and widespread pressure pain sensitivity in patients with episodic Cluster Headache (CH).

Methods: Men with episodic CH were included. Static pressure pain thresholds (PPT) were bilaterally assessed over temporalis muscle, cervical spine, and tibialis anterior muscle with a digital pressure algometer (Somedic®). Dynamic pressure pain sensitivity was assessed over trigeminal area with a dynamic pressure algometry set (Aalborg University®, Denmark) consisting of 8 rollers with the following pressure levels (500 g, 700 g, 850 g, 1350 g, 1550 g, 2200 g, 3850 g, 5300 g). Each level roller was moved at a speed of 0.5 cm/sec over a diagonal line covering the temporalis muscle from an anterior to posterior direction. The dynamic pain threshold (DPT), i.e., load of the first painful roller, was calculated. Participants were assessed in a remission phase.

Results: Forty men with episodic CH were included. Significant positive associations between DPT and widespread PPTs were observed (temporalis r : 0.665, $P < 0.001$; cervical spine r : 0.368, $P = 0.020$; tibialis anterior muscle r : 0.285, $P = 0.045$): the greater the widespread static pressure pain sensitivity, the higher the dynamic sensitivity to pressure pain in the trigeminal area.

Conclusion: This study found that dynamic pressure pain sensitivity was associated with widespread sensitivity to pressure pain supporting that dynamic algometry can be as valid as static algometry for assessing sensitivity to pressure pain in patients with primary headaches.

Disclosure of Interest: None Declared

IHC-PO-016

Repeated greater occipital nerve (GON) injections in medically intractable chronic cluster headache

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Objective: To assess the effectiveness of repeated injections of the greater occipital nerve (GON) with steroids and/or local anaesthetics in medically intractable chronic cluster headache (MICCH).

Methods: We retrospectively identified all cluster headache patients who received a GON-injection between January 2014 – June 2018 at Leiden University Medical Center Headache Clinic. Data were collected from patients' medical records on diagnosis, number and timing of GON-injections, frequency, duration and intensity of attacks, subjective response, adverse events, current and previous use of prophylactic medication.

Results: We collected data from 180 injections in 122 patients ($n = 70$ chronic cluster headache (CCH) and $n = 52$ episodic cluster headache (eCH)). Median number of injections per patient was 1 (range 1–8). Any improvement was reported for 119/180 (66%) of injections, with complete remission for 56/180 (31%) injections. Both endpoints were similar in CCH and eCH. In total 33/122 (27%) patients received repeated injections. Response rates were 80/122 (65%, 1st injection), 22/33 (67%, 2nd injection), 9/15 (60%, 3rd injection), 3/4 (75%, 4th injection) and 2/3 (67%, 5th injection). Mild to moderate adverse events were reported in 46/180 (26%) injections in (32/122 (26%) patients). There were no serious adverse events. Repeated injections did not increase adverse event rate. There were 40 patients with MICCH who received 68 injections (median = 1, range 1–5). Any improvement was reported for 39/68 (57%) injections in 22/40 (55%)

patients, with complete remission in 19/68 (28%) in 12/40 (30%) patients

Conclusion: GON injections afforded at least some improvement in two thirds of patients with episodic or chronic cluster headache and in more than half of patients with MICCH. Complete remission was seen for one third of injections. Repeated injections were well tolerated and associated with at least some improvement in two thirds of injections.

Disclosure of Interest: None Declared

IHC-PO-017

Light sensitivity is increased in cluster headache

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Objective: Because attacks of cluster headache may be associated with visual aura and photophobia we wanted to assess sensitivity to light and patterns in patients with cluster headache during and in between attacks.

Methods: We used the validated Leiden Visual Sensitivity Scale (L-VISS) (1) to assess sensitivity to light and pattern in 139 patients with cluster headache from a previous study on aura in cluster headache (2). L-VISS scores were compared with existing L-VISS scores in 86 matched non-headache controls who were investigated in a previous study (1). Participants were divided in five groups: controls, episodic cluster headache (ECH) without aura, ECH with aura, chronic cluster headache (CCH) without aura, and CCH with aura. ECH patients were investigated in a cluster period during and outside an attack, and in an attack-free period. CCH patients were investigated in and outside an attack.

Results: L-VISS scores were obtained for 139 patients (76 with ECH without aura, 42 with CCH without aura, 11 with ECH with aura and 9 with CCH with aura) and compared with the scores from 86 controls. For both ECH and CCH, L-VISS scores were higher during an attack compared to outside an attack and compared to controls (both $p < 0.001$). Patients with ECH had higher L-VISS scores in a cluster period (but outside an attack) versus an attack free period ($p < .001$). Patients in an attack free period had similar L-VISS scores as controls. L-VISS scores did not differ between CCH and ECH between patients with versus without aura.

Conclusion: ECH patients in a cluster period have increased sensitivity to light and pattern during an attack. CCH patients have increased light sensitivity both during

and outside an attack. Outside an attack, both during a cluster period and an attack free period, ECH patients have normal sensitivity to light and pattern.

Disclosure of Interest: None Declared

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IHC-PO-018

Suicide risk in refractory chronic migraine, refractory chronic cluster headache, and refractory trigeminal neuralgia. Which is the “suicide disease”?

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Objective: Suicide has been classically related to trigeminal neuralgia (TN) although there is no conclusive scientific data. Instead, recent studies suggest an association with cluster headache (CH). We analyze and characterize suicidal risk in patients with refractory rTN, refractory rCH and refractory chronic migraine (rCM).

Methods: Patients with CM, CH and TN according to ICHD3 criteria with suicide risk detected by anamnesis. CH and CM were considered refractory (r) according to EHF-2014 criteria, and TN according to SFEMC-2018 criteria.

Results: We interviewed 963 patients in their first visit to the Headache Unit (February2018-February2019). We diagnosed: CM-191, CH-72, and TN-91. 78 patients presented rCM-40.84%, 29 rCH-40.28% and 33 rTN-36.26%. We detected suicide risk in 9 patients: 2 patients with rCM-2.56%, 6 with rCH-20.69% and 1 with rTN-3.03%. Of these 9 patients with suicide risk: 55.5% were women (mean age: 44.3 years-old), mean evolution of headache/neuralgia: 14 years, 33.3% had psychiatric history, 100% presented death passive ideas, 88.8% presented unstructured autolytic ideation and the 22.2% had structured autolytic ideation, 66.6% kept these ideas in free-pain periods, and 22.2% reported autolytic attempts in the past. The psychiatric diagnose was: major depressive disorder 5/9, adaptive disorder 3/9, anxiety-depressive

disorder 1/9. We did not detect autolytic attempts during the follow-up.

Conclusion: The suicide risk is more frequent in cluster headache than in migraine or in trigeminal neuralgia when they achieve the refractory scenario. Psychiatric history was presented only in one out three patients. Therefore, the suicide behaviour appears reactive to a bad evolution of the pain control in the majority of cases.

Disclosure of Interest: None Declared

IHC-PO-019

Suboccipital steroid injections for treatment in cluster headache: an observational prospective study

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Objective: Greater Occipital Nerve (GON) injections with corticosteroids can be used for transitional treatment in cluster headache (CH). The aim of this observational prospective study is to evaluate the effectiveness and safety of repeated suboccipital injections with methylprednisolone in CH.

Methods: We consecutively enrolled all patients accessed to our Headache Centre for episodic or chronic CH without contraindication to steroid treatment. Patients underwent to three injections in suboccipital area of slow-release methylprednisolone 60 mg on alternate days. Primary outcome was the complete absence of CH attacks at one month from the injections. Secondary outcome was the reduction of at least 50% of daily attacks.

Results: A total of 50 patients were enrolled, between November, 2017 and February, 2019: 42 with episodic and 8 with chronic CH. Twenty-three patients (46%) were attacks free at one month, reaching the primary outcome. In the 21 non-responders patients (2 were lost to follow up, 4 dropped out) the daily frequency of attacks decreased from a median of 1.75 (IQR: 1–3) to 1.00 (IQR: 0.3–2) ($p < 0.006$), and 6 (29%) reached the secondary outcome. The intensity decreased from a median of 8 (IQR: 7–10) to 7 (IQR: 5–8) ($p < 0.023$). We find no significant difference in responsiveness rate in chronic patients compared to episodic ones.

No serious adverse events were reported: 31 patients (62%) had mild adverse events; neck stiffness/pain was the most common.

Conclusion: In our sample, at one month after GON injection, the 46% of patients were attacks free and the

29% of non-responders showed a reduction of at least 50% of daily attacks. Our findings suggested that suboccipital methylprednisolone injections may have an important role as transitional CH management, due to its rapid and good effectiveness in both chronic and episodic patients. Effectiveness of this infiltration protocol need to be confirmed in larger and controlled studies.

Disclosure of Interest: None Declared

IHC-PO-020

Acute and preventive treatment patterns in episodic cluster headache: findings from the United States, United Kingdom and Germany

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Objective: Patients with episodic cluster headache (ECH) can experience multiple, excruciatingly painful, unilateral headache attacks a day. Treatment options for cluster headache (CH) have limited supportive data and the standard of care may differ by region. The objective of this study was to describe regional treatment patterns for episodic cluster headache.

Methods: Data were drawn from the Adelphi 2017 CH Disease Specific Programme, a cross sectional survey including physicians and their CH patients from Germany, UK and US. Physicians reported on the full acute and preventive treatment history for their next 10 consulting CH patients. Data was analyzed descriptively.

Results: The majority of ECH patients in Germany (N = 309), the UK (N = 328) and US (N = 375) received acute therapy only (53%, 48%, 43% respectively), a combination of acute and preventive therapy (34%; 37%; 42%), or preventive therapy only (10%, 8%, 12%). Most frequently prescribed acute treatments were sumatriptan, oxygen and zolmitriptan. Oxygen was prescribed more often in Germany (45%) and UK (33%) vs. US (19%). Verapamil was the most commonly prescribed preventive therapy (34%, 29% and 25% of patients in Germany, US and UK respectively) followed by topiramate and lithium. Fewer UK patients reported taking their preventive therapy as advised vs. Germany and US (32% vs. 60% and 80% respectively). Key reasons for non-compliance across geographies: forgetfulness, not feeling like a dose was needed and side effects experienced. Over half of patients in the UK (60%) and US (54%) reported the need to take an extra dose of their acute medication to relieve pain symptoms, compared with 30% in Germany, and 13% in the US

indicated they did this ‘all the time’ or ‘nearly all the time’ (vs. 2% in Germany and 7% in UK).

Conclusion: The treatment of ECH is marked by high use of acute medications and lower use of preventive treatments, despite recommendations, suggesting the need for additional preventive options.

Disclosure of Interests: JM, JSA, RN, and AT are employees and/or shareholders of Eli Lilly and Company. JJ, SC, JC, and ZP have no conflict of interest to disclose.

IHC-PO-244

Prediction of the sphenopalatine ganglion localization in computerized tomography images

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Objective: The sphenopalatine ganglion (SPG) is a target for several headache syndromes. Most of the groups targeting the SPG do not localize it directly, and this might account for some therapeutic failures. As the SPG cannot be seen on computerized tomography (CT) scans, magnetic resonance image (MRI) must be used to visualize the ganglion.

Objective: to describe anatomical landmarks that help predict the location of the SPG on CT scans.

Methods: We localized the SPG in 21 Caucasian patients (21 right and 17 left ganglia; total 38) in 3 tesla MR images subsequently fused with CT scans. We measured the distance from the SPG to two bony landmarks identified on CT scans. We then applied the average distances to find an estimated position of the SPG. The first landmark was the center of the anterior opening of the vidian canal (VC). The second landmark was a point on the sphenoidal bone, defined in an axial plane at the level of the center of the VC (S-point). The predicted position of the SPG measured from the VC and the sphenoidal bone were referred to as, respectively, vcSPG and sSPG. Finally, the distances between the SPG, as seen on MRI, and predicted vcSPG/sSPG were calculated.

Results: The average distance between SPG as seen on the MRI images and the estimated position based on CT images were 1.82 mm (SD 0.83, range 0.22–3.57 mm) for vcSPG and 2.09 mm (SD 0.99, range 0.71–4.79 mm) for sSPG.

Conclusion: The localization of the SPG can be predicted on CT images using bony landmarks. Localization of the SPG may be important in achieving successful therapeutic

outcomes for treatments that are directed toward the SPG.

Disclosure of Interest: None Declared

IHC-PO-245

The prophylactic effect of Zoster vaccine live attenuated in patients with episodic cluster headache

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Objective: We had ever reported that seizures of episodic cluster headache (ECH) might be probably triggered by reactivation of subclinical Varicella Zoster Virus (VZV) in trigeminal ganglion which would induce abnormal CGRP release via peripheral neuron by pre-post measuring trends on titers of VZV in 27 patients suffering from ECH. Furthermore, it was also reported that preliminary use of valaciclovir hydrochloride (dosage: 1500 mg BID for five days) for the onset of VZV's reactivation probably shortened duration on seizures of ECH.

Considering from the recent efficacy of vaccine for patients with VZV, also evaluate subclinical VZV in trigeminal ganglion that would probably have some relation to the onset of ECH.

Methods: This time, 68 patients (42 men and 24 women) who was diagnosed ECH by the International Classification of Headache Disorder IIIβ Edition had annually experienced 1.74-time seizure with 4.84-week period per seizure on average before vaccinated. Almost all patients were prescribed as prophylactic treatment in pre-vaccinated. After vaccination, all patients were checked antibody of VZV (IgG, IgM) before and after vaccinated, to confirm the efficacy for the prevention of ECH.

Results: Finally, approximately 99% of patients improved and experienced attack free term from their ECH's seizures by vaccinating in 48-month observation without no prophylactic medication nor abortive medication.

Only one patient experienced the recurrence of severe cluster headache attack who was vaccinated within a month after cluster period for patient 's desire.

Proper term of vaccination would 2 or 3 month ahead after the end of last cluster attack considering stabilized term of reactivated VZV in trigeminal ganglion.

In second look, injection of vaccine may sometimes have considered due to different taking titer of antibody to the individual.

Conclusion: Furthermore, long term and large number evaluation will be needed to confirm the efficacy of Zoster

vaccine to the prophylactic effect for cluster headache attack.

Disclosure of Interest: None Declared

IHC-PO-246

Misdiagnosis and physicians seen prior to the correct diagnosis of cluster headache: a systematic literature review

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Objective: To identify, appraise and synthesise clinical studies on the delays in diagnosis, misdiagnosis and mismanagement of cluster headache (CH).

Methods: The systematic review was prepared, conducted and reported in accordance with the Preferred reporting items for systematic review and meta-analysis (PRISMA). It was registered with International Prospective Register of Systematic Reviews (PROSPERO). Medline, EMBASE, PsycINFO, PubMed, CINAHL, BNI, HMIC, AMED, HBE and Cochrane Library databases were systematically searched. Reference lists of relevant articles were hand searched.

Results: Fifteen studies, including 4661 patients, met the inclusion criteria; 13 case series and two surveys. Delays in diagnosis, misdiagnosis and mismanagement have been reported in Europe, Japan and the USA, all with well-developed health services. Patients consulted on average 3 clinicians and waited a mean time from three to nine years (ranges between 0–48 years) prior to being correctly diagnosed. Patients performed multiple invasive procedure before the correct diagnosis was made. Both patient and physician factors account for the delays in diagnosis.

Conclusion: Diagnostic delays, misdiagnosis and mismanagement of CH is widespread and both patients and clinicians are responsible for the delays in diagnosis. Patients with CH consulted many clinicians before the correct diagnosis was established and underwent multiple invasive procedures.

Disclosure of Interest: None Declared

IHC-PO-247

Galcanezumab treatment patterns in episodic cluster headache: findings from a Phase 3b multicenter, single-arm, open-label safety study of galcanezumab

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Objective: To describe galcanezumab (GMB) treatment patterns for prevention of episodic cluster headache (CH) within the context of a study allowing monthly dosing based on investigator judgment.

Methods: Study CGAR (NCT02797951) is an ongoing Phase 3b single-arm, open-label safety study in outpatients with episodic or chronic CH who completed one of the Phase 3 double-blind, placebo-controlled studies, CGAL (NCT02397473) or CGAM (NCT02438826). Patients enrolled could receive GMB 300 mg subcutaneously once monthly. The decision to dose at each monthly interval (visit) was determined by the study investigator based on clinical symptoms and response. CH status, treatment patterns and Patient Global Impression of Improvement (PGI-I) were described for the subset of episodic CH patients with data available in the present interim analysis.

Results: Thirty-one patients completed CGAL and had entered the CGAR treatment phase at the time of this interim analysis. The majority of patients were male (71%) and European (67.7%). Mean age was 46.9 years with an average of 13.1 weekly CH attacks at CGAL baseline. All patients had a median (Quartile 1, Quartile 3) of 9 (5, 13) visits and 54.8% experienced one active cluster period, while 29.0% and 12.9% experienced two, and more than two active periods, respectively. Median (Quartile 1, Quartile 3) duration of active periods was 2 visits (1, 3). GMB was administered in 98.1% of active status visits and 42.4% of remission visits. Among 26 patients who enrolled in active status with available data, 53.8% (14/26) reported feeling “very much/much better” on the PGI-I scale at one month.

Conclusion: In a treatment setting, which more closely approximated that of clinical practice, GMB treatment patterns varied in relation to cluster status, and a majority of patients reported an improvement in their condition.

Disclosure of Interests: D. Kudrow has been an advisory board member for Alder, Amgen, Biohaven, Eli Lilly and Company, and Xoc; a speaker for Amgen, Eli Lilly and Company, and Teva; and a clinical research investigator for

Alder, Amgen, Biogen, Biohaven, Eli Lilly and Company, Roche-Genentech, Teva and VM Biopharma. JSA, MR, TO, JNB, RW, D. Kuruppu and JM are employees and minor stockholders of Eli Lilly and Company.

IHC-PO-248

Misdiagnosis of cluster headache in Russia

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Objective: Cluster headache (CH) is a comparatively rare, severe primary headache. Despite striking features and recognizable criteria, it remains underdiagnosed in many countries, including Russia. CH patients may face unnecessary investigations and delays in accessing adequate treatment. This study was conducted to investigate the occurrence of diagnostic errors.

Methods: Medical records were retrospectively analyzed in 144 patients with CH defined by ICHD-3 diagnostic criteria in the headache clinic in Moscow between September 2016 and December 2018. All patients had a neurological examination and questionnaire survey.

Results: The male to female ratio was 8:1. Mean age at onset was 27 (SD 9) years. Russian CH patients had pronounced seasonal periodicity, and high frequency of migraine-like features. The time between the first episode and the diagnosis ranged from 1 year to 21 years (median 9 years): 40.8% had consulted an ophthalmologist, 29.8% an ENT specialist, and 10.4% a dentist before the diagnosis was established. One patient had consulted a psychiatrist. The initial diagnosis was “cluster headache” in 16%, “TGN” in 30.5% “migraine” in 27.7%, “sinusitis” in 16.6%, “dysautonomia” in 17.3%. One patient was misdiagnosed with “psychoorganic syndrome”. A high rate of responders had undergone instrumental investigations: 70% had brain MRI, 19.4% had CT of the sinuses. Photophobia, phonophobia, nausea, and sex were among the factors that increased the diagnostic delay.

Conclusion: CH remains misdiagnosed in many cases for many years. Correct diagnosis is critical, because long-standing morbidity is associated with this intense pain. Careful adherence to the IHS criteria can resolve questions and will result in fewer diagnostic errors. Despite the stereotyped clinical picture, atypical features are often present and may result in diagnostic problems. More attention should be paid to educate first line physicians to recognize CH.

Disclosure of Interest: None Declared

IHC-PO-249

Acute and preventive treatment use in a phase 3 randomized trial of galcanezumab in chronic cluster headache

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Objective: To evaluate the use of concomitant acute and preventive treatments with galcanezumab (GMB) in adults with chronic cluster headache as defined in ICHD-3 beta.

Methods: Data are from an ongoing phase 3, double-blind, placebo-controlled trial with a prospective baseline (BL), 12-week treatment period, and 12-month open-label extension. Patients were randomized to monthly subcutaneous (SC) GMB 300 mg (N = 117) or placebo (PBO) (N = 120). Certain acute treatments and up to 6 pre-specified preventives were allowed. While the primary endpoint was not met, subgroup analyses investigated potential influences of acute and preventive treatments.

Results: Of the 150 patients who used preventive treatment at BL, 72% used one preventive and 24% used two. Preventive use was stable during treatment with similar frequency between GMB and PBO treatment groups. Verapamil was the most common (50%), then lithium (13%), topiramate (9%), valproate (6%), gabapentin (3%), and melatonin (3%). Pre-specified subgroup analysis for the primary efficacy measure showed no significant subgroup-by-treatment interaction by BL verapamil use (interaction p-value = 0.64), as did a post-hoc subgroup analysis based on any preventive use.

Patients most commonly used SC sumatriptan (62.9%) and oxygen (59.1%) for acute treatment during BL and also in the treatment phase (SC sumatriptan: GMB: 67.5%; PBO: 67.5% and oxygen: GMB: 65.0%; PBO: 53.3%). There were no statistically significant differences between treatment groups for any acute treatment. Post-hoc analysis showed a greater mean reduction in weekly attack frequency for GMB versus PBO in patients with high-frequency (>7 weekly uses) BL SC sumatriptan use compared to low-frequency users (interaction p-value = 0.033).

Overall, GMB-treated patients reported more treatment-emergent adverse events, including injection site erythema (GMB: 7%; PBO: 1%, p = .018).

Conclusion: Oxygen and SC sumatriptan were the most common acute treatments. While up to 6 preventive treatments were allowed, most patients used one preventive, and verapamil was by far the most common choice.

Disclosure of Interest: None Declared

IHC-PO-250**Images portraying headache pain – a tool to aid the diagnosis of cluster headache**

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Objective: We developed a new visual screening tool with images portraying pain with two objectives in mind: (1) to determine how healthy participants rated the pain severity depicted on six images; (2) to test the visual tool on patients with cluster headache (CH) and migraine to determine which image best represented their headache attacks.

Methods: In the first phase of the study, six images portraying people with pain, adapted from real life pictures and online images, were tested on 150 healthy participants to determine that these images depict a range of pain intensity. The healthy participants were asked to rate the images as mild, moderate, severe or excruciating pain. In the second phase, the images were further tested on 116 headache patients (16 patients with CH, 100 patients with migraine). The patients were recruited prospectively from a tertiary headache center at Hull Royal Infirmary (UK) between April-August 2017. The participants were asked to choose which image best illustrated their headache attacks.

Results: The results from the first phase showed that the images represent a range of headache pain severity from mild to excruciating as rated by healthy participants. They rated two images as excruciating, one image as severe, one image as moderate/severe, one image as moderate and one image as mild. In the second phase, there was consensus among patients in the two groups. One of the images depicting excruciating pain was predominantly chosen by both groups of patients.

Conclusion: We developed a screening tool with six drawings depicting headache pain severities from mild to excruciating. This was tested on healthy participants ($n=150$) and on CH and migraine sufferers ($n=116$). The two groups of headache patients chose the same image that represented 'excruciating pain', although the intensity of pain is a key difference between these two conditions. The reason why migraine patients have chosen the image depicting excruciating pain as the most representative for their attacks is not known and will be further explored in a larger follow-up study in which we will also establish the exact potential of the use of images for the diagnosis of CH.

Disclosure of Interest: None Declared

IHC-PO-251**The differences of the clinical features between drinker and nondrinker with cluster headache in Japan**

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Objective: The present study aimed to clarify the alcohol-related clinical features of cluster headache (CH) patients and reveal any features that may be peculiar to the differences of the clinical features between drinker and nondrinker.

Methods: The study population comprised of patients who were diagnosed with CH according to the criteria of the ICHD-3 beta. Data pertaining to the following variables were collected from medical records and/or by patient interview: age; age at onset; sex; body mass index (BMI); type of CH; laterality and sites of headache; pain intensity; autonomic features; additional symptoms (nausea, vomiting, photophobia, phonophobia, feeling of restlessness/restless behavior during attacks); duration of attacks; time of onset of attacks; history of alcohol intake; history of new attack triggered by drinking; and abstinence from alcoholic drinks during cluster period. Pain intensity was estimated using a visual analog scale (VAS).

Results: Out of 131 patients, 33 (25%) patients had no history of alcohol usage. In the study group, the drinkers had a significantly higher proportion of men and BMI as compared to that among the nondrinkers (83% vs. 57% [$p=0.001$] and 22.7 ± 2.7 vs. 21.1 ± 3.3 [$p=0.017$], respectively). Conjunctival injection was significantly more common among drinkers, while nasal congestion, vomiting, and photophobia were significantly less common among drinkers as compared with their incidence among nondrinkers (43% vs. 21% [$p=0.037$], 31% vs. 52% [$p=0.0037$], 11% vs. 30% [$p=0.014$] and 29% vs. 45% [$p=0.008$], respectively).

Conclusion: Our study showed that conjunctival injection was significantly more common among drinkers, while nasal congestion, vomiting, and photophobia were significantly less common among drinkers as compared with their incidence among nondrinkers. Current drink may alter the different response of cranial autonomic reflex between conjunctival injection and nasal congestion.

Disclosure of Interest: None Declared

IHC-PO-252**Post-hoc outcomes from a Phase 3 randomized, double-blind, placebo-controlled study of galcanezumab in patients with episodic cluster headache**

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Objective: Galcanezumab (GMB) previously demonstrated significant reduction in cluster headache (CH) attack frequency for patients with episodic CH. Post-hoc outcomes may further characterize the clinical importance of GMB treatment.

Methods: Study CGAL (NCT02397473) was a Phase 3 randomized, double-blind study of GMB in patients with episodic CH. Patients randomly (1:1) received placebo or GMB 300 mg once monthly during 8-week treatment period. Post-hoc analyses were performed to compare pooled acute medication use frequency (oxygen, subcutaneous sumatriptan, oral/nasal triptans, NSAIDs/acetaminophen) across weeks 1–3 and median time-to-first occurrence of $\geq 50\%$, $\geq 75\%$, and 100% reduction from baseline CH attack frequency. Responder definition of CH attack reduction was estimated using the median CH attack reduction across weeks 1–3 of patients who reported a response of “much better” on the Patient Global Impression of Improvement (PGI-I) at week 4. Responder analyses were subsequently performed.

Results: The weekly frequency of using pooled acute medications was lower across weeks 1–3 for GMB versus placebo (mean difference = -5.52 , 95% CI: -10.01 to -1.02). Time-to-response analyses demonstrate the median time-to-first occurrence of $\geq 50\%$, $\geq 75\%$, and 100% response was approximately 10 days sooner with GMB than placebo. Patients reporting “much better” on the PGI-I experienced a median weekly CH attack reduction of 43% from baseline. Greater proportion of GMB patients achieved this responder definition of 43% reduction across weeks 1–3 versus placebo (odds ratio 2.6, 95% confidence interval: 1.27–5.31).

Conclusion: Post-hoc analyses support the clinical meaningfulness of GMB treatment. Lower frequency of pooled acute medications use, faster median time-to-first occurrence of response rates and a greater proportion achieving a response anchored by patient-reported improvement was observed for GMB compared to placebo.

Disclosure of Interests: D. Kudrow has been an advisory board member for Alder, Amgen, Biohaven, Eli Lilly and Company, and Xoc; a speaker for Amgen, Eli Lilly and

Company, and Teva; and a clinical research investigator for Alder, Amgen, Biogen, Biohaven, Eli Lilly and Company, Roche-Genentech, Teva and VM Biopharma. JSA, MR, CZ, TO, JNB, RW, D. Kuruppu and JM are employees and minor stockholders of Eli Lilly and Company. RR has nothing to disclose.

IHC-PO-253**Reason for consultation to the headache unit: trigeminal neuralgia. but... what was the final diagnosis?**

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Objective: Trigeminal neuralgia (TN) is an overdiagnosed disease due to the ignorance of its criteria and the disorders that make up its differential diagnosis. We analyse the referral requests to our Headache Unit with the epigraph TN as diagnostic suspicion, and we analyse the pathologies with which they were confused. Moreover, we classify the grade of the diagnostic mistake.

Methods: Patients sent to our Headache Unit with the diagnostic suspicion of TN; and final diagnosis applying the ICHD3 criteria. We defined the grade of diagnostic mistake based on three categories (1-point par every category): A. Lack of knowledge of trigeminal anatomy, B. Ignorance of IASP criteria for neuropathic pain, and C. Prescription of ineffective drugs to the true disorder that the patient presented. Classification: mild (1 point), moderate (2 points) and severe (3 points).

Results: We evaluated 963 first consultations (February 2018–February 2019): 226 with the TN heading in the referral request (23.46%). They were sent by general practitioners (GPs)-58% and by neurologists-42%. Correct diagnoses of TN-141 (62.4%) and incorrects-85 (37.6%): neuralgia of other cranial nerves-16, trigeminal autonomic cephalalgias-29, epicranial headaches-16, secondary headaches-19, persistent idiopathic facial pain-5, others-5 (5 patients had two disorders). The mistakes were: mild-25 (29.4%), moderate-52 (61.2%) and severe-8 (9.4%). Mistakes committed by GPs-70 (82.4%), by neurologists-15 (17.6%). Severity: mild: GP-75% / neurologists-25%; moderated: GPs-63.5% / Neurologists-36.5%; and severe: GPs-100%.

Conclusion: One out of every three patients who get to the Headache Unit with the diagnostic suspicion of trigeminal neuralgia does not have it. The percentage of diagnose mistakes, especially the severe, is greater in general practitioners than neurologists. Trigeminal autonomic

cephalalgias, other cranial neuralgias and the new epicranial headaches, are the main confounding factors. We confirm the overdiagnose of trigeminal neuralgia and the need for training in this entity.

Disclosure of Interest: None Declared

IHC-PO-254

Symptomatic SUNA heralding a Lateral Medullary Infarction: A Case of a Sentinel Trigeminal Autonomic Cephalgia

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Objective: Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) is a trigeminal autonomic cephalgia (TAC) presenting as unilateral periorbital pain lasting 1–600 seconds with autonomic symptoms. “Salt and Pepper on the face” was originally described as facial pain preceding or representing medial brainstem ischemia.¹ At least 12 further cases have described facial pain preceding brainstem strokes.^{1–7} SUNA preceding brainstem stroke has not been described, though other TACs associated with brainstem ischemia have been described.^{2,3}

Methods: Case report.

Results: The patient is a 71 year-old male who awoke with right ear fullness, conjunctival injection, periorbital redness, edema, and burning pain. He then experienced recurrent stereotyped paroxysms of severe unilateral (right) peri- and retroorbital pain lasting 10–15 seconds with accompanying right ear fullness and right eyelid trigger zone without a refractory period. Two weeks later, he experienced a right lateral medullary infarction with symptoms and neurological signs consistent with a classic Wallenberg’s syndrome. He continued to experience recurrent episodes consistent with SUNA.

Conclusion: This case illustrates the potential for SUNA to be a sentinel presentation of an impending brainstem stroke. This case is consistent with other symptomatic TACs associated with brainstem ischemia and underscores the importance of a vascular evaluation in elderly patients with vascular risk factors who present with a new onset TAC.

Disclosure of Interest: None Declared

IHC-PO-255

Differences in symptoms exhibited by episodic cluster headache and chronic cluster headache patients during an episode and how family history may affect this.

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Objective: To examine symptoms exhibited by cluster headache (CH) patients during an episode, and the relationship these may have with family history of headache/migraine.

Methods: Results are from the Ipsos Healthcare Cluster Headache Therapy Monitor. Physicians involved in the treatment management of both episodic (ECH) and chronic (CCH) cluster headache patients provided demographic, disease and treatment data on the last cluster headache patients aged over 18 seen in their practice. Data were collected online in EU3 from n=154 Neurologists and n=102 GPs, providing information on 1,432 CH patients [United Kingdom (UK): n=458; Germany (DE): n=450; Spain (ES): n=524].

Results: The number of patients experiencing a symptom during their migraine episode was found to differ; both between ECH and CCH patients, and between those with or without family history of migraine.

The most common symptoms experienced during a migraine episode are consistent across the CH patients sampled. Significantly more ECH patients suffer from Unilateral pain (68% vs 55%), pain centred over one eye (66% vs 52%) and redness in the eye (58% vs 45%), compared to CCH patients. Whereas significantly more CCH patients suffer from other, less common symptoms such as memory loss (14% vs 8%) or depression (21% vs 13%). Certain symptoms present more in patients with family history of headache/migraine. These patients with family history of headaches/migraines are significantly more likely to exhibit redness in eye (57% vs 51%), nausea/vomiting (43% vs 34%), light sensitivity (58% vs 40%), noise sensitivity (44% vs 25%) and depression (20% vs 14%), than those without family history.

Conclusion: This study highlights the symptoms exhibited during a CH episode, how these can vary between ECH and CCH patients and the effect of family history on symptoms exhibited during an episode. The most commonly experienced symptoms are consistent across the CH sample however, differences are seen dependent on patient type. Family history of headache/migraine influences the kinds of symptoms patients exhibit during their episodes.

Factors such as these can influence the treatment decisions of physicians when considering therapies for their CH patients as well as side effects patients experience on certain drug therapies.

Disclosure of Interest: None Declared

IHC-PO-256**Impact of galcanezumab on total pain burden: findings from a Phase 3 randomized, double-blind, placebo-controlled study in patients with episodic cluster headache**

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Objective: A composite measure that incorporates multiple dimensions of pain (severity, duration, frequency) may better characterize the pain burden experienced during a cluster headache (CH) attack. Here, we describe the development and application of total pain burden in episodic CH.

Methods: Study CGAL (NCT02397473) was a Phase 3 randomized, double-blind episodic CH study of galcanezumab (GMB). Patients randomly (1:1) received placebo or GMB 300 mg once monthly for an 8-week (wk) treatment period. Total wkly pain burden was calculated by multiplying three attack quantities measured daily: average duration (hours; hr), number, average pain severity (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain, 4 = very severe pain); and summing these over the days in a wk. Attack pain severity and duration represents the patient's average over 24 hr regardless of acute medication use. Least square (LS) mean change from baseline in total wkly pain burden across wks 1–3 was compared using a post-hoc analysis. Average total wkly pain burden scores across Wks 1–3 were stratified by the Wk-4 Patient Global Impression of Improvement (PGI-I) responses to explore construct validity.

Results: Baseline mean (standard deviation) total wkly pain burden scores were similar for GMB and placebo; 41.5 (39.3) vs. 43.3 (44.0) severity-weighted hr. The LS mean change (decrease) from baseline in wkly total pain burden across Wks 1–3 was 11.18 severity-weighted hr larger for GMB than placebo (95% confidence interval: 0.83, 21.53). Median total pain burden scores across Wks 1–3 increased across the range of PGI-I response options at Wk 4, from 5.0 severity-weighted hr for patients who responded as feeling “very much better”, to 33.6 severity-weighted hr for those who responded as “very much worse”.

Conclusion: Greater total pain burden reduction was seen with GMB treatment. Construct validity was demonstrated but requires further validation. Total pain burden may provide an approach to holistically describe the pain experienced in episodic CH.

Disclosure of Interests: D. Kudrow has been an advisory board member for Alder, Amgen, Biohaven, Eli Lilly and Company, and Xoc; a speaker for Amgen, Eli Lilly and Company, and Teva; and a clinical research investigator for Alder, Amgen, Biogen, Biohaven, Eli Lilly and Company, Roche-Genentech, Teva and VM Biopharma. JSA, MR, TO, JNB, RW, D. Kuruppu and JM are employees and minor stockholders of Eli Lilly and Company. CG has received honoraria for consulting and lectures within the past 3 years from Allergan Pharma, Ratiopharm, Boehringer Ingelheim, Eli Lilly and Company, Novartis, Desitin Arzneimittel, Cerbotec, Bayer Vital, Hormosan Pharma, electroCore, Grünenthal, Reckitt Benckiser, and Teva. He does not hold any stocks of pharmaceutical companies or medical device companies.

IHC-PO-257**Cluster Headache in Kuwait: A Hospital-Based Study**

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Objective: study demographics, clinical characteristics and treatment modalities of CH patients referred to Headache Clinic in Kuwait

Methods: cross-sectional study included all CH patients referred to headache clinic at the tertiary neurology centre in Kuwait in the period between January 2016 to September 2018. The diagnosis of CH was re-challenged and confirmed by headache specialist based on the CH diagnostic criteria of IHS, 3rd edition (ICHD-3-beta). The demographics, clinical characteristics and treatment modalities of CH patients were recorded

Results: 46 patients were diagnosed with CH which constituted (1.7 %) of all headache patients and (0.1 %) of all visits to Neurology clinic. M: F ratio was 15.3:1. Mean age of the patients 40.1 ± 10.7 years and mean age at onset 29 years (20–49). Family history positive in only (6.5%). Smoking seen in (63.0%) of patients while (6.5 %) reported alcohol intake. CH was episodic in (84.4%) and chronic in (15.2%). Seasonal predilection was seen in all our patients; the most frequent season was Autumn (47.8%), followed by Winter (32.6%), Spring (15.2%) and the least frequent was Summer (4.3%). The mean duration of the cluster bouts was 6 weeks (2 to 12 weeks). The mean duration of the attack was 60 minutes (15 to 180 minutes). Number of attacks per day ranged from 2 to 10 attacks with a mean of 5 attacks/day. The median of attack severity by Visual Analog Scale (VAS) was 8.5 (7–10). The time taken to diagnose the patients ranged from 1 year to 12 years with a mean of 4 years. Among autonomic features in patients, tearing was found in (97.8%), conjunctival injection in (95.7%), rhinorrhea and nasal congestion in all

patients. Ptosis and miosis were only found in (21.7 %) patients. Agitation during the attack occurred in (89.1%). Chronic CH was found to have a statically significant relation with smoking ($P=0.036$), older age ($P=0.027$) and longer time taken to diagnosis ($P=0.026$) compared to episodic CH.

Conclusion: Our results coincided with other clinical studies published in many aspects, including the prevalence and clinical characteristics of CH. However, it was different in the highest proportion between men and women and in a less positive family history. Smoking is a significant risk factor for chronicity in patients with CH in addition to advanced age, a higher age at onset of the disease and a longer time of diagnosis.

Disclosure of Interest: None Declared

IHC-PO-258

Exploratory study of the efficacy of oxygen therapy using home oxygen concentrators as abortive therapy of cluster headache

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Objective: Oxygen therapy is most effective established abortive therapy for cluster headache. Oxygen concentrators (OC) can concentrate the oxygen from ambient air by selectively removing nitrogen through filter. We aim to test the efficacy of oxygen concentrators in the patients with episodic cluster headache.

Methods: A total of 6 patients with episodic cluster headache were recruited. Intervention was oral triptans or oxygen therapy based one or two OC through non-rebreathing oxygen mask for 30 minutes at the start of an attack of cluster headache because applied one OC could generate about 90% oxygen at a rate of 5 L/min. We analyzed pain relief (less than 3 out of 10 as visual analogue scales) at 15 minutes, pain free at 15, 30 minutes after the start of treatment based on headache diary.

Results: Among 6 patients, 4 patients treated with OC and 2 did not treated with OC due to the end of cluster

period. Among 20 treatments with two OC in 3 patients, pain relief was recorded in 80%, pain free in 10% after 15 minutes of treatment and pain free was recorded in 55% after 30 minutes of treatment. Among 8 treatments with one OC in 1 patient, pain relief was recorded in 75%, no pain free after 15 minutes of treatment and pain free was recorded in 63% after 30 minutes of treatment. After 22 treatments with oral triptans in 3 patients, no pain relief nor pain free after 15 minutes of treatment and pain free was recorded in 5% after 30 minutes of treatment. The duration of cluster headache was 27.8 ± 5.5 (15–40) minutes after treatment with two OC, 41.9 ± 12.8 (30–60) minutes after treatment with one OC, and 64.1 ± 23.9 (20–120) minutes after treatment with oral triptans. One patient reported no efficacy of OC without written headache diary

Conclusion: In this exploratory study, oxygen therapy with two OC seems to be effective in reduction or cessation of pain of cluster headaches and reducing the duration of cluster headaches. OC can be considered as a safe alternative of oxygen cylinder for cluster headache.

Disclosure of Interests: The study was supported by a grant from Korean Headache Society. No other financial support from the SL medicare company except providing oxygen concentrators during the study period.

IHC-PO-259

a case of secondary cluster headache induced by stenting in a patient with the idiopathic carotid artery vasospasm syndrome

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Objective: We present a case of secondary cluster headache induced by stenting in a patient with the idiopathic carotid artery vasospasm syndrome.

Methods: Case report

Results: A 48year old female had a cluster headache after stenting the carotid artery as therapy for the idiopathic carotid artery vasospasm syndrome. At age 41, she developed hypoesthesia on the left side of the body as the result of cerebral infarction caused by vasospasm of the right carotid artery and underwent stenting of that artery. A week later, she felt tingling sensation on the right side of the head, which spontaneously remitted in three months. She had a nearly identical episode three years later. At age 47, she again developed sensory disturbance with paresthesia on the right arm and scintillation affecting the right visual field. These symptoms improved in several hours

followed by pain, which, originating in the right retro-orbital portion, spread to the entire head. The headache abated by the next day. Magnetic resonance imaging showed cerebral infarction involving the left parietal lobe, and magnetic resonance angiography revealed vasospasm affecting the cervical portion of the left carotid artery. At age of 48, she had the left carotid artery stented at the cervical level. Postoperatively, she developed ptosis and stinging pain in the ipsilateral periorbital area on the left, associated with blurred vision and stuffy nose on day 16 and the first episode of a cluster headache on day 19, which consisted of severe pain at the left retro-orbital portion, accompanied by ipsilateral nasal congestion. The attack, lasting for about 30 minutes, returned almost daily thereafter. A therapeutic attempt with sodium valproate worked well with cessation of further attacks.

Conclusion: The pathophysiology of cluster headache still remains unclear. Previous studies have shown that pain associated with carotid dissection and endarterectomy may mimic a cluster headache. In these cases, injury to the carotid artery may activate the trigemino-autonomic reflex, which, in turn, causes cluster like headache. The present case document that irritation of the carotid artery by stenting can trigger a postoperative cluster headache, providing further evidence for a peripheral cause.

Disclosure of Interest: None Declared

IHC-PO-260

Cluster and Hemicrania Continua like Headaches Secondary to Posterior Scleritis

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Objective: A 49 year old lady presented to emergency department with a 23 day history of new recurrent right orbital pains associated with conjunctival injection, rhinorrhea and lacrimation. She was restless. They occurred 6 times a day and would last for 3 hours each. In addition, there was a constant background right orbital pain.

Methods: Initially, ophthalmology diagnosed posterior scleritis in the right eye and prescribed prednisolone 50 mg with a view of tapering down. Steroids improved her ophthalmic appearances on examination but her headaches continued and so Neurology reviewed. It was felt her headaches were cluster like episodes precipitated by the posterior scleritis. Oxygen therapy was helpful but subcutaneous sumatriptan did not bring any relief. Verapamil was started. For the constant right sided background pain, indomethacin was started.

Results: An MRI scan of the brain with contrast showed enhancement of the right posterior sclera in keeping with

scleritis. Blood tests for autoantibodies, Toxoplasma, Syphilis and CMV were all negative.

Two months later, she continued to have daily cluster like headaches despite long term steroids and verapamil. Home oxygen therapy was arranged as it continued to be helpful. Weaning from the steroids did cause a recurrence in her headaches as well as a deterioration in her episcleritis clinically. For the ongoing severe scleritis she was referred to the Rheumatologists and received cyclophosphamide infusion. Eventually, the headaches did stop. Weaning off the verapamil did not cause a recurrence of her headaches. Any reduction of indomethacin or any omission of her indomethacin would cause a recurrence of her headache. She appeared to have 2 different types of headaches (cluster like and hemicrania continua like) which responded to their specific treatments.

Conclusion: To our knowledge there is only one other report in the literature who described cluster like headaches caused by posterior scleritis (Choi et al., 2009). The current case is unusual in that there is both cluster like and hemicranias continua like characteristics. The cluster like episodes were responsive to oxygen and steroids but unresponsive to sumatriptan and verapamil. The unilateral continuous headache did respond to indomethacin and recurred on its withdrawal.

Disclosure of Interest: None Declared

IHC-PO-261

Neurofibroma causing Secondary SUNCT syndrome

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Objective: Short-lasting Unilateral Neuralgiform headache with Conjunctival injection and Tearing (SUNCT) syndrome is a rare headache disorder classified under the category of Trigeminal Autonomic Cephalalgias.

Most cases of SUNCT is idiopathic but rare secondary cases have been reported due to posterior fossa vascular aetiology and pituitary tumours.

We present an update on a gentleman who originally presented with secondary SUNCT related to nerve sheath tumours in the right pterygopalatine fossa and behind the right maxillary sinus. This tumour was later histologically confirmed to be a neurofibroma

We believe this case raises the importance of investigation in any SUNCT syndrome. This case report will also discuss the current management guidelines on nerve sheath tumours, a neurological topic which is sparsely covered.

Methods: We present a patient with this condition, including his journey from first diagnosis, eventual brain imaging and his management plan, 2 years after he was first presented including the biopsy results.

Results: N/A

Conclusion: Secondary SUNCT is a very rare condition which can be easily overlooked. It is important to following the local and national guidelines on investigations and management. We will talk about the latest guidelines in our presentation.

Disclosure of Interest: None Declared

Comorbidity of Primary Headaches

IHC-PO-021

Effect of sleep quality on migraine treatment outcome: a longitudinal follow-up study

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Objective: Sleep disturbance is a common comorbidity of migraine. It is known that poor sleep quality is associated with a higher headache frequency and severity. However, there is no prospective study to test the effect of sleep quality on the treatment outcome of migraine.

Methods: In this longitudinal study, we recruited new patients with migraine in the Samsung Medical Center between October 2015 and May 2018. Patients were prospectively followed-up using a structured follow-up questionnaire at 1 month and 3 months after the baseline visit. Sleep quality was assessed using the global Pittsburgh Sleep Quality Index (PSQI) score. We performed a mixed model to test the longitudinal association of the baseline sleep quality and changes of monthly headache days. Age, sex, BMI, caffeine consumption, preventive medication, depression, and anxiety were considered as covariates.

Results: A total of 498 patients (304 episodic migraine and 194 chronic migraine) were included in this study. The mean global PSQI score was 9.0 ± 3.7 , 8.2 ± 3.3 , 10.2 ± 4.0 in total, episodic and chronic migraineurs, respectively. In patients with episodic migraine, a global PSQI score was associated with higher headache frequency and a significant negative interaction with time on the change of monthly headache days (interaction coefficient = -0.216 , SE = 0.092 , p for interaction = 0.021). In contrast, a positive interaction between global PSQI and time was found in patients with chronic migraine (interaction coefficient = 0.355 , SE = 0.173 , p for interaction = 0.041).

Conclusion: In this longitudinal study, impact of sleep quality on treatment outcome differed according to migraine subtype (episodic vs. chronic). The poor sleep

quality was associated with the higher headache days at baseline but more rapid reduction of headache days in patients with episodic migraine, suggesting a reversible association between sleep and headache. In contrast, poor sleep quality has further deteriorating effects on treatment outcome in patients with chronic migraine. The effect of sleep on hypothalamic modulation may differ between episodic vs. chronic migraine, warranting a different treatment strategy.

Disclosure of Interests: This study was supported by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (Nos. 2017R1A2B2009086 and 2017R1A2B4007254).

IHC-PO-022

Photic allodynia as a potential marker of severity in chronic migraine

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Objective: Allodynia pain from a normally non-noxious input is common in migraine. When discussed it is generally in the context of tactile allodynia. Here we explore phenotypic associations of head pain being worsened by light: photic allodynia.

Methods: The clinical characteristics of chronic migraine patients with photic allodynia ($n=23$) were reviewed. Patients were age and sex matched with a group of chronic migraine patients ($n=23$) who had neither photic allodynia nor photophobia. Statistical analyses included paired Student t test, Wilcoxon signed-rank test and Pearson correlation coefficient as appropriate.

Results: Disease duration was more in the photic allodynia group (median difference: 12 years; $p=0.018$) with an earlier age of onset. Patients with photic allodynia reported more associated symptoms such as cutaneous allodynia ($r=0.563$; $p<0.001$), phonophobia ($r=0.661$; $p<0.001$), osmophobia ($r=0.458$; $p=0.002$), visual blurring ($p<0.001$; $r=0.590$), movement sensitivity ($p<0.001$; $r=0.531$) and vomiting ($r=0.341$; $p=0.031$). Overall, aura ($p=0.017$), premonitory ($p=0.04$) and cranial autonomic symptoms ($p=0.032$) were more represented in the photic allodynia group, in which the consumption of triptans was comparatively higher.

Conclusion: Patients with photic allodynia had had attacks for longer and had a richer phenotype compared to chronic migraine patients without photic allodynia. The presence of allodynia other than the cutaneous form in

these patients supports the idea of a multisensory sensitization and, specifically, photic allodynia, as a marker of migraine severity.

Disclosure of Interest: None Declared

IHC-PO-023

Calcitonin Gene-related Peptide on the arterial vasodilation in the eye: implications for retinal ischemia

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Objective: CGRP is a peptide with strong vasoactive effects. We have previously shown that the ocular vasculature responds to exogenous CGRP, leading to changes in retinal function and increased photosensitivity. Retinal ischemia is a leading cause of blindness and visual impairment. With the known role of CGRP in ischemia, and increasing number of migraine patients being treated with blockers of the CGRP pathway, it is important to understand the significance of CGRP modulation in relation to ischemic disorders. We aimed to determine whether applying exogenous CGRP or the CGRP blocker olcegepant will affect retinal function following ischemia.

Methods: Vasoconstrictive peptide endothelin-I (ET-I) was injected intravitreally to create a translatable model of retinal ischemia. The eyes were pre-treated with intravitreal CGRP, subconjunctival CGRP or intravitreal olcegepant. Retinal ischemic outcome was monitored by electroretinogram (ERG).

Results: On day 21, photoreceptor activity, represented by the A-wave amplitude, showed significant functional deficit when comparing ET-I induced ischemic eyes to the control eyes. In relation to retinal function, adding CGRP intravitreally or topically had a strong protective

effect. Importantly, pretreatment with intravitreal or topical CGRP greatly reduced the damage to photoreceptors (A-wave amplitude) and bipolar cells (B-wave amplitude), compared to ET-I ischemic eyes at day 21. Applying the CGRP receptor inhibitor Olcegepant did not affect the ET-I induced damage on day 21, when comparing either A-wave amplitude or B-wave amplitudes to the ET-I ischemic eyes.

Conclusion: Both intravitreal and subconjunctival applications of CGRP to rat eyes resulted in dilation of the ciliary artery. Furthermore, pre-treatment with CGRP reduced the ET-I induced ischemic retinal damage. The data show that CGRP has protective effect on ischemia damage when applied exogenously and that exogenous CGRP in patients could be used as a treatment to improve retinal function. Regarding blockage of CGRP receptors, it does not appear that endogenous retinal CGRP is an important mechanism normally used by the retina to reverse ischemic damage, as blocking the CGRP receptor *per se*, did not affect retinal ischemic outcome.

Disclosure of Interest: None Declared

IHC-PO-024

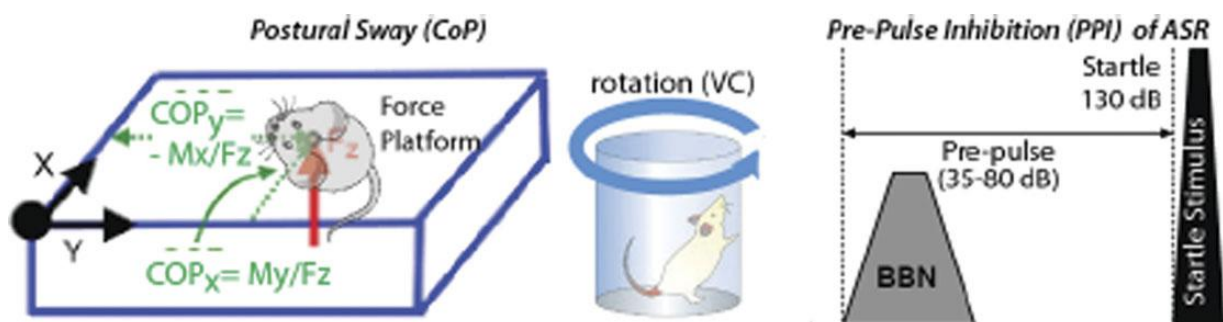
Systemic injection of CGRP increases postural sway and auditory sensitivity in mice

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Objective: About 42% of people with migraine have a vestibular component causing balance problems and dizziness, termed vestibular migraine (VM). In fact, VM is a major cause of vertigo in dizziness clinics and is estimated to affect 1% of the overall population. The most common symptoms of VM were unsteadiness and balance disturbances. When balance disturbances were quantified, VM patients swayed more than migraine-only or healthy controls when challenged. In addition, patients with migraine,



Abstract number: IHC-PO-024

exhibit heightened (phonophobia) or extreme sensitivity (hyperacusis) to sound. Behavioral evidence of hyperacusis and phonophobia in mice can be inferred from pre-pulse inhibition (PPI) of the acoustic startle reflex (ASR).

Methods: We studied 40 wildtype C57BL/6J (JAX 664) mice (20F/20 M). For postural sway or center of pressure (CoP) testing, mice were placed on force plate (AMTI Biomechanics) and we recorded forces for 1 sec, with measurements repeated 12 times. We also obtained CoP measurements after a brief 30-sec vestibular rotation (125 rpm), and repeated testing. For PPI/ASR testing, we determined target reception thresholds in dB for prepulse inhibition (that gives $A' = .75$ or 50% inhibition) for each animal. One week after initial testing, the same mice were systemically injected IP with 0.1 mg/kg rat α -CGRP (Sigma) and weresubjected to the same postural sway and ASR/PPI procedures.

Results: We determined that female mice swayed more than male mice after a vestibular rotation as well as after a systemic CGRP injection (2-fold increase in CoP area). In addition, both male and female mice were more sensitive to sounds (5 dB SPL) after a single systemic CGRP injection.

Conclusion: In conclusion, systemic CGRP injection increased both motion sensitivity (as measured by postural sway) and sound sensitivity (as measured by ASR/PPI). Experiments are underway to determine what effects systemic-delivered CGRP antagonists and triptans may have on these CGRP-induced sensitivities.

Disclosure of Interests: Research supported by NIH R01 (AL) and grants from the Kearns Center and Discovery grants (University of Rochester)

IHC-PO-025

Effect of sleep quality on headache-related impact in primary headache disorder

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Objective: Sleep disturbance is common in patients with primary headache disorders. We questioned if poor sleep quality could affect patients directly or by increased frequency and severity of headaches. In this study, we investigated direct and indirect effects of sleep quality on headache-related impact among patients with primary headache disorders. Poor sleep quality can directly increase headache-related impact in patients with migraine and tension-type headache. Proper management of sleep

problems is required to reduce the impact of headache among these patients.

Methods: We analyzed patients with migraine and tension-type headache using the prospective first-visit headache registry of the Samsung Medical Center headache clinic from January 2015 to May 2018. All patients completed the interview and questionnaire that recorded the monthly headache days, severity, and psychological status. Sleep quality and headache-related impact were measured using the Pittsburgh sleep quality index and headache impact test-6 score, respectively. We performed path analyses using headache days and severity as covariates to determine the direct effect of sleep quality on headache-related impact and indirect effects mediated by increased headache days and severity.

Results: A total of 915 (784 with migraine and 131 with tension-type headache) patients were included in the analysis. Sleep quality was independently associated with headache-related impact in both patients with migraine ($\beta = 0.146$, $p = 0.001$) and those with tension-type headache ($\beta = 0.217$, $p = 0.006$). Path analysis revealed a direct effect (standardized $\beta = 0.207$) of sleep quality and indirect effect mediated by headache days and severity (standardized $\beta = 0.067$) on headache-related impact in patients with migraine. In patients with tension-type headache, only direct effects of sleep quality on headache-related impact were significant (standardized $\beta = 0.224$).

Conclusion: Poor sleep quality can directly increase headache-related impact in patients with migraine and tension-type headache. Proper management of sleep problems is required to reduce the impact of headache among these patients.

Disclosure of Interests: This study was supported by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (Nos. 2017R1A2B2009086 and 2017R1A2B4007254).

IHC-PO-026

Contrast threshold at 15 Hz correlates with key symptoms of visual snow syndrome and is able to confirm the diagnosis in individual patients

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Objective: Patients with visual snow syndrome (VSS) suffer from a continuous TV snow-like visual disturbance (VS) in the entire visual field and additional visual symptoms including palinopsia that both might reduce contrast sensitivity. So far, VSS is a pure clinical diagnosis. Objective

measures are needed to confirm the diagnosis in clinical practice. Here, we investigated whether the threshold for detecting visual contrasts is increased in patients with VSS and if this allows confirming the diagnosis in the individual patient. In a second step, we tested the hypothesis that the contrast threshold correlates with specific clinical characteristics of VSS, namely the density and speed of VS and the presence of palinopsia.

Methods: Twenty patients with VSS were compared to 20 age-, gender-, migraine- and aura-matched controls. Ordinal scales were used to assess VS density (7 point) and speed (5 point). Palinopsia was coded binary. Subjects were randomly presented vertically left or right tilted bars, at different contrasts, and flickering at four different frequencies (15Hz, 20Hz, 25 Hz, 30 Hz). The contrast threshold was measured in a two-alternative adaptive forced-choice procedure (QUEST) for the discrimination between the two image orientations. The threshold was defined as the log10 (Michelson-Contrast) necessary to achieve the correct response in 75% of the cases.

Results: The 75% contrast threshold at 15 Hz was higher in VS patients (Mann-Whitney-U: median (p25;p75) -1.94 (-1.84 ; -1.99) vs. -2.14 (-1.95 ; -2.6); $p=0.012$, Bonferroni-corr.: $p=0.048$). The AUC for the ROC curve of 75% contrast threshold at 15 Hz was 0.73 ± 0.09 . A contrast threshold of -2.00 was able to support the diagnosis of VS in an individual patient with a sensitivity of 80% and a specificity of 70%. The contrast threshold correlated with VS density ($r=0.36$, $p=0.027$), VS speed ($r=0.44$, $p=0.006$, spearman-rho), and presence of palinopsia (Mann-Whitney-U: $p=0.025$).

Conclusion: In individual patients, the 75% contrast threshold at 15 Hz might be the first technical test confirming the hitherto purely history-driven diagnosis of VSS. The dependence of contrast threshold on key symptoms of VSS suggests that the test validly measures VSS.

Disclosure of Interests: Supported by Federal Ministry of Education and Research, Baasch Medicus Foundation, German Migraine and Headache Society, Eye on Vision Foundation.

IHC-PO-027

Pilot Exploration of migraine aura characteristics in patients with ischemic strokes

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Objective: There is an association between migraine aura and stroke. It is unknown if certain aura characteristics portend a higher risk for stroke. This study describes migraine aura characteristics in patients with migraine

with aura and ischemic stroke to address the current literature gap.

Methods: From a pilot 10-year retrospective chart review of 46,689 Mayo Clinic patients with migraine with aura, 30 patients were selected via simple random selection with stratification on stroke status, age, and sex. Demographics and clinical characteristics were compared between migraine with aura patients who had stroke (MwA + S) and those who did not (MwA) using Wilcoxon rank sum test or Fischer's exact test. All hypotheses were two-sided with $p < 0.05$ considered statistically significant.

Results: There was no difference in migraine features between groups though a trend toward increased photophobia, phonophobia and osmophobia was seen in MwA + S. For visual aura (83.3%), 44% reported positive symptoms, 32% negative, and 24% a combination with no difference between groups including aura description. 69.2% of MwA patients had vague blurry vision compared to 50% of MwA + S patients. For sensory aura (36.7%), 18.2% reported positive symptoms, 63.6% negative, and 18.2% a combination. Other types of aura were the same between groups: 16.7% language, 16.7% brainstem, and 13.3% hemiplegic. Aura frequency in the full cohort was 4.3 days per month with a mean duration 324 h and median 30 h. Three patients reported aura change in the 4 weeks prior to stroke onset including change in aura type or description, new onset aura, and increased frequency. Triptans were used in 20% ($n=3$) of MwA versus 40% ($n=6$) of MwA + S ($p=0.4270$). Substance use (marijuana, cocaine and methamphetamine) was only seen in MwA + S ($n=2$). Sleep apnea was only seen in MwA + S ($n=4$). There was no significant difference in other stroke risk factors between groups.

Conclusion: The data demonstrate several trends that may be clinically meaningful if looked at in a larger analysis and warrants further study. There is a trend toward higher likelihood of stroke with more migraine features, substance use, and sleep apnea. Three patients experienced change in aura in the 4 weeks prior to stroke.

Disclosure of Interest: None Declared

IHC-PO-028

Relations between left temporal lobe epilepsy and headache

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Objective: The relationship between epilepsy and headache remains controversial. Ictal pain is one of several types of somatic sensation felt during a partial seizure. The aim of this study is to estimate the prevalence and electroencephalographic features of headache cases.

Methods: This is a descriptive, retrospective study from medical record of patients with headache who underwent electroencephalography (EEG) in Airlangga University Hospital, Surabaya Indonesia from 2015 to 2018.

Results: Out of 30 patients, 46.67% had abnormal EEG results. 10 of 14 EEG results show a potential epileptogenicity in the left temporal region (71.43%). From brain imaging of these patients, there are no abnormalities in the left temporal region. "Epileptic headache" appears to be an appropriate term to clearly define the phenomenon of an epileptic (EEG-confirmed) manifestation, clinically represented by headache. Left temporal lobe epilepsy may also be presented with somatosensory seizure include headache.

Conclusion: Headache can be ictal symptoms of left temporal lobe epilepsy. Epileptic pain is usually associated with other seizure symptoms, but sometimes it could be the sole manifestation of epilepsy. Therefore, headache is often misdiagnosed and patients go through unnecessary diagnostic procedures before the correct diagnosis is made. EEG is mandatory in those case presenting with refractory headache, if epilepsy is suspected.

Keywords: Temporal lobe epilepsy, Headache, Ictal, Electroencephalography

Disclosure of Interest: None Declared

IHC-PO-029

Restless legs syndrome predicts headache-related disabilities in patients with migraine: a prospective 7-year follow-up study

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Objective: To prospectively evaluate the impact of restless legs syndrome (RLS) on headache-related disability in migraine patients.

Methods: A total of 101 patients with migraine who were evaluated for RLS twice at 7-year intervals in a university hospital setting were included in this study. RLS group was defined as positive for RLS at either baseline and follow-up, and non-RLS group was defined as negative for RLS at both baseline and follow-up. The Migraine Disability Assessment (MIDAS) questionnaire, Beck Depression Inventory (BDI)-II, Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS) were administered to all patients.

Results: The RLS prevalence was 16.8% at baseline and 20.8% at follow-up. Compared to non-RLS group (n = 27), RLS group (n = 74) showed significantly higher rate of

smoking and higher scores of MIDAS and BDI-II at 7-year follow-up. A significant reduction in scores of MIDAS and BDI-II at 7-year follow-up compared with those at baseline was observed in RLS group, but not non-RLS group. Non-RLS group showed a significantly lower MIDAS score at 7-year follow-up compared with RLS group, after adjusting for confounding variables such as age, gender, smoking status, ESS, and PSQI, using analysis of covariance.

Conclusion: RLS had a significant impact on headache-related disability in migraine patients.

Disclosure of Interest: None Declared

IHC-PO-030

Motor control reactions and balance sensorial organization of patients with migraine

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Objective: To assess the balance and postural reactions of patients with migraine.

Methods: Ninety women with migraine aged between 18 to 55 years were recruited from a tertiary headache clinic in Brazil and divided into three groups according to migraine subtype: with aura (MA), without aura (MoA) and chronic migraine (CM). Thirty headache-free controls were also recruited. They performed the Sensory Organization Test (SOT) and the Motor Control Test (MCT) in the Equitest System[®], guided by a blinded examiner. For the SOT, patients were assessed in six balance conditions, resulting in scores of the individual contribution of the vestibular, visual and somatosensory systems to patients' balance, ranging from 0 to 100. For the MCT, the latency to react from a platform sway (milliseconds) was measured in six conditions: small, medium and large platform excursion forwards (FS, FM and FL) and backwards (BS, BM and BL). A composite score of both tests was calculated and groups were compared using ANOVA with Bonferroni corrected *post-hoc* tests, in SPSS 21.0, at $\alpha = 5\%$.

Table 1. Mean and SD of the Sensorial Organization Test (SOT, score 0-100) and Motor Control Test (MCT, latency ms) among migraineurs and controls.

		CG	MoA	MA	CM
SOT	Somatosensory	97.9 (1.8) [#]	96.6 (2.9)	93.4 (6.8)	95.7 (4.7)
	Visual	89.6 (6.7) [*]	83.2 (12.1)	68.6 (18.7)	71.9 (18.0)
	Vestibular	75.9 (7.5) [*]	67.3 (11.0)	55.7 (14.5)	58.4 (15.7)
	Composite	82.4 (4.22) ^{**}	76.5 (6.6)	66.4 (9.4)	69.1 (10.0)
MCT	BS	133.8 (14.4)	129.7 (16.9) ^{##}	142.8 (21.3)	137.3 (20.0)
	BM	124.8 (10.2) [#]	129.8 (10.1)	138.0 (27.6)	130.8 (13.8)
	BL	122.7 (12.4) [#]	125.6 (18.1)	130.0 (18.1)	124.7 (12.9)
	FS	142.5 (15.9)	149.0 (23.4)	159.0 (36.0)	149.7 (17.2)
	FM	133.5 (10.3) [#]	140.0 (21.7)	150.0 (27.7)	141.0 (17.0)
	FL	126.0 (11.4)	132.3 (15.3)	135.5 (17.8)	128.5 (13.7)
	Composite	126.7 (8.5) [#]	132.0 (12.3)	138.4 (18.2)	131.3 (11.9)

^{**}CG vs. MoA, MA, CM, $p < 0.02$; [#]CG vs. MA, $p < 0.001$; ^{*}CG vs. MA, CM, $p < 0.0001$; ^{##}MoA vs. MA, $p = 0.04$.

Abstract number: IHC-PO-030

Results: Somatosensory SOT scores were lower in MA compared to controls ($p = 0.001$). Visual and vestibular scores were lower in MA and CM groups compared to controls ($p < 0.0001$). However, SOT composite scores were lower in all migraineurs ($p < 0.02$). In the MCT test, MA had a greater composite score than controls ($p < 0.0001$) and they took more time to react after the platform perturbation in the situations BM, BL, FM ($p < 0.0001$). No differences among migraine groups were verified, except in the situation BS, where MA patients exhibited greater latency than MoA ($p < 0.04$) (Table 1).

Conclusion: Patients with migraine, especially with aura and chronic migraine, exhibited balance changes due to impairment mainly of the vestibular and visual systems. Patients with migraine with aura present an impairment of the postural responses after ground perturbations compared to controls.

Disclosure of Interest: None Declared

IHC-PO-031

Visual Snow syndrome: comparison between an Italian and English population

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Objective: Patients with Visual Snow (VS) suffer a pan-field, dynamic visual disturbance described as continuous TV-static-like tiny flickering dots. Current diagnostic criteria require at least two additional visual symptoms from: palinopsia (afterimages and trailing), entoptic phenomena (floaters, blue field entoptic phenomenon, photopsia, self-light of the eye), photophobia and nyctalopia. Migraine and tinnitus are common comorbidities of visual snow, reported in up to three-quarters of patients. Our objective was to compare the phenotype of VS in an Italian and British population.

Methods: VS patients were characterized clinically with regards to the current criteria (Schankin 2014). An online survey was prepared in collaboration with the patient group Eye-on-Vision. Patients were directed to the site after they contacted us by email asking to be involved in research. The study was approved by the KCL Research

	UK (n=100)	IT (n=100)	p
Female	52	53	0.88
Age	30 ± 10	32 ± 10	0.09
History of disease			
Sudden onset	32	51	0.009
VS age of onset	24 ± 10	22 ± 10	0.44
Disease years	19 ± 14	15 ± 14	0.09
Visual Snow Type			
Black and white	65	58	0.30
Black and white coloured	40	43	0.01
Flashing	50	44	0.39
Transparent	41	54	0.06
Number of Visual Snow types	1.96 ± 1.1	1.79 ± 1.1	0.28
Visual Snow Symptoms			
Afterimages	83	70	0.30
Trailing	66	53	0.06
Blue field entoptic phenomenon	78	76	0.73
Floaters	83	93	0.03
Self-light of the eye	70	65	0.45
Flashes (spontaneous photopsia)	70	52	0.009
Nyctalopia	80	76	0.49
Photophobia	75	87	0.03
Tinnitus	79	63	0.01
Number of Visual Snow symptoms	6.0 ± 1.6	5.9 ± 1.8	0.63
Medical History			
Migraine	68	70	0.84
Previous use of recreational drugs	26	21	0.40

Table. Demographical and clinical data of two populations of patients affected by visual snow syndrome: 100 patients from United Kingdom (UK) and 100 patients from Italy (IT). UK patients were matched for gender and age with our Italian sub-population. Due to multiple testing over nineteen variables, adjusted p-values based on the Bonferroni correction were considered. The significance level was therefore lowered to $p < 0.0025$ ($p=0.05/20$).

Abstract number: IHC-PO-031

Ethics Panel. Following data collection, we compared the phenotypic characteristics of British versus Italian patients. As we expected more responses from the UK, we matched one-hundred UK patients for gender and age with our Italian sub-population. Due to multiple testing over twenty variables, adjusted p-values based on the Bonferroni correction were considered. The significance level was therefore lowered to $p < 0.0025$ ($p = 0.05/20$).

Results: Patients were enrolled from the UK ($n = 100$) and Italy (IT) ($n = 100$). Table shows demographical and clinical data. The distribution of the variables was similar between two groups.

Conclusion: This is the first study comparing the phenotype of VS syndrome in two distinct populations. Our findings suggest that the visual snow phenotype, as well as migraine comorbidity, is similar across the two groups.

Disclosure of Interest: None Declared

IHC-PO-262

The presence of neck pain does not change the cervical range of motion in patients with episodic migraine

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Objective: To investigate the global active range of motion (ROM) of the cervical spine in individuals with neck pain, with episodic migraine, with both pain conditions and healthy individuals without neck pain and episodic migraine.

Methods: We evaluated 100 women divided into 4 groups: control (28.5 years old; SD: 7.2), neck pain (32.9 years old; SD: 10.2), episodic migraine without neck pain (33.4 years old; SD: 10.5) and episodic migraine with neck pain (28.9 years old; SD: 4.1). Women with episodic migraine were diagnosed according to the International Classification of Headache – 3rd edition. Neck pain was assessed by reporting neck pain for more than 3 months and intensity ≥ 3 on the numerical scale of pain. The global active cervical ROM was assessed using a cervical range of motion device (CROM[®]). Total ROM was compared among groups by the one-way ANOVA and the Bonferroni post-hoc tests, adopting a significance level of 0.05. This study was approved by the local ethics committee (No 1100/2017).

Results: Reduced active cervical ROM was observed in the neck pain group compared to the control group and to the migraine group with neck pain for extension (control: 81°, neck pain 65°, migraine with neck pain: 76°, $p = 0.002$) and for left rotation (control: 74°, neck pain: 65°, migraine with neck pain: 70°, $p = 0.001$). For the right lateral flexion, neck pain group differed only from controls (control: 50°, neck pain: 43°, $p = 0.019$). For the right rotation the control group presented greater ROM than the neck pain and migraine groups with and without neck pain (control: 72°; neck pain: 65°; migraine without neck pain: 68°, migraine with neck pain 68°, $p < 0.000$).

Conclusion: The coexistence of neck pain in individuals with episodic migraine may not be associated to a lower cervical ROM as observed in individuals with only neck pain.

Disclosure of Interest: None Declared

IHC-PO-263

Morning Tension Type Headache and Orofacial Pain in Patients with Temporomandibular Disorders: Dental, Neurologic or Infectious Problem?

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Objective: Orofacial pain (OP), temporomandibular disorders (TMDs) and tension type headache (TTH) are common problems found in 17–80 % of general population. TTH may originate from pericranial muscles and

may be experienced with other phenomena as tinnitus and vertigo. There is an evidence for increasing prevalence of Lyme disease (LD). The aim of the study was to assess the coexistence of morning TTH with various forms of OP, tinnitus, vertigo, tooth substance loss and LD.

Methods: A group of morning TTH patients (N = 52) was selected out of 200 patients with TMDs. Subjects were examined clinically, radiologically and laboratory tests were performed. Patients with confirmed radiologic reasons for headaches, tinnitus, vertigo were excluded from the study. Subjects with TTH in temporal/frontal area were ascribed to GROUP A (anterior TTH, nA = 13), with TTH in occipital or parietal area to GROUP P (posterior TTH, nP = 12), with both posterior and anterior TTH to group AP (nAP = 27). A coexistence of different kinds of orofacial pain, tinnitus, vertigo, dental substance loss and the presence of morning TTH was analyzed and the coexistence probabilities were calculated. Statistical analysis was based on binomial distribution, probability, χ^2 tests. Confidence interval (CI) was set on 95% and 99%.

Results: Six highest probability scores of TTH coexistence were found in the group AP: for the jaw pain/discomfort $p = 0,48$, rest and orthostatic vertigo $p = 0,26$, low pitch tinnitus $p = 0,3$, high pitch tinnitus $p = 0,26$, posttraumatic neuropathic pain $p = 0,22$, tick bite $p = 0,52$). In the group P the highest probability of coexistence with TTH was found for orthostatic vertigo $p = 0,6$, low and high pitch tinnitus $p = 0,17$, persistent idiopathic facial pain $p = 0,17$ and tooth substance loss $p = 0,42$. In group A the only parameter with highest coexistence probability was rest vertigo $p = 0,38$. Interestingly, the probability of previous tick bite in groups with the highest aforementioned scores for all kinds of tinnitus, vertigo and neuropathic pain was at least 50%.

Conclusion: The results may support the need for an extended evaluation in patients with TTH, with a special emphasis on neurologic signs and neuroinfections, particularly in patients with diffuse form of TTH. The limitation of the study is a relatively small number of patients.

Disclosure of Interest: None Declared

IHC-PO-264

Primary headaches in epilepsy outpatients clinic

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Objective: To determine the prevalence of primary headaches in patients from an epilepsy clinic. As secondary objectives we analyzed demographic and headache or epilepsy-related characteristics.

Methods: 65 patients were reviewed, using their clinical visits and medical history. The period of recruitment was 3 months in a row.

IHS and ILAE classification were used to diagnosed patients.

Results: Prevalence of primary headaches was 28% (migraine 18%, tension-type headache 6%, primary stabbing headache 4%). Median age was 41 years old (16–68). All of the patients were females. The most frequent epilepsy type was idiopathic focal epilepsy (55%) and idiopathic generalized epilepsy (33%) with 13 years after diagnosed of epilepsy. One patient was finally diagnosed of non epileptic seizures. According to seizures classification, focal onset to bilateral tonic-clonic were 55.5% followed by focal onset seizures (38%). 89% suffered from impaired awareness. Most of the patients were seizure free for more than a year. 33% suffered from anxiety-depressive disorders.

According to headaches, episodic headaches were more frequent (83%) than chronic ones (17%). We found no abuse related headaches and only 16% were using a headache preventive treatment (amitriptyline). Only 58% of migraine patients used triptanes for symptomatic treatment and there were only one patient who was treated with onabotulinumtoxinA.

Conclusion: As we can see, headaches in special migraine is as prevalent in epilepsy patient as in general population or even more. We analyzed patients from an epilepsy clinic, who are usually more treated than epilepsy patients that are followed in general neurology clinics. They also use to have more comorbidities than healthy people, such as affective disorders.

Headaches need to be diagnosed and treated in epilepsy patient, in special drug-resistant epilepsy, because they can worsen quality of life and make epilepsy control worse. Further studies need to be done.

Disclosure of Interest: None Declared

IHC-PO-265

Electroencephalogram pattern in Migraine

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Objective: Migraine is a common primary headache disorder, ranked as the second most disabling disorder worldwide and associated with a variety of electroencephalographic pattern. Lack of evidence supporting relationship between migraine and epilepsy as paroxysmal brain disorder. Most guidelines stated that the use of electroencephalography (EEG) in routine diagnosis of migraine was questioned. Insufficient evidence supporting the utility of EEG, even in migraine with brainstem aura and hemiplegic migraine. This study aims to evaluate EEG pattern in migraine patients diagnosed by the International Classification of Headache disorder 3rd edition.

Methods: Descriptive, retrospective study from medical record of migraine patients who underwent EEG in Airlangga University Hospital, Surabaya Indonesia (December 2016–December 2018).

Results: There were 19 migraine patients who underwent EEG. Abnormal EEG results in 42.11% patients with 5.26% migraine without aura; 5.26% migraine with aura; 26.31% migraine with brainstem aura and 5.26% chronic migraine. Normal EEG results in 57.89% migraine patients with 15.79% migraine without aura; 5.26% migraine with aura; 31.58% migraine with brainstem aura and 5.26% chronic migraine. The abnormal EEG patterns were shown mainly in temporal lobe. Migraine like headaches are quite frequently seen in the epileptic post-ictal period, sometimes a seizure occurs during or following a migraine attack.

Conclusion: EEG appears to be useful in distinguishing between migraine subtypes and epileptic seizures. There were relationships between temporal electroencephalographic patterns and epileptic seizures in migraine, specifically before, during, after or interposed between the epileptic episodes. The clinical criteria, sometimes, are not conclusive therefore ictal EEG could be assessed epileptic origin of aura symptom. Keywords: Migraine, Electroencephalographic pattern, EEG

Disclosure of Interest: None Declared

IHC-PO-266

Effect of smartphone use on primary headache: A cross sectional study

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Objective: The aim of this study was to assess if smartphone usage is associated with occurrence of new onset headache or increase severity in adults with primary headache.

Methods: This was an observational cross-sectional study conducted over 18 months (June 2017 to December 2018) at a tertiary care center in New Delhi, India. The inclusion

criteria were age ≥ 14 yrs, new onset headache of at least 3 months duration or worsening of primary headache. Patients with secondary headache were excluded. Patients were divided into 2 groups; smartphone users (SU) and non-smartphone users (NSU). SU were further categorized into low smartphone (LSU) and high smartphone users (HSU) as per Smartphone addiction questionnaire based on DSM V criteria for substance use disorder. The primary objective was whether smartphone usage is associated with new onset headache or increase severity of primary headache. New onset headache secondary to smartphone usage was defined as primary headache becoming chronic or getting significantly worse. The secondary objective was whether smartphone use is associated with increased requirement of acute medication and prophylaxis.

Results: 400 patients were included in study out of which 206 were smartphone users (SU) and 194 were non-smartphone users (NSU). Out of 206 SU 76 were LSU and 130 were HSU. Episodic followed by chronic pattern was reported by 41 (21.1%) NSU compared to 39 (18.9%) in SU which was not statistically significant. Also, there was no significant difference in the number of patients complaining of worsening of headache [NSU:139 (71.6%) vs SU:148 (71.8%) p value:0.96]. SU had significantly longer duration of headache episode and clustering of attacks compared to NSU group [NSU:37 (19.1%) vs SU:64 (31.1%); p value:0.006]. There was no difference in frequency of episodes per month, mean HIT6 (Headache Impact Test) score and VAS (Visual Analogue Scale) score between the two groups. SU were taking a greater number of pills for acute treatment as compared to NSU group (SU:8 (0; 50), NSU group: (5(0; 30), p value <0.001].

Conclusion: The use of smartphone is associated with increase severity of headache in form of increased duration of episode and clustering of attack. Also, higher smartphone usage is associated with increase in requirement of acute medication and lesser relief with acute medication.

Disclosure of Interest: None Declared

IHC-PO-267

Migraine characteristics and association with metabolic syndrome; an observational study

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Objective: To study migraine characteristics and association with metabolic syndrome in 200 migraine patients.

Methods: 200 patients of age group 18 years to 60 years who met ICHD [International classification of headache disorder] criteria for migraine with aura or without aura coming to medicine and neurology opds of Maharaja Yashwantrao hospital were taken. This was questionnaire based prospective study. Parameters like Body mass index, blood pressure [systolic and diastolic], waist circumference, random blood sugar, total cholesterol, triglycerides, LDL and HDL were taken. Data was collected in form of demo-

Parameter	Value
Systolic blood pressure [mmhg]	119.

graphic characteristics, characteristics of migraine headache, precipitating factors, clinical and laboratory characteristics, prevalence of migraine in family members, current therapy and presence of metabolic syndrome.

Value of clinical and laboratory parameters

Results: Among the selected patients maximum number of patients 46% lies in the group of age 21 to 30 years and least number of patients 8% were reported in the age group of 51 to 60 years. Among the selected population 69% female and 31% male were present. Headache was unilateral in 138 patients [69%] and was bilateral in 62 patients [31%]. Out of selected patients 144 [72%] had pulsatile headache and 56 [28%] had constricting headache. Photophobia [178 patients 89%], phonophobia [154 patients 77%], nausea [148 patients 74%] and vomiting [92 patients 46%] were most common symptoms. Travel [84 patients 42%], tension [64 patients 32%] and hunger [48 patients 24%] were most common precipitating factors. Total 46 patients [21%] were found to have family history of migraine sufferer. Out of 200 patients 40 were having metabolic syndrome. and 160 patients were not detected of having metabolic syndrome.

Conclusion: Out of 200 selected patients in present study prevalence of metabolic syndrome was 20% [40 patients] with 22% in female patients and 18% in male patients. Some components of metabolic syndrome like

high BMI and high waist circumference were significantly more frequent in migraine patients.

Disclosure of Interest: None Declared

IHC-PO-268

Migraine comorbidity with anxiety disorder, a study in Regional Hospital Durres, Albania

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Objective: Many migraine patients often suffer from symptoms of anxiety. Patient with migraine have more possibility for symptoms of anxiety than patients without migraine. About 50% of patients with migraine have anxiety. Maybe this comorbidity between migraine and anxiety is because of brain chemicals involved of serotonin and some hormone changes in woman, that can stimulate both conditions. Symptoms of anxiety are most common in patients with chronic migraine, more than 15 days a month. In these patients headache treatments don't get well when anxiety is not treated. These patients have less response to headache medications and have more relapse. Physical symptoms such fatigue, trouble concentrating, appetite, and sleep changes are very common in these patient.

Methods: In our study we have seen 400 patients with migraine in ambulatory policlinic in Regional Hospital Durres in year 2017. 330 (82.5%) patients were female and 70 (27.5%) male. From all patients 208 (52%) have migraine accompanied with anxiety disorder (180 female (86.5%) and 28 male (13.5%)).

Middle age of patients with migraine and anxiety was 32.6 years and for patients without anxiety was 38.1 year. All patients of migraine and anxiety had preventive therapy with amitriptyline 25 mg per day for a group of them, and escitalopram 20 md per day for others (for long time treatment 6–12 months).

Results: The mean frequency of crisis in patients with anxiety was 15.4 days and without anxiety 4.3 days a month. After treatment of anxiety for one year the mean frequency of crisis was lower 13.6 days.

Conclusion: We need to understand better the impact of treating anxiety in patients with headache comorbidity

because so we can to obtain best treatment for each disorder. Effective drugs and behavioral therapies are available to have good results and less crisis of migraine.

Disclosure of Interest: None Declared

IHC-PO-269

Prevalence and clinical profile of migraine with aura in a cohort of young patients with stroke: a retrospective analysis

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Objective: Patients with Migraine with Aura (MA) are at increased stroke risk. however, an MA phenotype predisposing to stroke has not been identified yet. We aimed at exploring if MA patients suffering from stroke display peculiar clinical profiles and remarkable MA characteristics.

Methods: We retrospectively searched our clinical electronic dossiers for patients younger than 60-year-old diagnosed with “acute stroke” and for patients with MA patients who had also undergone testing for patent foramen ovale (PFO) in our Hospital. We defined three groups: stroke patients without (S+MA-) and with (S+MA+)MA history, MA patients (S-MA+). We collected vascular risk factors, the results of PFO detection tests and thrombophilic screening, stroke severity, etiology, and vascular territory. In S+MA+ and S-MA+ patients, we recorded MA onset age, type of aura, attack frequency, aura duration.

Results: We found 175 stroke patients and 105 MA patients without stroke (S-M+). Prevalence of MA subjects in our cohort of stroke patients was 6.3%. S+MA+ patients resulted younger than S+MA- patients ($p = .01$), more frequently female ($p = .026$), less frequently hypertensive ($p = .049$). No differences were observed in stroke severity (NIHSS). Moreover, S+MA+ presented a higher prevalence of PFO (χ^2 test, $p < .0001$). Time from MA onset age to stroke was 20.7 ys (sd 13.1). Compared to S-MA+ subjects, S+MA+ patients presented a higher prevalence of the exclusive visual type of aura (χ^2 test, $p = .019$) and a shorter aura duration (median 12.5 min IQ 21.2 min vs to 30 min IQ 28.8 Mann-Whitney test, $p = .038$) and similar MA attack frequency and onset age

Conclusion: Our findings suggest that PFO represents a relevant pathogenetic mechanism subtending the increase in stroke risk in MA patients. Short visual aura seems to be a remarkable phenotype in MA patients experiencing a stroke. The factors converting PFO from bystander to causative factor are yet to be discovered. Although the screening for PFO detection is not advisable in all MA patients, future studies are needed to circumstantiate a subset of patients where it can have a pivotal clinical value.

Disclosure of Interest: None Declared

IHC-PO-270

A case of Parkinson's disease started with headache

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Objective: We experienced Parkinson's disease started with headache.

Methods: 68-year-old woman.

In July of X-1, she visited our outpatient clinic for the first time because of a chronic headache. We diagnosed with chronic tension-type headache (ICHO-II 2.2.1) and started treatment with Tizanidine 3 mg/day. Her symptoms improved temporarily, but the next month, she was exacerbated by stress exposure, which made her headache worse again. We added treatment with Loxoprofen. But it did not get enough improvement even after adding Loxoprofen treatment. We examined her with DSM-IV. As a result she was a Major depressive episode (19 points on HAM-D/ The Hamilton Depression Scale). We started treatment with Duloxetine 20 mg/day for her from September. As a result, in the two weeks after the initiation of treatment, the headache improved from 10 to 5 in Visual Analog Scale (VAS), and the depression also improved from 19 to 7 in HAM-D. After that, the same state was maintained for a while.

In July X, resting tremor appeared in her left upper limb. Furthermore, bradykinesia appeared in August and the rigidity and postural instability of both upper limbs appeared in September. We suspected Parkinson's disease and underwent ¹²³I-MIBG scintigraphy and Brain MRI.

Results: As a result, we diagnosed her with Parkinson's disease and began treatment with Rotigotine. We started Rotigotine from 4.5 mg/day and titrated weekly to 13.5 mg/day. And we maintained it 13.5 mg/day. As a result, UPDRS part 3 improved from 27 points to 4 points three months after the start of treatment. In addition, the remaining headache and depression almost disappeared (VAS: 0 HAM-D: 2).

Conclusion: Depressive state is one of the important comorbid disorders of headache. In addition headache is thought to be a manifestation of depression since headache and physical symptoms in depression. Also, Parkinson's disease is often accompanied by depression, but it has been reported that in 1 to 5% of cases, depression appears before exercise symptoms. It's suggested that this case may be Parkinson's disease started with depression accompanied by headache. Depression associated with Parkinson's disease tends to be inconspicuous in the characteristic symptoms of endogenous depression including depressive state, so we need to be careful at the time of the examination.

Disclosure of Interest: None Declared

IHC-PO-271

Sleep disturbances in migraine w/o aura and tension-type headache. Results from premecef in a mexican population

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	Migraine without aura (N = 51)		Tension-type headache (N = 95)		p value
	Frequency	Percentage	Frequency	Percentage	
Sleep 4 to 6 hours	10	19.6%	41	43.2%	0.004
Sleep 6 to 8 hours	40	78.4%	46	48.4%	0.000
Restful sleep	18	35.3%	16	16.8%	0.012
Initial insomnia	10	19.6%	39	41.1%	0.009
Sleeping meds	5	9.8%	2	2.1%	0.038
Movements during sleep	10	19.6%	2	2.1%	0.000

Objective: Sleep disorders are common among headache patients. Different sleep disturbances have been described with different connotations on headache evolution. There is no information about this issue in México or Latin America. PREMECEF (*Primer Registro Mexicano de Cefaleas, First Mexican Registry of Headaches*) is the first Mexican effort to gather information about headaches. It serves as an e-medical record and the information is entered by physicians. We have presented global results previously. We describe sleep abnormalities within the subgroup of migraine w/o aura and tension-type headaches.

Methods: Until Feb/19, there were 489 registries with 97 migraine diagnosis and 212 tension-type headaches. Of these, we had complete data of different sleep parameters in 51 and 97 patients, respectively. Data were analyzed with chi square and the comparisons are presented.

Results: Main results are shown in the table. There were several striking differences, mostly against tension-type headache. Snoring, bruxism and daytime sleepiness were not significant.

Conclusion: Sleep disturbances are acknowledged as a factor in headaches evolution. However, it is not known if they have etiological role or are a consequence. Our results show highly significant differences between both entities studied, mostly against tension-type. We suggest that the sleep disturbances observed may be a manifestation of the same etiological process of the headache. We are currently studying if correction of the sleep disturbance can improve the headache evolution.

Disclosure of Interest: None Declared

IHC-PO-272

Endurance of cervical muscles in women with migraine after a craniocervical exercise protocol – a pilot study

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Objective: To verify the effect of a craniocervical exercises protocol on the endurance of cervical flexors and extensors in women with migraine.

Methods: Fifteen women with a diagnosis of migraine with a mean age of 31.9 (SD = 9.95) years and a frequency of 10.67 (SD = 8.86) days with headache per month were

assessed. The endurance test of the cervical flexors was performed with the volunteer in supine position; and for the cervical extensors the volunteer was placed in prone, supporting a weight of 2 kg. Both tests were started with the head in neutral position. The holding time (s) and the report of headache during the test (numerical scale of pain) were recorded. Pre and post-treatment results were compared by the Wilcoxon test and the significance level adopted was $p < 0.05$. The study was approved by the local ethics committee (No. 6146/2016).

Results: The mean holding time of the cervical flexor pre-treatment was 46 seconds (SD = 45), while the mean after treatment was 58 seconds (SD = 44). To cervical extensors, the mean pre-treatment was 185 seconds (SD = 144); in turn, the mean after treatment was 235 seconds (SD = 170). Despite the observed increase in both holding time, the difference was not statistically significant ($p > 0.05$). However, a significant decrease could be observed to the intensity of the headache report during the flexion test, with a mean pre-treatment of 1.9 (SD = 2.9) and mean post treatment of 0.8 (SD = 1.9) ($p = 0.04$). For the extensors, the intensity of headache reported showed no significant difference ($p > 0.05$), the mean pre-treatment was 1.1 (SD = 2.1) and a mean post-treatment of 0.8 (SD = 2.4).

Conclusion: Although we did not observe a significant improvement in the endurance cervical muscles values after the application of a craniocervical exercise protocol, a significant reduction of headache was observed when the cervical flexor endurance test was performed. However, this is a pilot study and by increasing the sample, the endurance gain of the cervical muscles might be noticeable.

Disclosure of Interest: None Declared

Genetics and Biomarkers of Headache Disorders

IHC-PO-032

Circulating MicroRNA Signature in Patients with Reversible Cerebral Vasoconstriction Syndrome

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Objective: The pathophysiology of reversible cerebral vasoconstriction syndrome (RCVS) is elusive; no effective circulating biomarkers have been identified. We aimed to investigate the role of circulating miRNAs in patients with RCVS.

Methods: We prospectively recruited patients with RCVS and age- and sex-matched healthy controls from the headache clinics of Taipei Veterans General Hospital. In the screening phase, we performed miRNA sequencing on pooled samples of each group to identify differentially-expressed miRNAs, which were further confirmed in individual samples using quantitative PCR (qPCR) in the training phase. The candidate miRNAs were further investigated in two independent validation cohorts. The targeted genes and pathways were predicted using bioinformatics.

Results: Totally 88 RCVS patients were approached, and 75 of them (mean age: 46.7 ± 9.5 ; M/F: 22/53) (including 20 in screening/training phases, 23 in validation cohort-1, and 32 in the validation cohort-2) together with 76 age- and sex-matched controls were eligible for final analysis. Five miRNAs including miR-130a-3p, miR-130b-3p, miR-let-7a-5p, miR-let-7b-5p and miR-let-7f-5p were significantly upregulated in patients with RCVS during ictal stage in comparison with their remission stage or controls. The combined miRNA panel well differentiated patients from controls (area under curve of Receiver Operating Characteristic curve was 0.906, 0.890 and 0.867 in three different cohorts respectively.) Pathway enrichment analysis suggested that endothelin-1 (EDN1) and transforming growth factor-beta (TGF- β) signaling pathway might link these miRNAs to the pathogenesis of RCVS.

Conclusion: We identified the miRNA signatures associated with RCVS, which revealed excellent diagnostic performance, clinical relevance, and were functionally relevant to the putative pathomechanisms.

Disclosure of Interest: None Declared

IHC-PO-033

Procalcitonin levels in chronic migraine patients

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Objective: To compare procalcitonin (proCT) serum levels in a group of chronic migraine (CM) patients and a group of healthy controls in order to determine its potential role as a biomarker. We also evaluate its relation with systemic inflammation and trigeminovascular activation markers, such as interleukin 6 (IL-6), high sensitivity C-reactive protein (hs-CRP), soluble TNF-like weak inducer of apoptosis (sTWEAK) and Calcitonin gen-related peptide (CGRP).

Methods: Cross-sectional study including 117 CM patients (ICHD2013) (48.6 ± 11.2 years old; 97.4% women) and 70 healthy controls (47.4 ± 10.7 years old; 97.1% women). Blood samples were obtained during interictal periods. Serum proCT levels were measured using an electrochemiluminescence immunoassay. IL-6, hs-CRP, sTWEAK, and CGRP levels were measured using ELISA. Independent t-test and one-way analysis of variance were used to compare results between groups, and multiple linear regression analysis was used to test associations adjusting for potential confounding factors.

Results: Serum proCT levels were significantly higher in CM patients than in healthy controls during interictal periods (0.040 ± 0.019 vs. 0.030 ± 0.023 ; $p = 0.003$). proCT levels were correlated with CGRP levels ($r = 0.498$, $p < 0.001$), that were also higher among patients. Importantly, hs-CRP serum levels were not elevated in CM patients (0.32 ± 0.56 vs. 0.34 ± 0.65 , $p = 0.830$). We did not find any correlation between proCT levels and other biomarkers of inflammation as IL-6 or sTWEAK.

Conclusion: Our results suggest a potential role of proCT as an inflammatory migraine biomarker related to CGRP in migraine pathophysiology.

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IHC-PO-034

Comparing effectiveness of different prophylactic migraine drugs in treating hemiplegic migraine

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Objective: Hemiplegic migraine is a rare and severe subtype of migraine with aura characterized by auras with motor weakness. For prophylactic migraine treatment in

hemiplegic migraine often a trial-and-error strategy is used based on treatment guidelines for the common types of migraine or on limited clinical experience available from hemiplegic migraine cases. We retrospectively evaluated prophylactic treatments that were used for treating hemiplegic migraine.

Methods: A retrospective cohort study was performed on hemiplegic migraine patients, diagnosed at the Leiden University Medical Center Headache Clinic from August 2009 till July 2015. Assessment was made on: 1) possible treatment efficacy (as estimated by the treating physician and the patient after 3 months), and 2) registered moderate to severe side-effects (defined as side-effects that led to discontinuation).

Results: Our cohort consisted of 20 hemiplegic migraine patients (follow up: 74 person-years), with a median follow up of 2.3 years (IQR 1–5). Median hemiplegic migraine attack frequency was 10 attacks per year (IQR 6–12). Of these, 13/20 patients (65%) were prescribed prophylactic migraine treatment. Ten different drugs from seven drug classes were used for treating hemiplegic migraine (median: 3 drugs per patient (range 1–8)). In 62% of the treated patients, treatment was considered clinically effective by both the treating physician and patient. The most effective treatments were lamotrigine (3/4, 75%), sodium valproate (4/6, 67%), acetazolamide (2/3, 67%), and verapamil (1/3, 67%). Propranolol was not effective in any of the patients treated (n = 5). Reasons for discontinuation of prophylactics were lack of efficacy 55% or side effects 45%.

Conclusion: Our findings confirm the results of previous small studies showing that lamotrigine, sodium valproate, acetazolamide and verapamil may be effective in treating hemiplegic migraine patients.

Disclosure of Interests: There are no conflicts of interest.

IHC-PO-035

Salivary cortisol levels on awakening predict headache outcome in chronic migraine

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Objective: Disturbances in the hypothalamic-pituitary-adrenal (HPA) axis have been reported in various chronic pain disorders. Whether cortisol levels are correlated with treatment outcomes of chronic migraine (CM) has not been determined.

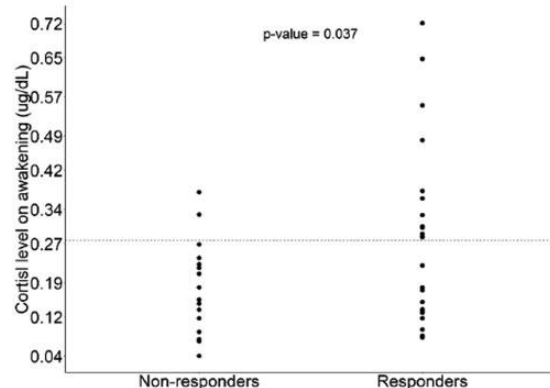
Methods: Newly diagnosed CM patients and healthy controls (HCs) were enrolled, and their baseline clinical

profiles and salivary cortisol levels were determined by questionnaires and ELISA, respectively. All patients were treated with flunarizine (5–10 mg/day), and were asked to keep headache diaries. Responsiveness was defined as $\geq 50\%$ reduction in moderate or severe headache days per month at 2 months compared to baseline. Comparisons were made between responders and non-responders. The cut-off value of cortisol levels was determined by using the receiver operating characteristic (ROC) curve, and the adjusted odds ratios (aORs) of prognostic factors were determined by multivariable logistic regression.

Table 1. Comparisons for baseline salivary cortisol levels at different time periods between responders and non-responders

Salivary cortisol levels	Non-responders (n = 16)	Responders (n = 22)	p-value
	Mean (SD)	Mean (SD)	
On awakening	0.18 ± 0.09	0.28 ± 0.18	0.037*
30 min after awakening	0.27 ± 0.19	0.32 ± 0.20	0.441
3 PM	0.07 ± 0.06	0.10 ± 0.11	0.341
Bedtime	0.09 ± 0.24	0.07 ± 0.18	0.674
Area under curve	110.4 ± 75.6	130.0 ± 87.8	0.478

Figure: Salivary cortisol levels on awakening at baseline between responders and non-responders



Results: In total, 38 CM patients (34F/4M, mean age 38.3 yrs) and 35 (31F/4M, mean age 42.5 yrs) HCs were recruited. There were no differences in salivary cortisol levels at different time periods between CM patients and

HCs. At 2 months after treatment, 22 (57.9%) were responders; whereas, 16 (42.1%), non-responders. There were no differences in age, psychological disturbance, sleep, disability or stress levels between responders and non-responders at baseline (data not shown). However, responders had higher salivary cortisol levels on awakening (0.28 ± 0.18 vs 0.18 ± 0.09 ug/dL, $p = 0.037$) than non-responders (Table). The cutoff value was determined at 2.76 ug/dL, above which 11 out of 13 patients (84.6%) were responders vs. 11/25 (44.0%, $p = 0.036$) in those below (Figure). The prognostic effect still remained after controlling for age (>2.76 ug/dL, aOR = 5.7, 95% CI 1.0–32.5, $p = 0.049$).

Conclusion: CM patients with lower salivary cortisol levels on awakening at baseline were more likely to have an unfavorable outcome to treatment, suggestive of possible HPA axis dysfunction. Whether this could serve as a marker for treatment responsiveness deserves further verification.

Disclosure of Interests: SJW has served on the advisory boards of Eli Lilly, Daiichi-Sankyo, and Taiwan Pfizer. He has received honoraria as a moderator from Allergan, Pfizer, Eli Lilly, Bayer, and Eisai.

IHC-PO-036

Is it useful to determine CGRP, VIP and PACAP in migraine? A cross-sectional study in chronic migraine patients

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Objective: VIP, CGRP and PACAP have important roles in migraine pathogenesis but their diagnostic value is controversial. Objective: To determine and compare these neuropeptides serum levels in a cohort of chronic migraine (CM), episodic migraine (EM) and healthy controls (HC).

Methods: Peripheral blood samples from 304 age and sex matched subjects (28 males and 276 females: 108 CM, 98 EM and 98 HC) were drawn, centrifuged, and stored at -80°C . ELISA-based assays were performed using BlueGene Biotech Co kit for PACAP and Cloud-Clone Corp kit for CGRP and VIP. Standardized values were compared using t-test for univariate analysis. A multinomial regression analysis was performed to identify predictors of clinical diagnosis. Pearson's "r" statistic was used for bivariate correlation analysis and Chi2 for categorical

variables. Area under the curve (AUC) in ROC curves were used to assess their diagnostic value.

Results: VIP, PACAP and CGRP were increased in CM vs EM and HC ($p < 0.001$), but not in EM vs HC. Age inversely correlated with PACAP and CGRP but not with VIP. Significant correlation occurred between VIP and PACAP ($r = 0.347$), VIP and CGRP ($r = 0.526$), and PACAP and CGRP ($r = 0.504$). Only VIP ($B = 0.009$) and PACAP ($B = 0.003$) predicted the clinical diagnosis for CM, but not EM. CGRP did not predict CM nor EM. Only 60.2% of CM, 68.8% of EM, and 15.5% of HC were correctly predicted. AUC were significant for VIP and PACAP (0.703 ± 0.33 , 0.739 ± 0.32 , respectively). Both had low sensibility for CM (0.53 and 0.50 respectively), and better specificity (0.83 and 0.939 respectively).

Conclusion: We found that VIP, CGRP and PACAP were significantly increased in CM. In the present study CGRP value as a CM biomarker was relatively low. Standardized techniques for analyzing these neuropeptides are strikingly needed.

Disclosure of Interests: Funded by ISCIII-FISS PI15/01285 and IDIVAL. None of the authors have any conflict of interests to declare.

IHC-PO-037

Isolated cerebrospinal fluid hypertension in chronic headache

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Objective: To identify the pressure-related features of Isolated Cerebrospinal fluid Hypertension (ICH) in order to differentiate headache sufferers with ICH from those with primary headache disorders.

Methods: In this prospective study, patients with refractory chronic headaches and suspected of having cerebrospinal fluid-pressure elevation without papilledema or sixth nerve palsy, together with controls, underwent one-hour lumbar cerebrospinal fluid pressure monitoring via a spinal puncture needle.

Results: We recruited 153 consecutive headache patients and 16 controls. Lumbar cerebrospinal fluid pressure monitoring showed high pressure and abnormal pressure pulsations in 97 (63%) patients with headache: 40 of these patients with the most abnormal pressure parameters (opening pressure above 250 mmH₂O, mean pressure 302 mmH₂O, mean peak pressure 400 mmH₂O, and

severe abnormal pressure pulsations) had the most severe headaches and associated symptoms (nocturnal headache, postural headache, transient visual obscuration); 57 patients with the less abnormal pressure parameters (opening pressure between 200 and 250 mmH₂O, mean pressure 228 mmH₂O, mean peak pressure 318 mmH₂O, and abnormal pressure pulsations) had less severe headaches and associated symptoms.

Conclusion: Nocturnal and postural headache, and abnormal pressure pulsations are the more common pressure-related features of ICH in patients with chronic headache. Abnormal pressure pulsations may be considered a marker of ICH in chronic headache.

Disclosure of Interest: None Declared

IHC-PO-273

Familial “Diplegic” Migraine – Description of a Family with a Novel CACNA1A Mutation

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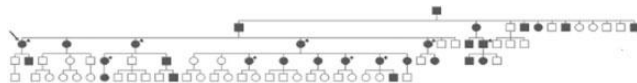
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Objective: Familial hemiplegic migraine (FHM) is a rare monogenic form of migraine with aura including fully reversible motor weakness affecting one side of the body. Three distinct genes have been associated with FHM. FHM type 1 (FHMI) is the most prevalent, and is caused by mutations in the CACNA1A gene that codes for a voltage-dependent calcium channel. More than 20 unique mutations of this gene have been described, some with distinct phenotypes. Here we describe a novel CACNA1A gene mutation associated with migraine aura including bilateral motor weakness (“diplegia”).

Methods: The proband had previously been diagnosed with FHM on clinical grounds, and reported multiple similarly affected family members. The proband underwent genotyping for FHM. To characterize phenotypes, semi-structured phone interviews were conducted with the proband and multiple affected family members.



Results: A novel CACNA1A mutation (c.622 isoform 1 G>A; p. Gly208Arg) was identified in the proband. A total of twenty-nine putatively affected family members, across five generations, were identified. The proband and eight affected family members were interviewed. All met ICHD-3 diagnostic criteria for FHMI. Six of nine subjects

described some, but not all, of their migraine attacks to include motor deficits affecting both sides of the body simultaneously. Subjects described three sequences by which diplegia occurs. In the more common motor aura sequence, weakness starts in a foot, progresses up the ipsilateral side of the body to the face, crossing to the contralateral side of the face, then down the contralateral side of the body to the opposite foot (in a single wave). A second, similar sequence was described except the wave starts and finishes on opposite sides of the face. The third sequence differs in that weakness starts in a foot, then as the wave progresses cephalad up the ipsilateral side of the body, a second wave of weakness starts in the opposite foot with the two waves moving up their respective sides of the body simultaneously at different levels.

Conclusion: We describe a large FHMI kindred with a novel CACNA1A mutation associated with migraine attacks including diplegic aura.

Disclosure of Interest: None Declared

IHC-PO-274

ATP1A2 from gene structure to clinical implications

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Objective: Mutations in the ATP1A2 gene have been associated with hemiplegic migraine type 2 (HM2), alternating hemiplegia of childhood (AHC) and hypokalemic periodic paralysis (HypoPP). ATP1A2 encodes the $\alpha 2$ -subunit of the Na⁺/K⁺-ATPase ion pump that plays a critical role in maintaining the sodium and potassium gradient across the basolateral membrane in all animal cells. To what extent mutations in ATP1A2 affect the function of the Na⁺/K⁺-ATPase and how these mutations contribute to the pathophysiology of HM2, AHC and HypoPP has not been completely elucidated. The aim of this study was to review current understanding of the structure and function of ATP1A2 and the clinical significance of mutations.

Methods: We conducted a systematic search for studies that reported a mutation in ATP1A2 associated with disease. The pathogenicity was assessed based on in silico pathogenicity prediction programmes and subsequent searches for functional *in vitro* tests.

Results: Ninety-five different mutations have been reported in ATP1A2 in patients. Most cases reported with a mutation in ATP1A2 have an HM2 phenotype of which about half show additional features, such as epileptic symptoms and/or developmental delay. The mutations are

localized in clusters at district sites (within the P domain and around the C-terminus) within the Na⁺/K⁺-ATPase crystal structure. The majority (ca. 70%) of the mutations has been reported only once. For 56 mutations additional *in vitro* tests were performed. We show that 52 of these functional assays have an effect on cell function, varying from reduced protein expression to a change in cation affinity.

Conclusion: No direct genotype-phenotype correlations could be made. However, our data suggests that amino acids changes in the P-domain and the C-terminus are more prone to cause a disease phenotype. Furthermore, mutations in *ATP1A2* are not merely the result of loss-of-function.

Disclosure of Interest: None Declared
IHC-PO-275

Does being a night owl in migraine have any connection to higher migraine-related disability?

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Objective: Our bodies have an internal biological clock, people's sleep schedules are defined as an early bird or a night owl depending on their circadian rhythm. People need to get up early to go to work or school in modern day life routine. We hypothesized that people sleep habits might have a role in their migraine. The aim of the study was to investigate whether being a night owl has a negative effect on migraine-related disability or not.

Methods: One hundred-forty-three patients with migraine [68 patients with episodic migraine (EM) and 75 patients with chronic migraine (CM);(34.1 ± 7.6)] and 62 healthy subjects (32.6 ± 9) were recruited in the study. Individuals were asked about their demographic characteristics. The patients with migraine were also assessed by Migraine-Related Disability Assessment Scale (MIDAS). All participants completed the Morningness–Eveningness Questionnaire (MEQ) and Pittsburgh Sleep Quality Index (PSQI).

Results: MIDAS of all migraine patients showed severe disability (24.6 ± 21.9) [EM patients (10.7 ± 10.3);CM patients (37.1 ± 22.1)]. Sixty-two percent of the migraine patients and 56.5% of the control group were classified as group 3 (intermediate type) according to their MEQ. MEQ was not statistically different for both groups (p = 0.594). Sixty-eight percent of the migraine patients and 63% of healthy subjects had poor sleep quality. PSQI was not found to be different between the migraine patients (7.2 ± 4.3) and the control group (5.9 ± 3.4) (p = 0.07).

The total scores of the MEQ and the PSQI showed statistical difference between EM and CM patients respectively, [(54.1 ± 9.5) vs. (51.01 ± 8.7); (p = 0.04)], [(6.1 ± 3.9) vs. (8.2 ± 4.5); (p = 0.006)]. In all migraine patients, the PSQI showed positive correlation with the MIDAS (r = 0.310, p < 0.01) and inverse correlation with the MEQ (r = -0.210, p = 0.01).

Conclusion: Most of our participants were classified as an intermediate type and we found no difference in patient and control chronotype composition. Migraine-related disability was correlated with poor sleep quality for all migraine patients. Being evening type in MEQ and poor sleep quality showed correlation for the migraine patients; however, we did not find any association between their migraine-related disability and their chronobiological features.

Disclosure of Interest: None Declared

IHC-PO-276

No association of RNF213 polymorphism with reversible cerebral vasoconstriction syndrome

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Objective: In Asian cohorts, reversible cerebral vasoconstriction syndrome (RCVS) is mostly idiopathic and its clinical presentation is benign, compared to reports from Caucasian cohorts. We aimed to investigate the association between RCVS in Korean population and the 14429G>A (p. Arg4810Lys) mutation of the Ring finger protein 213 gene (RNF213), the susceptibility gene for moyamoya disease (MMD), intracranial artery atherosclerosis and dissection which are more prevalent in Asians.

Methods: We prospectively collected patients who presented with thunderclap headache in Samsung Medical Center from November 2016 to January 2018. Causes of thunderclap headache were classified by using clinical presentation, brain MRI, MRA, and/or CSF analysis. Blood samples of the patients were analyzed to detect the presence of c.14429G>A (p. Arg4810Lys) mutation of RNF213. Genomic DNA was extracted from peripheral blood leukocytes using a Wizard Genomic DNA Purification kit and following the manufacturer's instructions (Promega, Madison, WI, USA).

Results: Among the 50 patients with thunderclap headache included in this study, 34 (68.0%) patients had RCVS, and seven (14.0%) had other secondary causes including intracranial arterial dissection (n = 4, 8.0%). The remaining nine (18.0%) patients were classified as having primary

thunderclap headache. Neither the patients with RCVS nor those with other primary or secondary causes of thunderclap headache had the c.14429G > A (p. Arg4810Lys) mutation of the RNF213.

Conclusion: The RNF213 polymorphism might not be the susceptibility gene related with RCVS in Koreans. The difference in demographics and characteristics of RCVS between reported cohorts may not be attributed to genetic predisposition but to study setting and social/environmental factors.

Disclosure of Interests: This study was supported by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (Nos. 2017R1A2B2009086 and 2017R1A2B4007254).

IHC-PO-277

Correlation between ADRB1, ADRB2 and ADRB3 gene polymorphisms and Cluster headache susceptibility

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Objective: Cluster headache (CH) is a primary neurovascular headache disorder. A genetic component was confirmed by family and twin studies. Since β -adrenergic receptors (ADRBs) are involved in nociception, polymorphisms in ADRB genes may be associated with CH susceptibility. The purpose of the present study was to investigate the correlation between ADRB genes polymorphisms and the susceptibility to develop CH in a Southeastern European Caucasian (SEC) population.

Methods: DNA from buccal swabs of 95 cluster headache patients and 730 non-related volunteers with SEC origin was collected and genotyped for ADRB1 (rs1801252, rs1801253), ADRB2 (rs1042713, rs1042714) and ADRB3 (rs4994) gene polymorphisms. Statistical analysis was performed using SPSS package (v.25).

Results: Although allele and genotype frequency distribution for each ADRB gene polymorphism showed no statistically significant differences between patients and general population ($p > 0.05$), heterozygosity in both rs1042713 and rs1042714 was 1.7 times more likely to appear in general population (OR: 0.582, $p = 0.05$).

Conclusion: Larger studies on ADRB2 gene polymorphisms must be conducted in order to confirm the heterozygosity protection against CH.

Disclosure of Interest: None Declared

Headache and Gender

IHC-PO-038

Sex Pairing and Migraine: A Population-based Twin Study

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Objective: Migraines are a common neurovascular disorder and are comorbid with other disorders. Evidence points towards migraine as a heritable condition and studies show that intrauterine hormones may transfer from male to female during opposite-sex twin pregnancies. Our objective is to determine a relationship between migraine risk and sex pairing among twins and to compare the heritability of migraine among American twins.

Methods: Survey data from the Washington State Twin Registry ($n = 19305$) was used in descriptive, bivariate and generalized estimating equations analysis. We used migraine risk as the dependent variable and independent variables included demographic characteristics, sex pairing and clinical conditions such as depression, chronic fatigue syndrome, temporomandibular disorder, and seizures.

Results: Both male-female sex paired twins (1.86, 95%CI 1.57–2.21) and female-female twins had a (2.34, 95%CI 2.06–2.66) higher odds of migraine compared to male-male twins. Depression, chronic fatigue syndrome, temporomandibular disorder, and seizures were found to be frequently comorbid in individuals with migraine.

Conclusion: Many factors influence risk of migraine including comorbid conditions and sex pairing of twins. Migraine risk increases in female-female twin pairs compared to pairs that have a male twin present, indicating a protective factor of male twins in the uterine environment. Evidence of heritability in this study indicates that migraine is affected by both genes and prenatal environment.

Disclosure of Interest: None Declared

IHC-PO-039

Anxiety, depression, headache severity and disability: Comparison of male and female migraineurs

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Objective: Migraine is a highly prevalent and disabling neurological disorder. The disease is more prevalent in female patients. The aim of the current study is to compare the prevalence of anxiety and depression and also headache severity and disability scores in male and female migraine patients.

Methods: In this cross-sectional study, migraine patients were enrolled based on ICHD-3 beta criteria. Hospital Anxiety and Depression Scale (HADS), MIDAS (Migraine Disability Assessment) score and Headache Impact Test (HIT-6) were fulfilled by the patients in order to evaluate anxiety and depression, migraine headache-related disability and severity respectively. Regards to odd questions summation of HADS scores' we determined depression score (patients with scores more than 7 were assumed as depressed) and we calculated anxiety score by summing the even questions of HADS scores (patients with scores more than 7 were assumed as anxious). Total scores of MIDAS and HIT-6 were used in the analysis. The student T-test was used to compare the means between two groups and the chi-square test was used to compare the frequency of anxiety and depression between the two genders. Informed consent to publish has been obtained from this patient.

Results: In this study, 126 migraineurs were enrolled. Mean (\pm SE) age of the participants was 32.44 ± 0.04 and 82 (65.1%) patients were female. No statistically significant difference was seen between male and females regarding the mean age ($P=0.163$). Mean (\pm SE) total MIDAS and HIT-6 scores for female subjects were 33.41 ± 4.77 and 64.41 ± 0.57 respectively and their difference with this scores in males (32.68 ± 5.16 and 62.66 ± 1.23 respectively) were not statistically significant ($P=0.922$ and 0.145 respectively). Of the females, 87.8% had anxiety and the difference with males (63.6%) was statistically significant ($P=0.02$). No statistically significant difference was seen between female (46.3%) and male (40.9%) subjects when comparing the frequency of depression ($P=0.346$).

Conclusion: Results of the current study showed that females with migraine experience more anxiety than male subjects. However, the two genders were the same regarding the frequency of depression and the level of headache-related disability and severity of attacks.

Disclosure of Interest: None Declared

IHC-PO-040

The course of chronic and non-chronic headaches during pregnancy. A population based prospective study from a large pregnancy cohort: The Akershus Birth Cohort – ABC study

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Objective: Headache is one of the most common health problems among women of child bearing age. The main focus of studies on headache during pregnancy has been migraine but chronic headaches also contribute. Few studies exist on the fate of these during pregnancy. Particular problems are use of analgesics and headache prophylactics. Our objectives were, in a large, prospective, epidemiologically recruited pregnancy cohort to examine the fate of chronic and non-chronic headaches. We also aimed to describe headache medication use through pregnancy.

Methods: This was a prospective study during pregnancy and postnatally at the Akershus University Hospital. The hospital serves a population of 400,000 and has 3,500 births yearly. Women were recruited at the routine fetal ultrasound, gestational week 17. Three prospective questionnaires were completed at week 17, 32 and eight weeks after birth. The headache situation pre-pregnancy was also queried. Questionnaires addressed migraine prevalence, monthly headache frequency, headache intensity (verbal rating scale) and frequency of medication intake. Descriptive statistics were used and for trend analysis a mixed linear model was used.

Results: 4,814 women were invited, 4,662 gave consent (97%). The response rate for each questionnaire was 80%. 1,981 (43%) returned all three questionnaires. 2% of the women had chronic headache before pregnancy (32% with migraine). 0.5% had medication overuse headache. Chronic headache frequency worsened up to week 17, improved before week 32 and then remained stable until 8 weeks post-partum. 4% of women with non-chronic headache had new incident chronic headache before week 17. Headache intensity for all women followed a similar pattern. Having migraine influenced headache intensity slightly, chronic headache cases had more severe headache throughout. Medication use was reduced through pregnancy but less among those with chronic headaches.

Conclusion: Chronic headache is common among pregnant women and its assessment and treatment needs more focus.

Disclosure of Interest: None Declared

IHC-PO-278**Gender dysphoria and headache**

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Objective: Gender dysphoria is the distress a person experiences as a result of the sex and gender they were assigned at birth. The prevalence and demographics of gender dysphoria vary according to geographical location and has not been well-documented in Turkey. There are also significant research gaps in headache and migraine's effect on transgender population. The aim of this study was to search for headache incidence and type in people with gender dysphoria (female-to-male) and association between headache and hormone replacement therapy (HRT).

Methods: A total of 50 patients (24.3 ± 3.8) who were diagnosed as gender dysphoria (female-to-male) and followed by Psychiatry Department of 9 Eylul University, Faculty of Medicine, Turkey were recruited in the study. Participants were asked whether they were currently receiving hormone replacement therapy or not. All patients filled out Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). Headache was diagnosed using a questionnaire which consisting of 40 questions and assessed by a neurology specialist.

Results: Forty percent of the participants ($n = 20$) were currently receiving hormone replacement therapy, while 60% of the patients were not. The mean score of the BDI and BAI were respectively, $[(8.27 \pm 7.37); (8.98 \pm 7.12)]$. The patients were classified as a tension type headache (TTH) ($n = 14$, 28%) and migraine ($n = 28$, 56%). Patients with TTH and migraine were mostly infrequent episodic type respectively, $[(n = 13, 93\%) (n = 24, 82\%)]$. The most common triggers for headache reported by the patients were stress and sleep disturbances. Twenty-two participants with migraine were currently receiving hormone replacement therapy (61%) and 68.2 percent of them ($n = 15$) reported that their headache frequency did not change after starting hormone replacement therapy.

Conclusion: Both episodic (48%) and chronic migraine (14%) prevalence of our patients with gender dysphoria was pretty higher compared to general population. The headache frequency of most of participants with migraine who were currently receiving hormone replacement therapy did not change with HRT according to the participants' statements. More studies need to be done in order to reach any further conclusion about headache in individuals with gender dysphoria.

Disclosure of Interest: None Declared

IHC-PO-279**Headache Prevalence in Transgender Youth: a Retrospective Chart Review**

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Objective: A sex difference in migraine prevalence arises in adolescence, peaking during mid-life with a female to male prevalence ratio of roughly 2. There is likely a hormonal contribution given its occurrence during reproductive years. Some research suggests that low testosterone (T) is associated with higher rates headache in males. We hypothesized that adolescents assigned male gender and given estrogen (E) as gender affirmation treatment will have a higher prevalence of headache than those with gender dysphoria who have not received E. We also hypothesized that adolescents assigned female gender and given T will have a higher prevalence of headache than those who are untreated.

Methods: All patients from 2007–2017 seen in the Gender Management Service (GeMS) clinic at Boston Children's Hospital were included. Data were collected on assigned gender and patients' treatment with sex steroids by GeMS. Patients with headache diagnosis in their chart were identified and charts validated by JAH. Statistical testing was a chi-squared analysis in Excel software.

Results: Results demonstrated that in those assigned male gender and treated with E, 6 of 119 had headache (5%). In those assigned male gender and untreated, 3 of 150 had headache (2%). In those assigned female gender and treated with T, 20 of 221 had headache (9%). In those assigned female gender and untreated, 10 of 255 had headache (4%). There was a statistically significant difference ($p = 0.001$) between expected and actual frequencies of headache in both comparisons.

Conclusion: However, headache prevalence was higher in both E and T treatment groups compared with untreated groups. There are limitations to this study, including the

small number of subjects, the retrospective nature of the study, and lack of a specific information about headaches. Our findings suggest that headache prevalence in transgender youth should be studied prospectively as the number of adolescents treated with gender affirmation hormones increases.

Disclosure of Interests: This study was funded by a grant from the Joan Alford Fund in the case of JAH, NIH grant T32-DK007699 in the case of KM, and NIH grant R01-HD082554 to YC.

IHC-PO-280

Gender differences in clinical and pharmacological response to triptans

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Objective: To examine the effect of gender on clinical response to triptans in migraine patients and to relate these gender differences to pharmacokinetics of triptans in men and women.

Methods: We performed a systematic search to identify clinical trials distinguishing clinical response to or pharmacokinetic parameters of triptans between men and women. Male-to-female pooled risk ratios (RR) were calculated for clinical outcomes and pooled ratio of means (RoM) for pharmacokinetic outcomes, using random-effects models.

Results: Out of > 1200 publications on clinical trials with triptans, 237 were identified after adding sex and gender related search terms. Of these, only 19 presented gender-specific results. No gender differences were found for 2-hour headache response and 2-hour pain free response. Women had a higher risk for headache recurrence within 24 or 48 hours (male-to-female RR 0.74, 95%CI:0.56–0.97) and adverse event frequency (male-to-female RR 0.82, 95%CI:0.76–0.89) than men. No gender-specific results were available on sustained pain free rates. Women had a higher AUC_{0-∞} (RoM 0.68, 95%CI:0.61–0.75) and C_{max} (RoM 0.72, 95%CI:0.65–0.79) than men. Gender differences remained in AUC_{0-∞} and C_{max} normalized to body weight (RoM 0.48, 95%CI:0.30–0.76 and RoM 0.65, 95%CI:0.47–0.91) (data only available for frovatriptan). No gender differences were found on T_{1/2} (data on frovatriptan and zolmitriptan available).

Conclusion: Given the widespread use of triptans and the large amount of literature on this topic, it is surprising that

there are only few publications about gender differences. Based on the limited data available, we conclude that women have a higher adverse event frequency than men, which may be due to a higher drug exposure. This higher drug exposure seems to exist regardless of body weight and is not accompanied by a higher response rate. Moreover, women have higher headache recurrence rates, which cannot be explained by a different initial response to triptans, but may hypothetically be due to longer attack duration related to sex hormonal changes.

Disclosure of Interest: None Declared

Headache Classification

IHC-PO-041

Tactile Acuity in Migraine: A Prospective Study

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Objective: Migraine is associated with structural and functional changes in the brain, including the somatosensory cortex. The primary aim of this study was to evaluate whether trigeminal tactile acuity, a cortical sensory sign, could serve as an objective clinical biomarker in the evaluation of migraine.

Methods: Consecutive patients meeting study inclusion criteria were consented to participate. Inclusion criteria included all patients 18 years or older fulfilling International Classification of Headache Disorders, 3rd edition criteria for a diagnosis of migraine with or without aura. Patients were excluded who had concurrent secondary headache disorders, cognitive impairment precluding participation in sensory testing, confounding neurologic disorders, including trigeminal neuropathy, and a history of structural facial deformation. Dynamic brush allodynia and 2-point discrimination (2PD) were assessed 1 cm above the supraorbital notch according to previously validated methodology. Predictors of 2PD were evaluated by multivariable logistic regression using standard least squares and backward selection. All statistical tests were 2 sided, with $p < 0.05$ considered significant.

Results: The cohort was comprised of 70 individuals with either episodic (36, 51%) or chronic (34, 48%) migraine, with a median MIDAS of 26 (10–50.25). Patients had a median age of 41.5 (24–52) and were mostly woman (82.8%). The median supraorbital 2PD threshold was 1.2 cm (0.82–1.6) with a median side-side difference of 0.2 cm (0–0.32). Significant univariate associations were identified between 2PD and age ($P = 0.028$), current headache intensity ($P = 0.024$), and PHQ-9 scores ($P = 0.01$). Associations between 2PD and gender, headache days, headache diagnosis, GAD-7, MIDAS and allodynia on

exam were non-significant. Headache intensity and PHQ-9 remained significant in multivariable logistic regression ($R^2=0.16$, $P<0.0001$). Greater side-side differences were observed in patients with a greater number of monthly headache days ($R^2=0.05$, $P=0.04$) and in patients with chronic migraine ($P=0.03$).

Conclusion: Tactile acuity may serve as an objective clinical biomarker in patients with migraine. In this exploratory cohort, headache intensity and depressive symptoms predicted 16% of the variance in supraorbital tactile discrimination.

Disclosure of Interests: Royalties from Up-To-Date, Inc. for the articles, "Acute treatment of migraine in adults" and "Preventive treatment of migraine in adults".

IHC-PO-042

Is the level of migraine aura complexity related to visual and somatosensory cortical thickness?

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Objective: Our goal is to categorize migraine patients into homogenous groups using newly developed Migraine Aura Complexity Score (MACS) and to compare those groups with respect to patient's cortical thickness.

Methods: Selected participants who have a migraine with aura (MwA) were interviewed after each attack in order to obtain characteristics of migraine aura. Thereafter, we scored the complexity of their auras by MACS. MACS was used to categorize patients into three groups: MwA-S (with simple aura – MACS ≤ 1 point), MwA-MC (with moderately complex aura – MACS between >1 and <4.5 points) and MwA-C (with complex aura – MACS ≥ 4.5 points). The Surface-Based Morphometric Analysis approach was used to estimate cortical thickness. We used General Linear Model (GLM) for comparing these groups in terms of cortical thickness, controlled for the effect of age and sex.

Results: The study included 32 patients with MwA (MwA-S = 14, MwA-MC = 9 and MwA-C = 9). Patients in the MwA-C and MwA-MC groups had a thicker cortex in the

left primary visual cortex with respect to MwA-S group (1.495 ± 0.063 vs. 1.397 ± 0.072 , $p=0.006$; 1.489 ± 0.066 vs. 1.397 ± 0.072 , $p=0.010$), respectively. In addition, patients in the MwA-C group have had thicker cortex relative to MwA-S group in the left secondary visual cortex (1.887 ± 0.095 vs. 1.754 ± 0.066 , $p=0.001$), right secondary visual cortex (1.943 ± 0.115 vs. 1.798 ± 0.056 , $p=0.002$), left visual area V5 (2.513 ± 0.152 vs. 2.332 ± 0.122 , $p=0.011$), right visual area V5 (2.424 ± 0.201 vs. 2.234 ± 0.115 , $p=0.013$), right somatosensory BA3a cortex (1.745 ± 0.082 vs. 1.654 ± 0.090 , $p=0.009$) and left somatosensory BA3b cortex (1.859 ± 0.129 vs. 1.725 ± 0.116 , $p=0.017$).

Conclusion: Our results show that the newly developed MACS can be used for the stratification of MwA patients. MwA-C group had thicker cortex in several visual and somatosensory cortical regions with respect to the MwA-S group.

Disclosure of Interest: None Declared

IHC-PO-043

Menstrually-related migraine: a comparison between self-reported diagnosis and prospective headache diaries

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Objective: Clinical and epidemiological studies suggest a prominent role for female sex hormones in migraine. The menstruation period may be an important trigger for attacks. In addition, menstrual migraine tends to be more severe, longer lasting and less responsive to acute treatment. According to the new International Classification of Headache Disorders (ICHD-3) appendix criteria no prospectively obtained evidence is necessary for a menstrually-related migraine (MRM) or pure menstrual migraine (PMM) diagnosis. The aim of this study was to investigate accuracy of non-diary self-reported diagnosis.

Methods: As part of our LUMINA programme female migraine patients were asked whether their attacks were associated with the menstruation. A subset of patients was prospectively followed during at least three months with daily headache e-diaries to confirm MRM or PMM diagnosis. MRM was defined as migraine attacks occurring on day -2 to $+3$ of the menstrual cycle in at least two out of three cycles, and additionally at other times of the cycle.

PMM was defined as attacks occurring exclusively on day -2 to $+3$ in at least two out of three cycles, and at no other times.

Results: A total of 5727 female migraine patients participated in this LUMINA sub analysis, of whom 58% reported to have MRM and 4% PMM. We collected prospective diaries for a random sample of 104 premenopausal women. Mean follow-up time was 124.4 ± 37.7 days. During follow-up women had on average 4.5 ± 1.5 menstrual bleedings, 6.8 ± 4.2 migraine days per month and 3.2 ± 1.4 migraine attacks per month. Women's self-reported diagnoses had a positive predictive value of 65% and negative predictive value of 50%. Sensitivity was 80% and specificity 33%.

Conclusion: Accuracy of self-reported menstrually-related migraine diagnosis is poor in female migraine patients. We suggest to reconsider the appendix criteria for menstrual migraine. A prospective diary is required not only for research purposes but also for an accurate clinical diagnosis.

Disclosure of Interest: None Declared

IHC-PO-044

Migraine with brainstem aura: defining the core syndrome

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Objective: Migraine with brainstem aura (MBA) is a rare sub-type of migraine with aura. Although this entity has been known for many years, its diagnosis and even its existence are still a matter of debate. Previous studies demonstrated that current diagnostic criteria for migraine with brainstem aura are too open and brainstem symptoms may originate within the cortex and not in the brainstem.

The aims of the present study were to analyze whether aura from the brainstem exists, how prevalent such a core syndrome is, to analyze if current diagnostic criteria define such a core syndrome and, if necessary, to develop new diagnostic criteria that define only the core syndrome.

Methods: We analyzed all cases with MBA in the literature described in detail, clinical cases from the Danish Headache Center(DHC) and our very large sample of telephoneinterviewed cases with migraine with aura. After collecting data, we selected the 20 most convincing cases from the literature and from DHC to develop diagnostic criteria for the core syndrome of MBA.

Results: Out of 79 MBA described cases in detail in the literature, 44 fulfilled the diagnostic criteria for MBA of the International Classification of Headache Disorders, 3rd

edition (ICHD-3) and most were convincing. In the DHC after face-to-face interview, neurological examination and imaging, only 4 MBA out of 293 (1.25%) with migraine with aura were found corresponding to 0,04% or less in the general population. Our telephone-interviewed cohort included 1781 subjects with a diagnosis of migraine with aura or probable migraine with aura. 228 of these fulfilled the diagnostic criteria for MBA of the ICHD-3. Thus, using interview diagnosis according to current diagnostic criteria, far too many get the MBA diagnosis. Therefore, we developed stricter diagnostic criteria in an attempt to include only those rare cases who really have aura originating from the brainstem.

Conclusion: Migraine with brainstem aura does exist but it is very rare. Existing diagnostic criteria are too unspecific, but it was possible to develop tighter criteria that define a core syndrome probably caused by brainstem dysfunction.

Disclosure of Interest: None Declared

IHC-PO-045

Persons who have never had a headache. Socio-demographic characteristics

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Objective: Headaches are extremely common illnesses that in population surveys have a lifetime prevalence of 90–99%. There are persons who never in their whole life have encountered a headache, so called headache resilient persons. This subgroup is 4–5% in the general population. To our knowledge research on resilient or immune individuals has so far been limited to infectious

disease, but it is obvious that factors that help individuals from getting a headache are very interesting. We utilized the Danish blood donor study and the unique Danish registries to estimate the prevalence of headache resilience and to describe the socio-demographic characteristics of headache resilient participants compared to non-resilient participants.

Methods: 33,110 Danish blood donors (1,364 cases and 31,746 controls) were included in the study. All donors answered a digital tablet-based questionnaire and consented to the use of their data from national registers. Headache resilient participants were identified based on the question “In your opinion, have you never, in your whole life, experienced a headache of any kind?”. Logistic regression was used to analyze for association to headache resilience, adjusted for age and sex.

Results: 4.1% of participants were identified as headache resilient with a female-male ratio of 1:2.2. Headache resilience was positively associated with an employment status as a student, a low level of income and a daily alcohol consumption. A high education was negatively associated with headache resilience. There were significant but numerically small differences between headache resilient participants and controls in health factors as well as in self-perceived physical health.

Conclusion: Headache resilience as a phenotype has not been studied before. 4.1% of blood donors were headache resilient and it is two times more prevalent in men. Headache resilient participants were slightly healthier than controls.

Disclosure of Interest: None Declared

IHC-PO-046

Exploring the structure of migraine diagnosis in ICHD-3: Factor analysis across a population-based sample

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Objective: In the absence of an etiologic gold standard of migraine, the ICHD-3 diagnostic criteria for migraine is

composed of headache features, associated symptoms, attack number, and attack duration. Factor analysis is a statistical method used to describe variability among observed variables in terms of a potentially lower number of unobserved variables. For a better understanding of the structure of ICDH-3 migraine diagnosis, we conducted an exploratory factor analysis of migraine diagnostic criteria using Korean Headache-sleep Study (KHSS).

Methods: We used the data of the KHSS. The KHSS is a nation-wide, cross-sectional, population-based survey on headache and sleep involving Korean adults aged 19 to 69 years. An exploratory factor analysis (EFA) using principal components analysis was conducted on 8 variables based on ICHD-3 criteria (unilateral pain, pulsating quality, mild-to-moderate pain, aggravation by movement, nausea, vomiting, photophobia, and phonophobia). A correlation matrix was analyzed by tetractrochoric correlation analysis.

Results: Of 2695 participants, 143(5.3%) were diagnosed as having migraine. A three-factor model emerged in Eigen values of tetractrochoric matrix analysis. Three-factor model corresponded sensory hypersensitivity and nausea (rotated component matrix, photophobia: 0.865, phonophobia: 0.635 and nausea: -0.869), unilateral pain (unilateral pain: 0.959) and pain severity (moderate-to-severe pain: 0.486, aggravation by movement: 0.419, pulsating quality: -0.519, vomiting 0.555).

Conclusion: The ICHD-3 diagnostic criteria for migraine could be parsed into 3 partially related factors across population sample. Identifying the association among migraine symptoms elucidate the structure of migraine diagnosis may be facilitated for understanding the nature of the disease.

Disclosure of Interests: Soo-Jin Cho was involved as a site investigator of multicenter trial sponsored by Otsuka Korea,

Eli Lilly and Company, and Novartis and worked as an advisory member for Teva, and received research support from

Hallym University Research Fund 2016 and a grant from Korean Neurological Association (KNA-16-MI-09).

Min Kyung Chu was a site investigator for a multi-center trial sponsored by Otsuka Korea, Novartis International AG and

Eli Lilly and Company. He worked an advisory member for Teva, and received lecture honoraria from Allergan Korea, Handok-Teva and Yuyu Pharmaceutical Company in the past 24 months.

The other authors, except for Soo-Jin Cho and Min Kyung Chu, declared no potential conflicts of interest.

IHC-PO-047**Analysis of vertigo in chronic migraine through extended phenotyping**

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Objective: Vertigo is a common symptom in migraine symptomatology but its frequency in patients with chronic migraine (CM) is not well studied. We aimed to research the frequency of vertiginous symptoms in a well-defined group of patients with CM and explored potential associations with other migrainous symptoms.

Methods: A retrospective cohort analysis was performed by assessing the patient files of a tertiary headache clinic. A query was performed searching for the words “chronic migraine” in clinic letters containing extended phenotyping from the King's College London Headache Group between January 2014 and November 2018. All letters found were opened, read, analysed and entered into spreadsheets manually. The patients had a diagnosis of CM only and new- daily persistent headache was excluded. Analysis comparing CM with vertigo (CMwV) patients versus CM without vertigo (CMoV) patients was performed using unpaired student's *t*-tests and chi-square tests, without testing for multiple comparison due to the exploratory nature of the research. Significance levels were set at 0.05.

Results: After screening all retrieved cases from the query ($n = 431$), 376 patients with an exclusive diagnosis of CM were included for analysis. For the total cohort, the mean age was 44.4 years (SD 14.8) and 81% were women. Vertigo was an associated symptom in migraine attacks in 44% of all patients, with a distribution of 50% internal vertigo, 44% external vertigo and 5% both. CMwV patients had significantly higher rates of associated symptoms such as movement sensitivity (86% vs 75%; $p < 0,01$), nausea (81% vs 69%; $p < 0,01$), cranial allodynia (77% vs 55%, $p < 0.0001$) and visual blurring (36% vs 20%, $p < 0.001$) compared to CMoV patients. Also, CMwV patients had

more frequent presence of aura (60% vs 42%, $p < 0.001$) and more frequent presence of premonitory symptoms (87% vs 76%, $p = 0.045$).

Conclusion: We found that vertigo is a frequent symptom in migraine attacks of patients with CM, and that vertigo is frequently associated with other migrainous phenomena and aura. In conclusion, our data suggests that vertigo in CM can be part of a more ‘enriched’ phenotype.

Disclosure of Interest: None Declared

IHC-PO-281**Advances in the Direction Towards an Objective EEG Test for Migraine: A Data Driven Approach for Subtyping Classification of Migraine**

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¹Research and Development

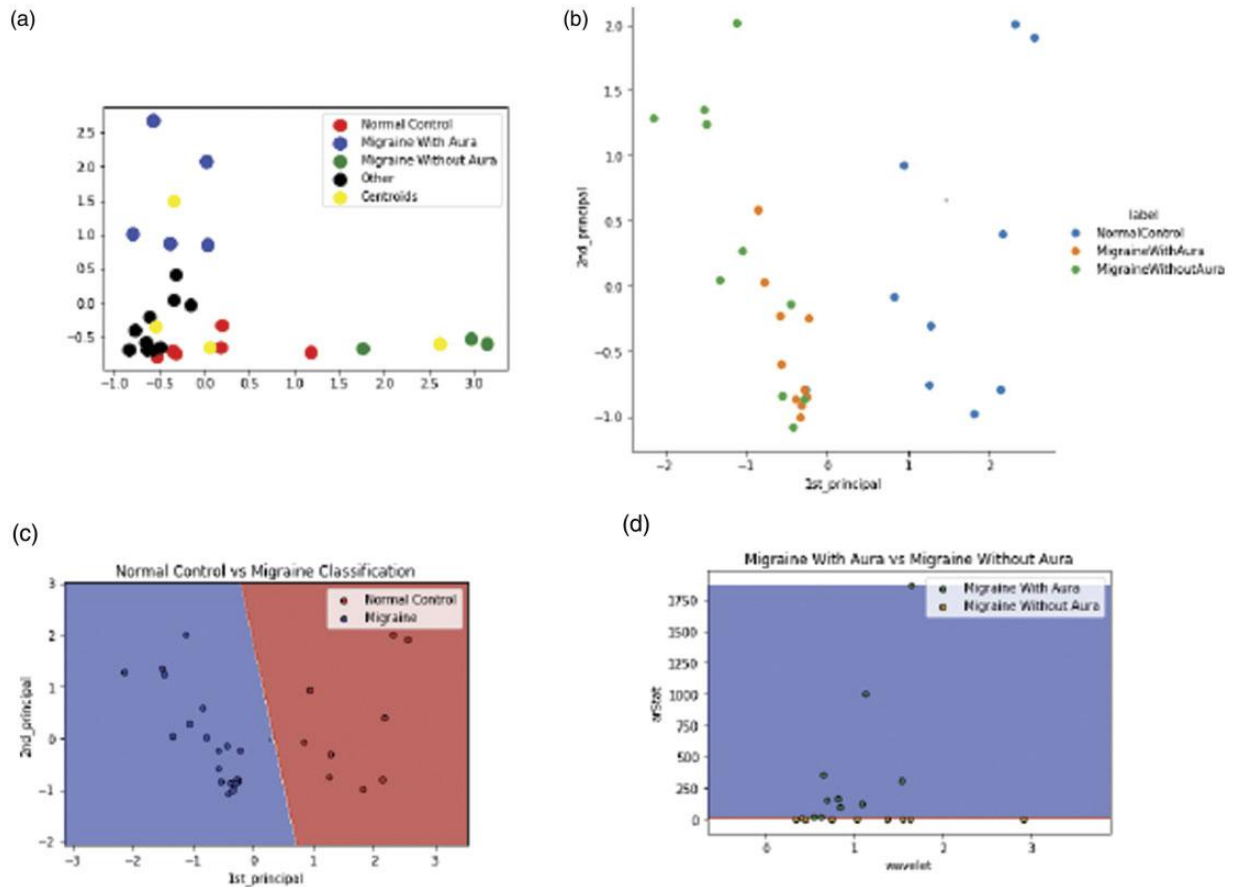
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Objective: Migraine has clinical subtypes with/without aura (MA/MwA). Objective quantitative features for subtypes could be an aid not only to diagnosis and monitoring but could also generate treatment targets for drug and non-drug treatments. Here we propose the use of electroencephalography(EEG) to perform a data driven approach that classifies patients into one of three categories: MA, MwA and normal control (NC).

Methods: Our dataset consisted of 10 MA, 10 MwA and 10 NCs. Migraineurs were screened using the ICHD-2 criteria. A two minute 32 electrodes (10–20 system) baseline recording was done. Three electrical characteristic features were obtained to characterize the EEG patterns: synchronization, transients, and frequency statistics. Feature selection and reduction techniques were performed on the sub-features of these 3 mutually independent features to preserve interpretability of the results. For the pattern classification portion of the algorithm, we used a two-step ensemble approach. Step one; use a linear support vector machine(SVM) model to differentiate M from NC using a projected 2D hyperplane of the combined effective features. Step two; use another SVM model to differentiate MwA and MwoA using 2 other electrical features.

Results: Performing direct 3 group separation using conventional techniques such as neural network, SVM, and decision trees, gave us a poor classification accuracy maximizing at around 67%. Our ensemble classification accuracy for step one and two were 97% and 83% respectively, resulting in an effective classification rate of 81%. To further illustrate the discrimination capabilities of our algorithm we plotted both our decision hyperplanes (Figure C,D).

Conclusion: We identified the existence of electrical subtypes for MwA using unsupervised clustering learning methods (Figure A,B). Using this knowledge we proposed



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a two-step classification algorithm to first separate NCs from Ms and then we subsequently separated the Ms into a MwA and MA group. This method has effective classification accuracy of 81%. This outperformed other known pattern classification techniques in differentiating NCs, MwA and MA. Future work may also look into optimizing error propagation as well as further reduction of overfitting of the models to the current data.

Disclosure of Interests: Mark Doidge is the president of Headache Science Inc.

IHC-PO-282

Elementary Visual Symptoms of migraine aura: A systematic review and proposal of an official list

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Objective: Visual disturbances are the most common feature of migraine aura (MA), occurring in 99% of auras. Visual aura symptoms are multifaceted, often complex, and highly variable. Studies of the clinical features of visual aura indicate that the perceived visual scenarios be effectively characterised by their basic features, “elementary visual symptoms” (EVS), such as zigzag lines, crescent shapes, and flickering lights. Our aim was to perform a review of all systematic recordings of visual disturbances in MA and to create an official list of EVS to guide future research and to improve the clinical characterisation of MA.

Methods: We performed a systematic review of previous prospective and retrospective recordings of visual aura symptoms to provide an overview of the different types of visual phenomena occurring during MA and their respective frequencies in patients.

Proposed Name	Description
1. Bright light [^]	Single area of bright light
2. Foggy/blurred vision	Foggy or blurred vision
3. Zigzag lines ^{^#}	Zigzag or jagged lines
4. Scotoma	Single blind area
5. Scotomata	Several blind/black areas
6. Small bright dots [^]	Small bright dots/stars
7. White dots/round forms ^{#*}	Medium sized white dots/round forms
8. Colored dots/round forms ^{^#*}	Medium sized coloured dots/round forms
9. Lines (colored lines) ^{^#*}	Lines (colored lines)
10. Geometrical shapes ^{^#*}	Geometrical shapes
11. 'Like looking through heat waves, water or oil'	'Like looking through heat waves, water or oil'
12. Visual snow	Dynamic, continuous, tiny dots usually black/gray on white background and gray/white on black background
13. 'Bean-like' forms ^{^#*}	'Bean-like' forms like a crescent or C-shaped
14. Hemianopsia	Blindness of half of the visual field
15. Deformed images	Deformed images (alteration of lines/angles)
16. Tunnel vision	Blindness in the whole periphery
17. Oscillopsia	Movement of stationary objects
18. Mosaic vision	Seeing mosaic-like
19. Fractured objects	Seeing fractured objects
20. Corona effect ^{^#*}	An extra edge on objects
21. Anopia	Total blindness
22. Micropsia	Objects appear smaller or more distant than they actually are
23. Macropsia	Objects appear larger or closer than they actually are
24. Like a negative film	Seeing like a negative film
25. Complex hallucinations ^{^*}	Visual perception of something not present (e.g. objects, animals, and persons)

Proposed list of all EVS of migraine aura and their description.

For some EVSs, when reported, patients should be asked about some additional features:

* colour;

internal pattern (suggested text: "If the inside of the EVS does not have a homogeneous color but is made up an internal pattern (for example zigzag lines or chessboard) please describe it in words") ;

[^] scintillation / flickering (suggested text: "Is/are EVS scintillating (like stars or intermittent lights) and/or flickering (as rapid movements like the wings of a butterfly)?");

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Results: We found 11 retrospective studies and three prospective studies. The number of EVS reported by patients in the studies ranged from two to 23. The total number of EVSs reported was 30. We combined 8 symptoms into four and we deleted one symptom as it was instead a feature that can be used for several EVSs (flickering/intermittent quality). In Figure we reported the final list, which contained 25 EVDs. We propose that some EVSs should be further characterized by the presence or absence of the features "scintillation" and/or "flickering" ([^]), and some EVS should be further characterized by their colour (^{*}) and "internal pattern" ([#]).

Conclusion: We created a comprehensive list of elementary visual symptoms reported by migraine patients based on all currently available data from clinical studies.

Currently, there is an unmet need of a common classification of visual aura symptoms to improve the clinical characterisation of the disorder and to aid future studies of migraine aura.

We propose that the present list should be implemented and further developed within the International Classification of Headache Disorders of the International Headache Society.

Disclosure of Interest: None Declared

IHC-PO-283**Changes in the characteristics of the aura as a presentation of migrainous infarction in a patient with migraine. Case report**

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and Lilia Nuñez-Orozco¹

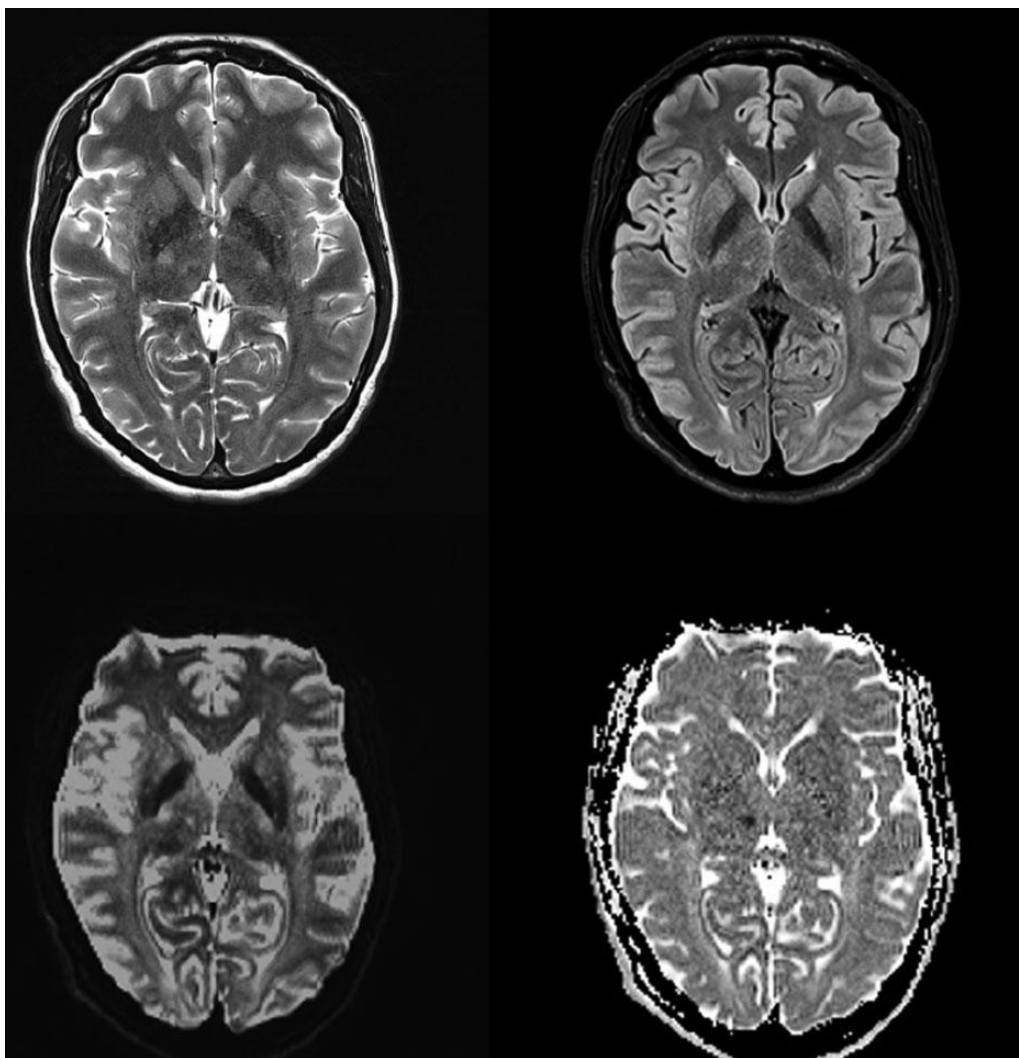
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Objective: We present the case of a patient with a diagnosis of migraine with aura who had a migrainous infarction which manifested as a typical aura with different characteristics from the usual ones, but without fulfilling ICHD3 criteria.

Methods: A 31-year-old woman with a history of recurrent headache since she was 10 years old. Her episodes begin with negative scotomas in the central region of the visual field lasting 15 minutes. Never had other symptoms

of aura. After this aura, she had pulsatile unilateral headache, intense, up to 48 hours lasting, 3 times per year. From the beginning of her disease she was in treatment only with analgesics in case of pain. Never used prophylactics. In march 2018 she presented episode of positive scotomas of intense brightness, with paresthesias of the left hand, ascending to the shoulder, and later difficulty in language articulating. The succession of these symptoms lasted 45 minutes, then complete remission of all symptoms. After this, she had headache of the same characteristics of her usual episodes of migraine. At the time of his attention, the neurological examination was normal and she had headache only.

Results: Although the patient presented a complete reversible typical aura according to the criteria of ICHD 3 and none of the aura symptoms persists more than 60 minutes, brain MRI was performed. It shows small acute ischemic lesion in the right thalamus.



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Conclusion: In this case, we can observe that the presentation of migraine infarcts can simulate a complete reversible typical aura and not meet ICHD 3 criteria. The clinical suspicion of migraine infarction, despite the criteria, could be based on the clinical presentation of the aura, different from the usual ones.

Disclosure of Interest: None Declared

IHC-PO-284

Headache and Work-related Stress in Nursing Staffs and the copying Strategy: Taiwan Data in a 1250-bed Medical Teaching Center

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Objective: Primary Headache is the most symptom for nursing staffs in their daily care for patients, while work-related stress played a major role in this healthcare issue

Methods: Semi-structure questionnaire were asked for nurses participants in a medical teaching center in southern Taiwan, including intrinsic stress (4 items), extrinsic stress (6 items), and perceived causes of headaches (5 items) and the copying strategy was also queried. By good validation (Cronbach coefficient = 0.89) in pre-tests and proper statistics by structure equation modeling (LISREL), stress and headaches relationship was estimated

the co-efficiency and its significance. The copying strategy for nursing staffs was also demonstrated.

Remark 1: KMO: Kaiser-Meyer-Olkin sets some samples as suitability measure and the information as the suitable guide of factor analysis.

2: KMO > 0.8 means this information is suitable for the factor analysis.

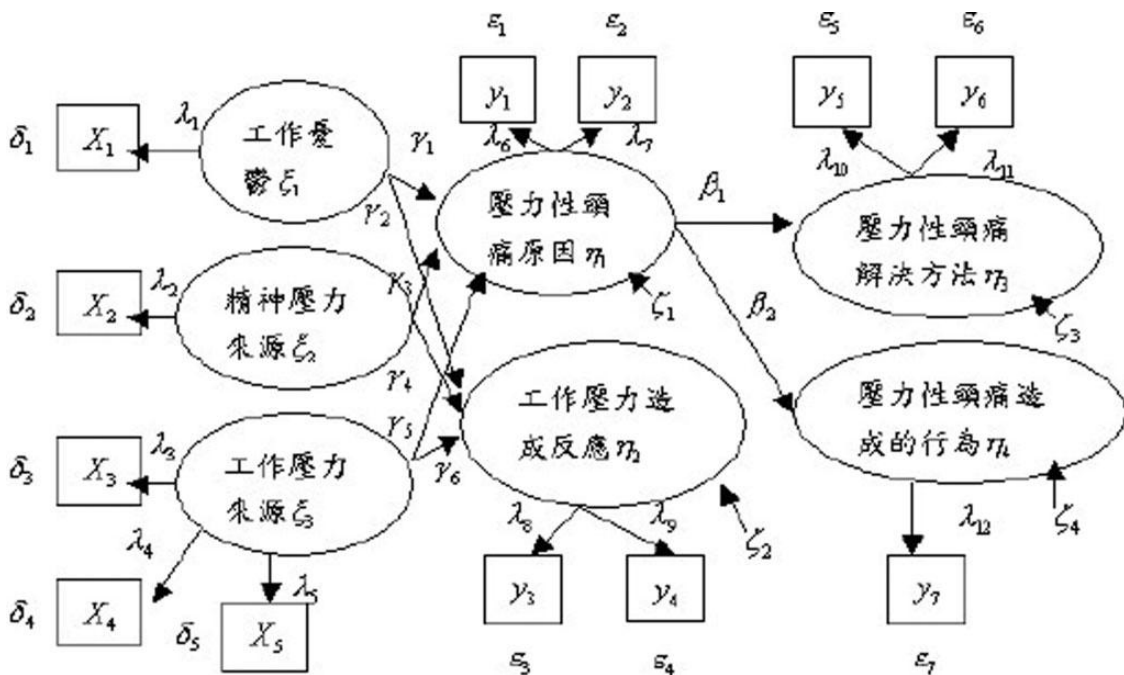
3: KMO < 0.5 means this information is not suitable for the factor analysis.

Results: 786 responders (84.6%) among 930 nursing staffs, and migraine headache (57.6%), tension-type headache (TTH)(27%), and mixed both (9.6%). Only 12 sufferers had chronic attacks based on ICHD-3 criteria, of who all took medications (topiramate 50–150 mg) with

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Table I. Factors analysis on TTH

Variable name	Accumulated variable (%)	KMO
Work melancholy	58	0.611
Physical tension source	54	0.787
Work stress source	60	0.689
TTH cause	69.3	0.841
Reactions on work stress	62.55	0.696
Coping strategies on TTH	61	0.527
Causal behaviors of TTH	60	0.839



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non-pharmacological methods for headache relief. In subgroup analysis, TTH was dominantly in un-married, female nurses, and aged 20–29 young staffs (80.8%), especially in ICU subdivision (21.2%). Work-stress came from duty-shifting, older aged, married, low-level staffs were statistically significant ($p < 0.05$). Work-stress came from prolongation of working time was significant in different subdivision of nurses, more occurred in ICU staffs (23.7%). The coping strategies for headaches in nursing staffs are sleep, medications, rest, doctor seeking and psychological help in sequences. They rarely seek for mindful-based stress reduction training.

Conclusion: The work stress in nursing staffs is statistically associated with primary headache and their daily healthcare job and coping strategy. The sources of stress including physical tension, melancholy, work overload, or time prolongation are all positively linked to. It warrants for further research for the health in nurses and their caring works.

Disclosure of Interest: None Declared

IHC-PO-285

Clinical differences between pulsatile and non-pulsatile migraine without aura. Results from a population in Mexico

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Objective: Information about headaches in México is scarce. In 2015 we launched PREMECEF (*Primer Registro Mexicano de Cefaleas, First Mexican Registry of Headaches*). It functions as an e-medical record and the information is entered by physicians. We have presented global results previously. We wanted to know if there was a difference in clinical features between pulsatile and non-pulsatile migraine w/o aura.

Methods: We collected from the registry all patients with the diagnosis of migraine w/o aura and compared the main clinical features with descriptive statistics.

Results: There were 489 registries, 97 patients with migraine w/o aura, 70 women with median age of 37.5 (men 31.9). The main differences were in the presence of kinesiophobia (22.2% vs 41.4%), the duration of pain (longer in the non-pulsatile group), and the presence of triggers: 41.4% vs 26%, pulsatile/non-pulsatile, with no food triggers in the non-pulsatile. There was only one patient with prodromal period in the non-pulsatile vs 7 in the pulsatile.

Conclusion: The origin of the pulsating quality of pain is not completely understood. We hypothesized that, although both diagnosis are based on the criteria of ICHD, there could be some differences between them. Our results show some, but nothing clearly convincing. Since there are no biological markers for migraine, we are currently analyzing the longitudinal data of treatment responses.

Disclosure of Interest: None Declared

IHC-PO-286

International Classification of Headache Disorders (ICHD-3): the nosological conflict between cervicogenic headache and other headache disorders

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Objective: The distinction between primary and secondary headaches is the principle forming respectively ICHD-3 Part 1 and Part 2. ICHD-3 recognises that a headache disorder, normally regarded as primary, may in fact be secondary, as per 'How to use this classification', paragraph 9. But when a patient with migraine or cluster headache has cervical signs, is it a primary disorder with coincidental neck symptoms or a cervicogenic, i.e. secondary, headache with a migraine or cluster phenotype? This question has been addressed before: preference should be given to the primary disorder until a firm diagnostic anchor for cervicogenic headache is found (Goadsby, 2003). Our objective is to highlight the value of invasive tests as advocated by Bogduk&Govind, 2009, and give more nosological weight to cervicogenic headache.

Methods: We report clinical observations of ICHD-3 Part 1 and Part 3 types, in theory non-cervicogenic, that show cervical signs and behave like cervicogenic headache.



Results: Case 1. F. 58, 1-year history, unilateral, not strict, severe, throbbing headache, mostly temple, every other day, with nausea, photophobia, avoidance of movement and ipsilateral lacrimation. *Chronic migraine, ICHD-3 1.3*

Case 2. M. 53, 3-year history, strictly unilateral, severe, throbbing pain, temple/peri-orbital, 'pushing the eye out', up to 2 h duration, 3–4 times a week, no spontaneous remissions, with restlessness and prominent ipsilateral cranial autonomic symptoms. *Chronic cluster headache, ICHD-3 3.1.2*

Case 3. F. 49, 2.5-month history, strictly unilateral, suicidal, short lasting, shooting pain, up to 1 min, limited to trigeminal distribution V2-3, and with prominent trigeminal triggers. *Trigeminal neuralgia, ICHD-3 13.1*

All three patients had ipsilateral neck complaints and/or cervical paravertebral tenderness. An immediate interruption of the headache pattern and subsequent remission was achieved by a single cervical medial branch block using plain L-bupivacaine (Figure) and continuous neck exercises.

Conclusion: ICHD-3 does acknowledge that migraine, cluster headache and trigeminal neuralgia can be secondary to another disorder, such as intracranial lesion or vascular pathology. Our cases illustrate the possibility of a cervical cause that should be recognised and treated accordingly.

Disclosure of Interest: None Declared

IHC-PO-287

Proposed new diagnostic criteria for chronic migraine

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Objective: ICHD-3 criteria for chronic migraine (CM) may include a mixture of migraine and tension-type-like headaches and do not account for patients who have a high frequency of migraine but no other headaches. We suggest classifying CM as ≥ 8 migraine days per month (proposed CM) disregarding the need for ≥ 15 headache days per month.

Methods: Patients from the Danish Headache Center and a Russian student population with CM were compared to patients with proposed CM. Danish registries were used to compare the socioeconomic impact of CM in these two groups.

Results: There was no difference in the demographic profile between the two groups; the number of lifelong or annual attacks ($p > 0.3$), comorbid diseases, or self-reported effect of triptans ($p = 1$). Proposed CM patients

purchased more triptans than CM patients ($p = 0.01$). CM patients received more early pension ($p = 0.00135$), but no differences with regards to sickness benefit ($p = 0.207$), cash assistance ($p = 0.139$), or rehabilitation benefit ($p = 1$).

Conclusion: Patients with proposed CM are comparable to CM patients with regards to chronicity and disability. Extending the definition of CM to include patients with proposed CM will ensure that patients with significant disease burden and unmet treatment needs are identified and provided appropriate access to the range of treatment options and resources available to those with CM.

Disclosure of Interest: None Declared

Headache Disorders in Children and Adolescents

IHC-PO-048

Is pediatric medication overuse headache really due to medication overuse?

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Objective: Medication Overuse Headache (MOH) is a headache occurring on ≥ 15 days/month in patients with pre-existing primary headache and developing as a consequence of regular overuse of symptomatic medication. Aim of this study was to analyze the clinical features of pediatric MOH, with particular emphasis on the applicability of ICHD-3 criteria.

Methods: We retrospectively analyzed clinical data of pediatric patients with MOH; the clinical diagnosis was verified according to ICHD-3 criteria. Although no more included in the diagnostic criteria, we analyzed how many patients presented a clinical benefit after discontinuation of overused medication.

Results: We identified 42 subjects diagnosed with MOH (31 F, 11 M), aged 8–17 years (mean 13.4 years). They all presented with chronic migraine, 9% fulfilled a diagnosis of migraine with aura. Photo- and photophobia were present in 81% of patients, nausea/vomiting in 30%, dizziness in 18%. ICHD-3 criterion A was fulfilled by 40/42 patients (95%), criterion B by 35/42 (83%), and criterion C by 40/42 (95%). Nineteen patients (45%) did not present an improvement of headache after medication overuse cessation.

Conclusion: The old criteria required a development or marked worsening of the headache during medication overuse, and a resolution within 2 months after medication withdrawal. Both these criteria disappeared in

ICHD-3. Our data show that, without the necessity of demonstrating a clear and direct correlation with abuse and discontinuation of symptomatic medications, a definite diagnosis can be achieved in a high rate of patients with a clinical suspicion of MOH. Nearly half of patients with MOH didn't improve after medication overuse cessation, thus raising the doubt of a true causal relationship between medication overuse and chronic headache. A high rate of patients with a definite diagnosis of MOH according to new criteria continued to present a high frequency headache despite the withdrawal of overuse.

Disclosure of Interest: None Declared

IHC-PO-049

Cyclic vomiting syndrome and benign paroxysmal torticollis are associated with a high risk of developing primary headache: a longitudinal study

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Objective: Periodic migraine variants are a group of disorders affecting patients with migraine or with an increased risk of presenting it, and likely represents an early life expression of migraine. Cyclic vomiting syndrome (CVS) and benign paroxysmal torticollis (BPT) are well characterized and represent a frequent cause of request for specialistic consultations. Aim of this study is to longitudinally assess the rate of headache in patients presenting with CVS and BPT during infancy, and to define the main clinical features of the disorder.

Methods: We administered a questionnaire to the parents of all our pediatric patients with previous diagnosis of CVS and/or BPT according to ICHD-3; questions were focused on the main clinical features of the disorder as well as the prognosis, with particular emphasis on the development of headache.

Results: For the final analysis we considered 82 patients with CVS and 33 with BPT. Seventy-nine percent of patients with CVS presented with headache during the follow-up, with a mean age at onset of 6 years; 67% of patients with BPT suffered from headache during the follow-up, with a mean age at onset of 5 years.

Conclusion: CVS and BPT are associated with a very high risk of developing headache, mostly migraine, later in life. In both groups of patients, the vast majority presented

with different periodic migraine variants at different ages, thus suggesting an age dependent evolution of migraine-like symptoms before the onset of clear migrainous headache.

Disclosure of Interest: None Declared

IHC-PO-050

Pediatric tension-type headache: the role of co-morbidity with emotional and behavioral disorders

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Objective: To assess in children and adolescents suffering from frequent episodic or chronic tension-type headaches (TTH) the incidence of co-morbid emotional and behavioral disorders and the patients' daily difficulties in emotions, concentration, behavior, or being able to get along with others.

Methods: 150 patients with TTH (75 male and 75 female) aged 8–16 years were included into the study. The severity of emotional and behavioral problems was analyzed in comparison with their healthy peers (103 boys, 117 girls) by means of parents' interviewing with the «Strengths and Difficulties Questionnaire» (SDQ) [Goodman R., 2001]. The 25 SDQ items are divided into 5 scales of 5 items: the Hyperactivity-Inattention scale, the Emotional symptoms scale, the Conduct problems scale, the Peer problems scale and the Prosocial Behaviour scale.

Results: Total difficulties scores measured by SDQ were significantly higher in boys ($16,2 \pm 0,7$) and girls ($14,3 \pm 0,7$) with TTH compared with their peers (respectively $7,9 \pm 0,4$ and $7,7 \pm 0,4$, $p < 0,001$). Patients with TTH had significantly more prominent manifestations than their peers ($p < 0,001$) on the four SDQ scales, including Hyperactivity and Inattention, Conduct problems, Emotional symptoms, Peer problems. However, they did not differ from the peers on Prosocial Behaviour scores. Clinical assessment revealed the following disorders in many patients with pediatric TTH: attention deficit hyperactivity disorder – ADHD (in 45,3% boys and 13,3% girls), oppositional defiant disorder – ODD (26,7% boys, 18,7% girls), with co-occurrence of ADHD and ODD in some (17,3% boys, 10,7% girls). Moreover, most patients with TTH had anxiety disorders (68,0% boys, 77,3% girls) and some adolescents had dysthymic disorder (4,0% boys, 2,7% girls) (Fig.1).

Conclusion: Pediatric TTH clinical manifestations may be dependent on the co-morbid emotional and behavioral disorders. Co-morbid disorders must be taken into

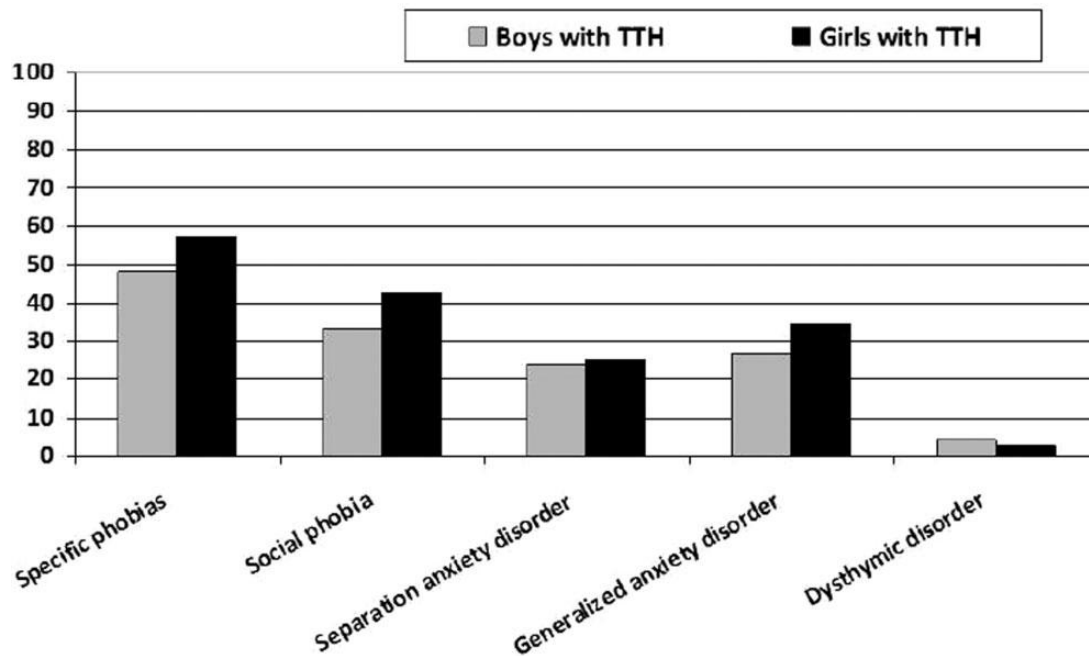


Fig. 1. The incidence (%) of emotional disorders in boys and girls aged 8-16 years with tension-type headaches.

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account for individualized treatment program including drug therapy and non-pharmacological approaches in TTH.

Disclosure of Interest: None Declared

IHC-PO-051

The usefulness of red flags in preschool headaches: a study in pediatric emergency department

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Objective: The aim of current study is to evaluate red flags' specificity and correlation with neuroimaging abnormalities in preschool children admitted in our Emergency Department for headaches. In literature we currently found no evidence regarding preschool children evaluated in Emergency Department, however several

works suggest an increased in incidence of dangerous headaches in this population.

Methods: We collected 377 clinical cases (168 Males – 209 Females) of children from 1 to 7 years old, suffering from headache, admitted in the Emergency Department of our Hospital (Ospedale dei Bambini, Palermo), from October 2015 to December 2018. Our sample represents 22,9% of total access for headache.

Results: We found that 56,23% of them (212 children) had one or more red flags from the list and 125 children between them (58,96%) underwent CT. We found several different outcomes: 103 children showed benign abnormalities (cerebellar tonsils ptosis, inflammatory processes of paranasal sinuses or nonspecific abnormalities) certainly not related with clinical presentation, 22 children showed no abnormalities, and only 3 children (0,8%) showed major abnormalities (2 tumors and 1 hemorrhage).

Conclusion: Our study, according to other studies, highlights that headache in preschool age is less infrequent than expected. We showed that several children (more than 50%) presented at least one red flag. The correlation between red flags and dangerous abnormalities in neuroimaging is not so direct; in addition, in this age the red flags does not increase the recognition of dangerous headaches. In conclusion, in presence of normal neurological

evaluation we can decide to avoid or postpone neuroimaging examination.

Disclosure of Interest: None Declared

IHC-PO-052

Sleep onset latency and sleep duration in Siberian adolescents with a tension-type headache and migraine

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Objective: Migraine and tension-type headache (TTH) may be associated with sleep disturbance. On the other hand, both headache and sleep disorder may be manifestations of the same mental conditions such as anxiety and depression. Sleep disturbance in adolescents with different types of headache is not studied well.

Methods: 52 urban Siberian (Krasnoyarsk, Russia) adolescents aged 12–18 attending a tertiary medical center for primary diagnosis of a tension-type headache (n=29, TTH, including the subtypes “frequent episodic TTH, chronic TTH”), migraine (n=12), and mixed type (n=11, TTH + Migraine). All of them and 44 healthy matched controls were asked “During the past month, how long (in minutes) has it usually taken you to fall asleep each night?” to estimate sleep onset latency. Bedtime and wake-up time on school days were assessed with the question: “At what times (hours:minutes) do you usually go to bed and wake up on school days?”. Data are shown as median (25–75% quartiles). Kruskal-Wallis test was used.

Results: Significant positive associations were detected between sleep onset latency and migraine presence: the time usually taken migraine adolescents to fall asleep were remarkable higher (in migraine and TTH + Migraine

groups, Table 1). Sleep duration exhibited lowering in hours in case of TTH presence (in TTH and TTH + Migraine groups, Table 1).

Conclusion: Sleep disturbance is different in adolescents with different types of headache: for migrainers is characteristic higher sleep onset latency (possibly, due to emotional problems presence [1]), while for adolescents with TTH is characteristic lower average sleep duration time. The reported study was funded by RFBR according to the research project № 18-29-22032\18.

Disclosure of Interest: None Declared

Reference

1. Tereshchenko S., Shubina M. Sleep onset latency and psychologic problems in Siberian adolescents: the school-based study // Journal of Sleep Research. – 2018. – Vol. 27 (Suppl. 1). – P. 328.

IHC-PO-053

Primary headache and pain-related non-cyclic functional gastrointestinal disorders assigned by questionnaire on pediatric gastrointestinal symptoms ROME-IV version (QPGS-RIV) in Siberian adolescents

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Objective: Many common complaints in adolescent medicine practice, such as recurrent headache and recurrent abdominal pain (RAP) have similar risk factors, accounting for emotional stress, anxiety and depression. Data regarding the association of recurrent headache and newly developed ROME-IV criteria for functional gastrointestinal disorders in children and adolescents are limited.

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Table 1. Sleep characteristics in adolescents with different types of headache.

Sleep characteristics	No headache (n = 44)	TTH (n = 29)	Migraine (n = 12)	TTH + Migraine (n = 11)	p (K-W test)
Sleep onset latency, minutes	17.2 (14.7–19.7)	20.6 (15.4–25.8)	27.9 (23.9–31.9)	34.5 (25.1–44.0)	0.002
Sleep duration, hours	8.4 (7.9–8.9)	7.5 (7.3–7.8)	8.4 (7.9–8.9)	6.6 (6.1–7.0)	0.025

Abstract number: IHC-PO-053**Table 1.** Relationship between primary headache and functional gastrointestinal disorders assigned by QPGS-RIV (%)

Headache	Functional Dyspepsia n = 44	Irritable Bowel Syndrome n = 17	Functional Abdominal Pain n = 1
No headache (0) n = 59	18.6 (10.8–30.4)	5.1 (1.8–13.9)	0
TTH (1) n = 55	21.8 (13.0–34.4)	7.3 (3.0–17.3)	0
Migraine (2) n = 35	37.1 (23.1–53.8)	8.6 (3.1–22.5)	0
TTH + Migraine (3) n = 28	28.6 (15.3–47.2)	25.0 (12.7–43.5)	3.6 (0.8–17.8)
p*	p0-2 = 0.049	p0-3 = 0.008 p1-3 = 0.027 p2-3 = 0.082	

*For ease of exposition, only p values ≤ 0.1 are displayed.

Methods: 118 urban Siberian (Krasnoyarsk, Russia) adolescents aged 12–18 attending a tertiary medical center for primary diagnosis of a tension-type headache (n = 55, TTH, including the subtypes “frequent episodic TTH, chronic TTH”), migraine (n = 35), and mixed type (n = 28, TTH + Migraine). All of them and 59 healthy matched controls were tested with QPGS-RIV. Data are shown as proportions (95% confidence interval). Two-tailed exact Fisher was used.

Results: Significant positive associations were detected between migraine and functional dyspepsia presence (p = 0.049, Table 1) as well as between migraine and irritable bowel syndrome which was more characteristic for TTH + Migraine group (Table 1).

Conclusion: Our study revealed a strong relationship between migraine and pain-related non-cyclic functional gastrointestinal disorders, which can result from the effect of these co-morbid diseases with emotional stress, depression, and anxiety. The high level of functional dyspepsia in headache adolescents may also result from analgesics overuse in “headachers”.

Disclosure of Interest: The reported study was funded by RFBR according to the research project № 18-29-22032\18.

IHC-PO-288**What are the primary concerns of children and parents attending a first appointment in a specialist children’s headache service?**

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Objective: Children and young people may experience difficulties in expressing their concerns verbally in an appointment with a professional team they are meeting for the first time. To support biopsychosocial assessment and multidisciplinary care, children and young people attending a UK specialist headache clinic and their parents were given the opportunity to record their key concerns in writing prior to the first appointment.

Methods: Parents and children were separately given a space to record in their own words up to three concerns. Questionnaires completed between January 2014 and March 2019 were included in the analysis. The responses were reviewed, key themes identified and each concern was categorised within these themes.

Results: 183 children and young people recorded at least one concern, with 437 concerns recorded in total. 216 parents recorded at least once concern and 564 parent concerns were recorded in total.

The following categories were identified: Health, Prognosis, Education, Cognition, Family, Friendship, Future, Weight/Physical Appearance, Emotions, Activities, Sleep/Tiredness, Other.

For children, 35.93% of concerns related to health or prognosis. The percentage of parent concerns relating to health or prognosis was higher at 48.58%.

Children recorded a higher proportion of education related concerns (27.69%). This included concerns about the impact of their headache condition on education and others which did not appear directly related.

Children were more likely to report concerns relating to friends or family (9.84%). Parents more frequently

highlighted concerns relating to emotions (10.46%) than children.

Conclusion: When given the opportunity to record their main concerns in advance of a first appointment parents and children recorded a range of concerns, enabling these to be recognised and responded to. There were differences between the frequency with which children and parents raised different areas of concern, highlighting the importance of supporting children to express their own concerns.

Disclosure of Interests: Hayley Bullock, Claudia Johnston, Clare Lasserson, Sophie Mitchell- none
Prab Prabhakar-

IHC-PO-289

Delayed Diagnosis in Pediatric Headache in India: An Outpatient Survey

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Objective: To study the factors associated with delayed diagnosis of pediatric headache among children attending a public hospital in India.

Methods: This study was conducted at the pediatric outpatient department of a tertiary-care public hospital over a 10-month period. Clearance was taken from the Institutional Ethical Committee and informed written consent from parents of the study subjects. Consecutive children, presenting to us for the first time, with a history of recurrent headache were evaluated. Children with secondary headaches were excluded.

Disability was assessed using PedMIDAS score, and headache severity was assessed using a 10-Point Visual Analogue Scale. We studied the association between delayed diagnosis and gender, headache type, previous Complementary and Alternative Medicine (CAM) use, parental education, family history of headache, and distance from hospital. All analyses were done by Epi Info software.

Results: 43 children aged 5–17 year (median age, 10.7 years; 22 boys) with recurrent headache were evaluated. 26 of these had migraine and 11 had Tension type headache (TTH) (ICHD III).

Majority of the patients (32, 74.4%) had waited for 1 to 3 years after onset of headache to seek medical attention. The median time of delay from onset of first episode of headache to definitive diagnosis was 14 (IQR 12–24) month. The commonest reason given for this delayed medical attention seeking was ‘no significant morbidity’ – all had PedMIDAS scores below 50. All were using CAM and/or Over-the-Counter (OTC) medications. Five patients (11.6%) were living in rural areas where medical facilities were far-flung causing delay in seeking medical help.

No relation was found between delay in diagnosis and patient age (correlation coefficient, $r=0.31$), distance from hospital ($r=0.22$), headache severity (VAS) ($r=-0.28$) and PedMIDAS score ($r=-0.01$). No association was found between the delay in diagnosis and gender (Mean delay, female vs male, 17.0 vs 17.5), religion (Hindu vs Muslim families, 17.7 vs 16.8), or family history of headache (family history vs no family history, 14.85 vs 18.3; $P=0.68$). No association was seen between the headache type and delay in diagnosis (Migraine vs non-migraine headache, $P=0.07$).

Conclusion: Headache is under-diagnosed in pediatric patients in our setting, which is frequently the result of reliance on CAM and OTC medications.

Disclosure of Interest: None Declared

IHC-PO-291

Are ICHD3 criteria suitable for primary headache diagnosis in children and adolescents?

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Objective: We conducted a series of studies aiming at investigating whether the ICHD3 criteria can be effectively used for the primary headache diagnosis in pediatric age.

Methods: Patients (0–18 years) referred to our Center with a primary headache were recruited. The ICHD3 and ICHD2 criteria were used for diagnosing the type of headache.

Results: When considering patients up to 6 years of age with episodic headache, the diagnosis remained undefined in around 32% of patients with both ICHD 2 and ICHD3 criteria. The main problem was the duration of the attacks which was often shorter than the lower threshold for both migraine and tension-type headache. In patients presenting with headache associated with aura, a definite diagnosis of typical migraine with aura was reached in 77.7% and 15.3% of patients with the ICHD3 and ICHD2 criteria, respectively. The ICHD3 criteria showed the advantage of not considering the headache attack characteristics for the final diagnosis. In children and adolescents with chronic headache, undefined diagnoses were more frequent with the ICHD2 than ICHD3 criteria, mostly due to the different classification of patients with medication overuse headache (MOH). It is to be underlined that in the younger children (up to 6 years of age) a defined classification of their chronic headache was hampered by the short

duration of their attacks. Lastly, in children and adolescents overusing drugs, a definite diagnosis of MOH was obtained in 76% and 43% of patients with the ICHD3 and ICHD2 criteria, respectively. The difference was due to the need of demonstrating a significant improvement with the drug withdrawal in the ICHD2 criteria.

Conclusion: Our studies show that, though providing an advance as compared to the ICHD2, the ICHD3 criteria show some limitations in pediatric age, especially for the youngest children. A greater attention to the specific characteristics of the primary headaches at this age would be hopeful in the future editions of the International Classification.

Disclosure of Interest: None Declared

IHC-PO-292

Effect of Cinnarizine for the Prophylaxis of Vestibular Migraine in Adolescents

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Objective: Vestibular migraine is a term used to describe episodic vertigo or vestibular symptoms attributed to migraine. Vestibular migraine is the most common cause of episodic vertigo among children and adolescents. Cinnarizine has acceptable effect on both vertigo and migraine. We designed a study to compare the efficacy of cinnarizine with that of well-known preventive agents in the prophylaxis of adolescent vestibular migraine.

Methods: This was a retrospective, single-center study of the effects of cinnarizine on vestibular migraine in adolescents. Adolescents (15–19 years) who experienced vestibular migraines were recruited into the study. The group taking cinnarizine stopped other preventive drugs and only kept cinnarizine. The control group that maintained the existing drug retained the existing drug without altering the drug. All groups were examined for sex, age, episodic or chronic status, accompanying symptoms, Visual Analog Scale (VAS) score, Pediatric Migraine Disability Assessment (PedMIDAS) scale, and headache day per month. These indicators were reevaluated after 3 months.

Results: The study included twenty subjects with the cinnarizine group and twenty-one subjects with the control group. The headache frequency was 20.0 ± 8.34 days per month in the cinnarizine group and 18.5 ± 7.74 days per month in the control group. The VAS score of the cinnarizine group was 7.2 ± 1.15 and the PedMIDAS score was 75.3 ± 12.82 . The VAS score of the control group was 7.2 ± 1.18 and the PedMIDAS score was 70.2 ± 18.12 .

There was no statistically significant difference between the two groups ($p = 0.917$ in VAS, $p = 0.315$ in PedMIDAS). After 3 months, many cinnarizine group patients showed improved accompanying symptoms. The headache frequency was 5.75 ± 6.46 days per month, VAS was 2.6 ± 2.06 , and PedMIDAS was 17 ± 20.80 ($p < 0.05$). When compared with the control group, these values showed better results in the cinnarizine group (headache frequency was 13.4 ± 8.70 per month ($p = 0.003$), VAS was 5.52 ± 2.20 ($p < 0.001$), and PedMIDAS was 40.0 ± 22.09 ($p = 0.001$)).

Conclusion: Although our study is a single institutional study with a small number of patients, this study confirmed that cinnarizine is a safe drug for adolescents. In addition, cinnarizine was found to be an effective drug for vestibular migraine in adolescents.

Disclosure of Interest: None Declared

IHC-PO-293

School attendance in children with headache disorders

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Objective: The burden associated with headache conditions is well recognised. In childhood education is one of the areas of life most affected and children accessing specialist headache services represent a group likely to be experiencing the greatest impact. To understand this impact the attendance levels of children attending a first appointment were collected and analysed.

Methods: Children and parents were asked to record school attendance over the last term within a pack of questionnaires completed as part of assessment. The Department for Education definition of attendance of 90% or less as 'persistent absence' was used in the analysis.

Results: Self reported: 161 children and young people recorded their attendance percentage. 103 (63.98%) reported attendance of 90% or lower, meeting the threshold for persistent absence. This was more common amongst females (74.76%) than males (47.27%) and amongst children of secondary school age (65.25%) compared to younger children (55%).

The mean attendance percentage was 73.26%. Attendance ranged from 0–100%, with a similar number reporting 0% ($n = 9$) and 100% ($n = 8$).

A higher percentage of children with persistent school absence reported symptoms leading to scores above the clinical threshold on each scale of the Revised Children's Anxiety and Depression Scale (Chorpita et al. 2000).

Parent reported: Attendance percentages were recorded by 180 parents, ranging from 0–100% with a mean of 76.65%. 111/180 parents reported persistent school absence.

The majority of parents indicated their child attended a mainstream school (151/180, 83.89%). 38/180 (21.11%) parents reported their child was accessing a psychology or counselling service, with this more frequently reported for those with persistent school absence (26.13%).

Conclusion: Many children accessing specialist headache services report levels of school attendance indicating persistent absence. Research into the long term impact of this for children with headache conditions would be beneficial. It would also be helpful to explore factors that may contribute to the wide variation in levels of attendance reported in order to support the development of services that best meet the needs of this group.

Disclosure of Interests: Hayley Bullock, Claudia Johnston, Sophie Mitchell- none
Prab Prabhakar-

IHC-PO-294

Telemedicine for Outpatient Headache Follow-up in a Community Pediatric Neurology Clinic

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Objective: Frequent headache follow-up may be crucial to decrease headache frequency in a pediatric population. For patients who live far from clinic or have disabilities, it can be challenging to return to care for a condition that is not life-threatening.

We conducted a pilot study to determine the feasibility of telemedicine for outpatient headache follow-up in a non-academic pediatric neurology clinic.

Methods: For nine months, we offered English-speaking patients aged 8–18 virtual telemedicine follow up for headache through a secure telehealth platform with a single provider. Patients were asked to fill out an anonymous 6 question survey about their telemedicine experience. No-show and late visits were compared to our in-clinic rates for headache follow-up. Reimbursement was also tracked. Many patients were offered telemedicine but preferred to follow up in clinic. Their reasoning was documented without a formal survey.

Results: Patients who chose telemedicine for headache follow-up were pleased with their experience, citing decreased transportation time and fewer days of school and work missed. Many patients who chose telemedicine lived far from clinic, but a large number lived within 5 miles of the clinic. No-show rate was extremely low and

patients were never late. Insurance reimbursed telemedicine visits with the same billing parameters as in-clinic visits, as required by parity laws in Oregon, USA.

Conclusion: We discuss the telemedicine experience for our physicians, clinic support staff, and patients. We found this to be an extremely successful pilot project. In the future, we intend to determine whether increased frequency of visits through telemedicine can improve pediatric headaches by encouraging healthy lifestyle choices.

Disclosure of Interest: None Declared

IHC-PO-053A

Altered sensory processing patterns correlate with disease severity and quality of life among children with Migraine

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Objective: Headaches are common among children and about 80% complain about headaches. Migraine and Tension Type Headaches are the most common primary headaches in children and the prevalence of migraine in about 8%. Sensory symptoms are common; before, during and after, the migraine attacks. They may be a part of a wider concept called sensory processing disorders that include extreme hyper or hypo sensitivity to sensations. However, the knowledge about sensory processing patterns of children and youth with headaches as well as its interaction with child's emotional aspects and quality of life is scarce.

Methods: 134 children between the ages of 8 and 12 participated in this study. 54 children (22 boys and 32 girls) with migraine were prospectively recruited from pediatric neurological clinics during the years 2014–2017. The control group included 80 healthy children. Both groups filled Health and demographic questionnaire, headache assessment including Ped-MIDAS, Short Sensory Profile, State-Trait Anxiety Inventory (STAI) for children, Pediatric Quality of Life Inventory.

Results: Children with migraine showed significantly higher sensory reactivity and lower quality of life compared to healthy controls. Among children with migraine, sensory reactivity significantly correlated with and lower quality of life. Quality of life among children with migraine was predicted by sensory reactivity.

Conclusion: Children with migraine show extremely different sensory patterns than healthy controls. There is a strong connection between the altered sensory profile and low quality of life among migrainers. The implication to the treatment of migraine in children needs further studies.

Disclosure of Interest: None Declared

Headache Education for Clinicians and Patients

IHC-PO-054

Children's Headache Training (CHaT) course in the United Kingdom: the first 5 years

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Objective: The British Paediatric Neurology Association (BPNA) recognised a need and desire for post-graduate training in the diagnosis and management of headache in children and young people. A one day interactive CHaT course for paediatric neurologists, paediatricians, and others working with children and young people with headaches was therefore designed. We will present data on the content, provision, uptake, and evaluation of CHaT.

Methods: A faculty of paediatric neurologists and paediatricians with clinical interest and expertise in paediatric headache and medical education was established by the BPNA. The scope and content of the one day course was established by the faculty. We included pre-course study materials, didactic lectures, small group facilitated workshops, quizzes, and anonymised participant feedback. The first course was launched in November 2012. The 2018 revision was based on participant and independent observer feedback.

Results: Over 6 years 26 CHaT courses have been hosted in 13 different UK and Republic of Ireland cities, reaching 916 participants so far. The majority of participants were paediatricians, but there were also paediatric neurologists,

trainee paediatric neurologists, specialist nurses, and ophthalmologists.

Feedback has been excellent: aggregated feedback on pre-course materials was good (score 8/10); on lectures and workshops was excellent (8–9/10); on the course overall was excellent (score 5/5); and on “would recommend to colleagues” was “definitely” (score 5/5).

Conclusion: The CHaT courses have proved popular with participants and faculty alike.

Future developments will include formative before-and-after assessments to evaluate knowledge transfer.

Further detailed results will be available by September 2019.

More information can be obtained from the BPNA: <https://www.bpna.org.uk/headache>.

Disclosure of Interest: None Declared

IHC-PO-055

Red ear syndrome – red flag or red herring?

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Objective: For our case, we present a 71-year-old lady who was referred to the neurology service initially in 2015 with two separate types of headaches, seen by me personally with a pre-referral diagnosis of tension-type and migrainous headaches.

The first headache was a daily pain near the centre of the head with no known triggers. It occurred any time in the day and pressing on her head took the pressure off. It was associated with autonomic features. The second headache was at the right frontal area described as sharp, lasting a few seconds waking her up at night. There were no specific triggers. There were no red flags or features in favour of trigeminal autonomic cephalalgia.

The patient was regularly followed up in the headache clinic usually by the specialist headache nurses and had tried propranolol, venlafaxine and different simple and combination painkillers although her compliance wasn't compliant of diary filling or following headache clinic recommendations. Eventually her headaches were controlled on a combination of amitriptyline and candesartan. She was continued to attend regularly.

After nearly three years under the neurology service, during a routine nurse-led headache clinic the patient reported that she had “for years” suffered from extremely severe pain in the right ear. The intensity was 10/10, waking her up from sleep. It was usually in the early hours and she had to “peel herself from the pillow”. She described it as a tearing pain on the outside of her ear. She used a cold flannel to try and control the pain. The ear got extremely red and the episodes lasted for 10 minutes during which the pain and redness gradually improved.

The patient was told by her GP that this was cluster headache and was specifically referred to the headache consultant. He diagnosed Red Ear Syndrome (RES) and the patient was started on gabapentin.

Methods: N/A

Results: N/A

Conclusion: RES is a rare condition causing a burning pain and erythema affecting one or both auricles. Both the duration and frequency are hugely variable. It is described in about 100 cases worldwide. Some cases appear to have a link with migraine, while others may have an association with trigeminal autonomic cephalalgias. There could also be secondary RES with musculoskeletal disorders affecting the temporo-mandibular joint or the cervical spine. Interestingly, our patient has a past history of cervical spondylosis.

Disclosure of Interest: None Declared

IHC-PO-056

Digital headache treatment pathway: key features based on health service context

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Objective: The objective of this research was to examine by interview how patients and professionals could benefit from a newly designed digital service for chronic headache in primary and occupational care.

The service offers information of the most common headaches like migraine, tension type, and medication overuse headaches. It provides an electronic headache diary, questionnaires, and multidisciplinary guidance. Support for the treatment and compliance for the service is enforced by text message communication with a nurse-coach and by automated feedback. The aim is to help patients better cope with headache challenges. Originally, the service has been designed for the purposes of tertiary care patients.

Methods: We conducted 16 semi-structured interviews, 10 within public primary care context and 6 within private occupational care context. We interviewed physicians, nurses, and management from each context about their opinion of the designed digital headache treatment pathway. The public primary care organizations were from several parts of Finland. The occupational care informants were from two major national service providers. Data was analyzed with Gioia-methodology and thematic analysis [1].

Results: There were six main findings. First, self-management was considered a key mechanism to better outcomes. Second, the tools for self-treatment were considered potential for preventing headache becoming chronic. Third, the service could reduce the need for appointments. Fourth, the service adds personalized headache information for the professional. Fifth, the digital pathway provides more comprehensive background information about the patients, as the regular appointments are short and fragmented. Sixth, the digital diary could help redirect the resources of professionals to patients needing more attention.

Conclusion: Digital headache treatment pathway can support patient care in different healthcare contexts. It may reduce the amount of appointments, provides more personalized information of the patient, and helps educate both patients and professionals in headache management.

Disclosure of Interests: This study was part of DiRVa project funded by Business Finland.

IHC-PO-057

Structured treatment plan of migraine for primary care and non-specialists

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Objective: In spite of considerable knowledge about migraine pathophysiology and primary headache disorders, patients still have difficulties finding medical professional help with diagnosing and modern treatment. Migraine has been known as a common, chronic but not malignant disease. It is also among the top 10 disorders worldwide causing most lifelong burden of disease as well as severe impact on socioeconomic costs. Despite this, it is not a prioritized disease at emergency room settings or at outpatients clinics. As soon as other differential diagnosis such as; stroke, meningitis, epilepsies and tumors are ruled out, very little knowledge and treatment is offered in these settings, often leaving patients back at square one. Better first line migraine care is needed to improve disease burden.

Methods: A first line treatment plan is developed together with the Swedish Headache Society. The treatment plan needed to fulfill the following criteria: a practical tool easy to access and include structured basic routines fulfilling most migraine patient needs in primary care.

The treatment plan is in accordance with the latest International Classification of Headache Disorder 2018 ICHD-3 and offers guidance for the first line physicians.

Results: A structured plan with diagnostic tools and a palette of up-dated treatments is presented. This includes a stepwise plan for setting a correct diagnosis, treating acute episodic migraine attacks, prophylactic treatments in severe cases of migraine, and information when to refer patients to headache specialists for more advanced treatments including newly developed CGRP- antibodies. The plan is implemented in primary care settings, at emergency rooms and at specialist clinics as a poster format and a pocket version.

Conclusion: There is overwhelming evidence that a structured plan and standardized treatment and care improves outcome in many chronic diseases. Improving first line care for migraine patients gives more patients access to correct treatment and a better selection of those in need of specialist care. The method optimizes existing resource distribution.

Disclosure of Interest: None Declared

IHC-PO-295

Headache training in Australia, New Zealand and Asia

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Objective: We aimed to assess 1) The quantity of teaching in headache subjects during undergraduate and postgraduate years; 2) The effects of teaching provided at the Headache Master School on knowledge and opinion.

Methods: This is a cross-sectional survey study where questionnaires were sent to 137 delegates from Australia, New Zealand and Asia, prior to the two-day Headache Master School in Sydney in August 2018. The Main outcome measured are recalled number of hours of teaching in undergraduate year and postgraduate years in: 1) Migraine; 2) Trigeminal autonomic cephalalgias (TACs); 3) Asthma; 4) Myasthenia gravis (MG) and performance in knowledge assessment before and after Headache Master School.

Results: The questionnaire response rate was 73% (100 of 137), of which 29 delegates were within 10 years of

completing their undergraduate degree. In undergraduate training, there was much greater quantity of teaching in asthma than migraine ($Z = 5.007$, $p < 0.000$) despite both being high-prevalent (asthma 11%, migraine 15–20%) conditions. Similarly, for diseases of medium-to-low prevalence, there was less training in TACs (1/1000), compared to MG (1.2/10,000) ($Z = 6.196$, $p < 0.000$). These major differences in training were also seen in postgraduate years even though overall headache teaching was greater in postgraduate than undergraduate training ($p < 0.000$). In the knowledge assessment, candidates improved their test score by a mean of 7.67 ($p < 0.01$) after training. Opinion questions also changed in key areas of migraine. Confidence improved from “mild confidence” prior to “moderate confidence” as a headache specialist after the HMS. The preferred mode of learning was in the workplace with mentors (54.25%; 51/94 responses).

Conclusion: Despite the high prevalence and morbidity of headache disorders, they receive less attention in training than conditions with similar prevalence. We propose that headache training opportunities should be improved in our region, particularly in the undergraduate course and through preceptorships or fellowships in postgraduate years. The Headache Master School has shown to be a highly effective method to enhance headache knowledge, at least in the short-term.

Disclosure of Interest: None Declared

IHC-PO-296

Strengths and limits in a 5 years' use of a digital platform in headache training

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Objective: The increasing development of social networks and in general of digital instruments led us to implement our project of a digital platform only focused on headaches, started in 2014, and the aim of this study is to analyze strengths and weaknesses in a 5 years' experience

Methods: Our platform is totally free. It is possible to access using website or smartphone app. It is divided in a section for pediatric and a section for adult headaches and contains more than 270 resources concerning headache. Each member can download or upload contents and discuss clinical cases. We alert members about new contribution by email and WhatsApp group. Administrators can

follow the members' activity (number of access, trend topics, uploaded/downloaded resources, discussions, average download for user). We monitored the evolution of the platform's activities over time and compared our experience with other digital platforms

Results: To this day the section dedicated to adult headaches includes 60 members and each did 14 downloads on average. The section dedicated to pediatric headaches includes 67 members with average of 19 downloads. We highlighted an increase in the number of users since the start of our project and in the number of downloads simultaneously with upload of new resources. The items that most capture the attention are PowerPoint presentations and resources closely related to common clinical cases or with short reading time. In each year the activity of the members during the summer appeared to be considerably reduced in number of downloads, uploads and new contributions

Conclusion: The increase in subscriptions shows that our social network dedicated to headaches is appreciated by the scientific community. Nevertheless, the activity does not appear equally increased and a considerable number of members rarely access the platform. Furthermore on average the number of uploads is remarkably lower than downloads, indicating passive use of the platform. In the other platforms discussions and downloads are considerably less than the number of subscribers, similarly to the activity of our platform. These results confirm the potential but also the limits of digital instruments in the training for specialists both in headaches and in other disorders

Disclosure of Interest: None Declared

IHC-PO-297

Impact assessment of clinic management interventions on efficiency in three headache centers

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Objective: Past research has shown that headache centers' capacity is highly saturated and as a result patient access can be limited. The objective of this analysis is to

investigate whether selected initiatives in clinical practice can improve efficiency and mitigate capacity constraints.

Methods: We have performed a retrospective analysis of selected interventions implemented by three headache/neurology centers. Data was collected from internal centers' databases both immediately pre- (point in time differs in the three centers, because of the different interventions implemented) and post-intervention implementation. Key performance indicators (KPIs) related to patient access to care and clinic management were measured to assess intervention impact.

Results: Case 1: Proactive patient data collection initiative allowed more appropriate patient triaging, ensuring the clinic focused on chronic migraine patients (from 13% to 44% of total migraineurs); effectiveness of new patient visits improved as more time (+33%) is dedicated to examination, diagnosis and treatment explanation instead of data collection; fewer visits were required to define appropriate treatment plan (from 3 to 1.8).

Case 2: Task delegation to specialized nurse increased time dedicated to new patient visit (+33%), allowed Neurologists to see more patients in the same amount of time (+36%), and increased follow-up patients under management (+57%).

Case 3: Opening a weekly specialized clinic with GP support decreased wait lists for headache patients by 45%, number of chronic patients under management increased (from 20% to 75%) as well as frequency of follow-up visits per year (from 1 to 3.5 on average).

Conclusion: In resource-constrained environments, select interventions can improve practice efficiency and increase patient access to headache services. Measurement of impactful KPIs helps ensure interventions' impact is verified and maintained over time.

Disclosure of Interests: Matias Ferraris is employed by Novartis Pharma AG in Switzerland, Niamh Murphy is employed by Novartis Ireland Limited in Ireland, Morag Nelson is employed by Novartis Pty Limited Australia in Australia, Marco Pedrazzoli is employed by LifeSciences Consultants in Italy, Marco Marchina is employed by LifeSciences Consultants in Italy, and Elia Lahouiri is employed by LifeSciences Consultants in Italy.

IHC-PO-298

Healthy eating plate for a healthy brain: the effect on migraine

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Objective: Diet has been often implied in Migraine pathophysiology and the therapeutic effects of certain diets have grown great interest in the patient community. However, noncontrolled diets can have harmful implications. This study aimed at evaluating the effect of education on the Healthy eating Plate on migraine frequency and disability.

Methods: We enrolled 160 Migraine patients (41.6ys SD 12.7, 84% female). At baseline, all patients underwent anthropometric assessment and filled a Frequency Food Questionnaire (FFQ) to assess their dietary habit and clinical scales (MIDAS e HIT-6) in the previous three months. All patients received prophylactic treatment if needed. After two months (T2) patients underwent anthropometric assessment, filled a Frequency Food Questionnaire (FFQ) and disability scales. They were educated about the healthy eating plate. Patients requiring a change in preventive therapy were considered dropouts. Three months later (T5), the enrolled patients returned for the control visit and underwent again the assessments.

Results: Baseline data showed average BMI of 24.33 ± 4.3 , mean migraine days per month 8.94 ± 6.98 , abortive drugs per month 8.77 ± 8.03 . At T2 we observed a drop-out of 42 patients for treatment failure while 20 patients failed to attend T2/T5 visits. The 98 patients completing T5 evaluations presented a reduction in BMI ($p = .029$), in Migraine attacks/month ($p = 0.017$) and in HIT-6 ($p = 0.026$). At T5, patients displayed a higher reduction in Migraine days if they had at least two servings of vegetables per day ($p = 0.005$), at least three servings of whole grain cereals ($p = .035$), at least two servings of fresh fish a week ($p = .006$), and a higher reduction in MIDAS B if they had less than two servings of red and processed meat per week ($p = .032$).

Conclusion: This study showed for the first time that a healthy diet may be a real help for migraine prevention. The shift from refined to whole cereals, fish and vegetable consumptions seems to play a relevant role independently of weight loss. The mechanism explaining the beneficial effect of whole grain cereal and vegetables is possibly based on a more steady glycemic control. Alternatively, we can speculate that a high fiber diet can modify gut microbiota and in turn have a detrimental effect on migraine.

Disclosure of Interest: None Declared

Headache Epidemiology, Outcomes and Burdens

IHC-PO-058

Demographics, Headache Characteristics, and Other Factors Associated With Opioid Use in People With Migraine: Results From the CaMEO Study

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Objective: To identify variables associated with opioid use among those using acute prescription medications for migraine.

Methods: The Chronic Migraine Epidemiology and Outcomes (CaMEO) study identified persons with ICHD-3 migraine from a Web panel demographically matched to the US population. We compared the features of self-reported opioid users (currently using opioids or having them on hand for migraine) with those of nonusers. Nested, multivariable binary logistic regression models evaluated opioid use/nonuse as the outcome. Covariates were entered in blocks (sociodemographics, headache and respondent characteristics, psychiatric comorbidities, emergency facility use for headache in the preceding 6 months, and ≥ 1 CV comorbidity). Nonsignificant socio-demographic variables were trimmed from the model.

Results: Of 2,388 people with migraine currently using acute prescription medications, 867 (36.3%) were opioid users. Factors significantly associated (odds ratio [95% CI]) with opioid use included male sex (1.74 [1.38, 2.19]), increasing BMI (1.02 [1.00, 1.03]), allodynia (1.39 [1.14, 1.70]), increasing monthly headache day frequency (0–4 days [reference] vs 10–14 days: 1.37 [1.02, 1.82]; ≥ 15 days: 1.62 [1.24, 2.13]), increasing Total Pain Index (TPI) (excluding head, face, neck; 1.32 [1.15, 1.52]), anxiety (1.37 [1.08, 1.73]), depression (1.49 [1.18, 1.89]), ≥ 1 CV comorbidity (1.56 [1.28, 1.90]), and emergency facility use for headache (1.73 [1.30, 2.31]). Physician-diagnosed migraine or CM (0.38 [0.30, 0.48]) and a lower migraine symptom severity score (0.94 [0.91, 0.97]) were associated with a significantly decreased likelihood of opioid use.

Conclusion: Opioid use is common among migraine patients using prescription medication and is generally associated with markers of worse health, including elevated BMI, CV and psychiatric comorbidities, elevated TPI, and emergency facility use. Modifiable variables

associated with opioid use include presence/absence of physician diagnosis and monthly headache days.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland

Author Disclosures:

Richard B. Lipton, MD, serves on the editorial boards of Neurology and Cephalgia and as senior advisor to Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS; serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache, 8th Edition (Oxford University Press, 2009), and Informa. He holds stock options in eNeura Therapeutics and Biohaven.

Todd J. Schwedt, MD, serves on the Board of Directors for the American Headache Society and the International Headache Society and on the editorial boards for Headache, Cephalgia, and Pain Medicine. He has received research support from the U.S. Department of Defense, the Patient Centered Outcomes Research Institute, National Institutes of Health, American Migraine Foundation, and the Henry Jackson Foundation. Within the past 12 months, he has served as a consultant or advisory board member for Alder, Allergan, Amgen, Dr. Reddy's, Eli Lilly, Ipsen Bioscience, Novartis, and Teva. He holds stock options in Aural Analytics, Nocira, and Second Opinion.

Benjamin W. Friedman, MD, reports no conflicts of interest.

Kristina M. Fanning, PhD, is an employee of Vedanta Research, which has received research funding from Allergan, Amgen, Dr. Reddy's Laboratories, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Novartis, via grants to the National Headache Foundation. Vedanta has received funding directly from Allergan for work on the CaMEO Study.

Michael L. Reed, PhD, is Managing Director of Vedanta Research, which has received research funding from Allergan, Amgen, Dr. Reddy's Laboratories, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Novartis, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study.

Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company.

Dawn C. Buse, PhD, has received grant support and honoraria from Allergan, Avanir, Amgen, Biohaven, Eli Lilly and Company, and Promius and for work on the editorial board of Current Pain and Headache Reports.

IHC-PO-059

Prevalence of Hypnic Headache in Iceland: Results of the Stress-And-Gene-Analysis (SAGA) Pilot Study

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Objective: To determine the prevalence of hypnic headache in Iceland in a population based sample. Hypnic headache is a rare headache disorder. The exact prevalence is unknown since there are no published prevalence studies.

Methods: Of 1398 invited adults, 921 (66%) participated; 402 men (average age 45.6 years, SD 13.2) and 519 women (52.6 years, SD 11.1). Age ranged from 18 to 69. Subjects answered an internet-based headache questionnaire including 16 screening questions on headache symptoms (based on ICHD-3 beta criteria) and 3 questions on headache treatment. The questionnaire included a screening question for hypnic headache: "Do you have a headache that occurs only during sleep and causes waking?" A neurologist (JHE) interviewed the participants who answered "yes" to the screening question for hypnic headache. Diagnosis of hypnic headache was made by clinical interview (JHE) using ICHD-3 beta criteria.

Results: Among 921 participants 6 screened positive for hypnic headache and of those two cases 0.22% (95% CI 0.06–0.79%) had probable hypnic headache, none had definite hypnic headache and four had migraine. Both cases of probable hypnic headache were women aged over 50 years and in both cases the criteria not fulfilled was the number of attacks (≥ 10 per month for 3 months).

Conclusion: Our estimate for the prevalence of probable hypnic headache is 0.22%, but we found no cases of definite hypnic headache, confirming that hypnic headache is a rare disorder. To find an accurate prevalence of hypnic headache a study with larger sample size is needed.

Disclosure of Interests: Drs. Eliasson, Scher, Launer, Valdimarsdottir and Gudmundsson have no disclosures.

Drs. Buse, Tietjen and Lipton have some disclosures including honoraria from industry. Dr. Lipton owns stock in pharmaceutical companies. Dr. Tietjen owns common stock in Johnson & Johnson and Stryker.

IHC-PO-060

Economic burden of migraine patients who failed two or more prophylactic treatments – a retrospective claims database analysis in the USA

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Objective: Migraine is a painful, debilitating neurological disease ranking among the top 10 leading causes of years lived with disability (YLD) worldwide, especially among individuals under 50 years of age. This study sought to characterize the healthcare resource utilization (HRU) and associated costs among migraine patients who had failed two or more prophylactic treatment failures (2+TF) versus matched patients with no treatment failures (0TF).

Methods: This retrospective cohort study used the IBM-Truven Health MarketScan[®] Commercial and Medicare Supplemental database to identify the number of prophylactic treatment failures during the 2 years following the initial migraine diagnosis in US. Migraine patients with 2+TF were randomly matched in a 1:1 ratio to migraine

patients with 0TF. Exact matching method on age and year at initial migraine diagnosis, gender, and region was used. The index date was defined as the time patient initiating the 3rd prophylactic treatment for 2+TF patients. The same index date was assigned to the matched 0TF patient. HRU and associated costs were assessed in the 12-month follow-up period post the index date.

Results: 17,010 migraine patients each were identified in the 2+TF and matched 0TF groups. The mean [SD] age was 44.4 [12.4] years and 85.5% were females. Compared with the 0TF group, the 2+TF group demonstrated a higher use in all aspects of healthcare resources including office visits, emergency room (ER) visits and hospitalizations. The migraine specific HRU in the 2+TF group was 4 to 5 times higher than the 0TF group. Similarly, the all-cause healthcare costs in the 2+TF group was almost thrice that of 0TF group (\$27,456 vs \$9,803).

Conclusion: Migraine patients with 2+TF impose a substantial burden through additional HRU and associated costs compared to those with 0TF.

Disclosure of Interest: None Declared

IHC-PO-061

The change of prevalence, the impact of headache and headache-related disability of primary headaches in Korea: data from 2009 and 2018 nation-wide surveys

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Abstract number: IHC-PO-060 HRU and costs among migraine patients with 2+TF vs 0TF

		0TF Patients (N = 17,010)		2+TF Patients (N = 17,010)	
		Migraine specific	All cause	Migraine specific	All cause
Visits, Mean (SD)*	ER	0.04(0.23)	0.45 (1.23)	0.14 (0.68)	0.83 (2.24)
	Hospital	0.00 (0.10)	0.34 (2.45)	0.07 (0.80)	0.75 (3.87)
	Office	0.62 (1.35)	6.86 (6.01)	2.82 (2.78)	12.56 (8.82)
	Other	0.28 (1.58)	10.39 (12.78)	1.37 (3.25)	17.40 (17.39)
Cost \$, Mean (SD)*	Medical	221 (997)	7,596 (19,542)	1,582 (3,975)	21,978 (52,731)
	Healthcare		9,803 (21,789)		27,456 (56,356)

*In a 12 month period, HRU: healthcare resource use, 2+TF: two or more prophylactic treatment failures, other visits: non-office visit type of outpatient visits.

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Objective: The prevalence of primary headaches in the general population has been assessed in several studies. Identifying changes in prevalence over time are an important basis for health policy as well as for understanding disease. Determining any change of prevalence over time requires comparable study designs in order to reliably compare prevalences. In 2009 and 2018, we conducted nation-wide surveys for primary headaches including migraine, probable migraine (PM) and tension-type headache (TTH) using the same strategies. The aim of the study is to assess any change in the prevalence, the impact of headache and headache-related disability of primary headaches over a 9-year period in Korea.

Methods: We used the data from Korean Headache Survey in 2009 and Korean Sleep-Headache study in 2018. We used the same questionnaire to assess diagnosis, the impact of headache, headache-related disability of migraine, PM and TTH in 2009 and 2018.

Results: The prevalence of migraine (6.0% vs. 5.0%, $p=0.159$) and PM (11.1% vs. 11.6%, $p=0.644$) did not significantly differ between 2009 and 2018. Nevertheless, the prevalence of TTH slightly decreased (30.7% vs. 22.0%, $p < 0.001$) over nine years. Impact of headache (Headache Impact Test-6 score) of migraine (51.5 ± 8.5 vs. 53.0 ± 8.9 , $p=0.210$), PM (49.7 ± 9.0 vs. 49.5 ± 8.3 , $p=0.795$) and TTH (44.01 ± 6.8 vs. 44.7 ± 7.5 , $p=0.155$) did not significantly change. The proportion of experiencing absenteeism or decrease work efficacy by headache among individuals with migraine (26.4% vs. 37.6%, $p=0.083$), PM (21.0% vs. 19.4%, $p=0.684$), and TTH (4.8% vs. 5.8%) did not significantly alter.

Conclusion: The prevalence of migraine and PM was stable for over nine years. The prevalence of TTH decreased.

Impact of headache and headache-related disability by migraine, PM and TTH did not significantly change.

Disclosure of Interests: Soo-Jin Cho was involved as a site investigator of multicenter trial sponsored by Otsuka Korea, Eli Lilly and Company, and Novartis and worked as an advisory member for Teva, and received research support from Hallym University Research Fund 2016 and a grant from Korean Neurological Association (KNA-16-MI-09). Min Kyung Chu was a site investigator for a multi-center trial sponsored by Otsuka Korea, Novartis International AG and Eli Lilly and Company. He worked an advisory member for Teva, and received lecture honoraria from Allergan Korea, Handok-Teva and Yuyu Pharmaceutical Company in the past 24 months.

The other authors, except for Soo-Jin Cho and Min Kyung Chu, declared no potential conflicts of interest.

IHC-PO-062

A Real-World Analysis of the Burden of Migraine in Patients with Prior Treatment Failure: Evidence from the BECOME Study

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Objective: Limited European data are available on the burden of disease and quality of life (QoL) in migraine

Abstract number: IHC-PO-062 PRO scores of Part 2 population set, overall and by PPTF and MMD

PRO questionnaires	Overall Part 2 (N = 2419)	1 PPTF (n = 1034)	2 PPTF (n = 690)	3 PPTF (n = 324)	≥4 PPTF (n = 371)	4-7 MMD (n = 806)	8-14 MMD (n = 605)	≥15 headache days/month, of which ≥8 were migraine days (n = 1007)
EQ-5D-5L utility index score	0.76 (0.22)	0.78 (0.22)	0.76 (0.22)	0.72 (0.24)	0.72 (0.22)	0.82 (0.19)	0.81 (0.19)	0.68 (0.24)
EQ VAS score	67.3 (20.36)	70.3 (19.85)	66.8 (20.07)	64.5 (20.31)	62.0 (20.94)	73.7 (17.88)	72.6 (17.74)	59.0 (20.71)
HIT-6 total score	65.2 (5.59)	64.6 (5.74)	65.1 (5.69)	66.4 (5.03)	66.3 (5.14)	63.6 (5.89)	65.0 (5.41)	66.7 (5.04)
MIDAS disability grade IV, n (%)	1982 (81.9)	802 (77.6)	565 (81.9)	283 (87.3)	332 (89.5)	583 (72.3)	492 (81.3)	907 (90.1)

All values are mean (SD) unless otherwise indicated. EQ-5D-5L, EuroQol 5 dimensions 5 levels; HIT, Headache Impact Test; MIDAS, Migraine Disability Assessment; MMD, monthly migraine days; N, total number of patients; n, number of patients; PPTF, prior prophylactic treatment failures; PRO, patient-reported outcomes; VAS, visual analogue scale.

patients with prior prophylactic treatment failure (PPTF). The aim of this analysis was to characterise the burden of migraine in patients with ≥ 1 PPTF and ≥ 4 monthly migraine days (MMD).

Methods: BECOME was a prospective, multicentre, non-interventional study in adult patients with migraine, conducted in two concurrent parts over 3 months across Europe and Israel. Part 1 assessed the characteristics of all migraine patients visiting headache specialist centres over a 3-month prospective period, including frequency of PPTF (results presented separately). Part 2 of the study examined burden of disease using patient-reported outcome questionnaires in visiting migraine patients with ≥ 1 PPTF and ≥ 4 MMD, identified by study investigators during Part 1.

Results: Overall, 20,837 patients were screened in Part 1; 2419 were included in the Part 2 analysis. The mean \pm SD age of patients in Part 2 was 43.0 ± 11.56 years; the majority were female (86.9%) and diagnosed with migraine without aura (53.4%). 23.6% patients reported medication overuse headache. Overall, Part 2 patients reported a EuroQol visual analogue scale (VAS) score of 67.3 ± 20.36 , severe impact (HIT-6 score 65.2 ± 5.59), and severe disability (MIDAS disability grade IV, 81.9% of patients) due to headache. The burden of disease generally increased in line with increases in PPTF and MMD (**Table**).

Conclusion: BECOME confirms the significant burden of disease among migraine patients who have failed prior prophylactic treatments and provides real-world evidence of the continuous need for improved treatment of patients with difficult-to-treat migraine.

Disclosure of Interests: This study was funded by Novartis Pharma AG, Basel, Switzerland.

Christian Lucas – collaboration as an expert, investigator or coordinator of clinical trials with Novartis, Teva, Sanofi, Grünenthal, Eli Lilly, Biogen, and Ethypharm. Patricia Pozo-Rosich – received honoraria as a consultant and speaker during the last 5 years for: Allergan, Almirall, Chiesi, Eli Lilly, Novartis and Teva. Her research group has received research grants from Allergan and has received funding for clinical trials from Alder, Boehringer Ingelheim, MSD, electroCore, Eli Lilly, Janssen Cilag, and Novartis. She is a trustee member of the board of the International Headache Society and a Member of the Council of the European Headache Federation. She is on the editorial board of *Revista de Neurologia*. She is an editor for *Frontiers of Neurology* and *Journal of Headache and Pain*. She is a member of the Clinical Trials Guidelines Committee of the International Headache Society. She has edited the Guidelines for the Diagnosis and Treatment of Headache of the Spanish Neurological Society. She does not own stocks from any pharmaceutical company. David Watson – received honoraria from Novartis, Teva and Allergan in the last 12 months for consultancy and educational work. Charly Gaul – received

honoraria for consulting and lectures within the past 3 years from Allergan Pharma, Ratiopharm, Boehringer Ingelheim Pharma, Eli Lilly, Novartis Pharma, Desitin Arzneimittel, Cerbotec, Bayer Vital, Hormosan Pharma, electroCore, Grünenthal, Reckitt Benckiser, and Teva. He does not hold any stocks of pharmaceutical companies or medical device companies. Emma Ramsden – provides services to Novartis Pharma AG. Paolo Martelletti – Section Editor, Medicine, Springer Nature Comprehensive Clinical Medicine; Editor-in-Chief, The Journal of Headache and Pain; Headache Books Series Editor, Springer; EU Expert, European Medicine Agency. Past-President of European Federation, Chairman of School of Advanced Studies of European Headache Federation. He does not hold any stocks of any pharmaceutical companies or medical device companies. Shannon Ritter and Josefin Snellman – employees and stocks: Novartis.

IHC-PO-063

Relationship between severity of migraine and vitamin D deficiency: a case-control study

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Objective: Even though it is well recognized that vitamin D deficiency is involved in chronic pain, whether there is a relationship between vitamin D deficiency and severity of migraine remains uncertain.

Methods: We prospectively examined the serum levels of calcium, parathyroid hormone, 25-OH vitamin D, and phosphorus of migraine patients and non-headache sufferers healthy controls. Migraine severity was measured by Visual Analogue Scale (VAS), headache frequency, and scores on the Migraine Disability Assessment (MIDAS) questionnaire, cutaneous allodynia (ASC-12); Beck Depression Inventory (BDI-II), Hamilton Anxiety Rating Scale (HARS) and medical overuse were compared with regard to the 25-OH vitamin D levels.

Results: Participants were grouped into 3 groups: Group 1 included 116 patients with chronic migraine (vitamin D 2.9 ± 5.4 ng/ml); Group 2 included 44 patients with episodic migraine (vitamin D 18.6 ± 6 ng/ml); Group 3 consisted of 100 non-headache controls (vitamin D 21.6 ± 6 ng/ml). Ninety-two migraine patients had vitamin D insufficiency (vitamin D levels between 10 and 20 ng/mL), whereas 40 had vitamin D deficiency (vitamin D levels < 10 ng/mL). Vitamin D deficiency was found in migraine

patients and less severely in non-headache sufferers control group. Serum 25-hydroxyvitamin D levels were negative related to headache frequency ($p < 0,001$). Moreover there was a negative relationship between serum vitamin D levels and BMI, HARS, BDI-II, MIDAS, VAS.

Conclusion: Our data indicate that severe vitamin D deficiency is associated with higher frequency of headache in migraine patients, suggesting that serum vitamin D levels correlate with severity of migraine. Vitamin D is implicated in descending modulation of endogenous pain control. Indeed 25-hydroxyvitamin D receptors and 1 α -hydroxylase are expressed in neurons of dorsal ganglia, limbic system, basal ganglia, cerebellum, cerebral cortex, substantia nigra, lateral geniculate nuclei, supraoptic and paraventricular nuclei in hypothalamus. We speculated that vitamin D deficiency may facilitate headache attacks and have a role in peripheral and central sensitization which lead to migraine chronification and other related phenomena such as cutaneous allodynia.

Disclosure of Interest: None Declared

IHC-PO-064

Headache at work, yesterday

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Objective: European estimates projected a productivity-loss related cost of €482 Million for headache, in Portugal, although no studies were performed in any European workforce.

This study aims to estimate the impact and work-related productivity loss to headache in the a Portuguese health-care provider company and to test it's methodology in order to plan for a similar country-wide study.

Methods: A questionnaire-based on-line survey using the "headache-yesterday" methodology was prompt to active employees of a nationwide health-care provider portuguese company.

Results: Participation rate was 5.4%, respondents were mostly female (254, 78.9%) aged 37.6 years, 63.9% had migraine. Point-prevalence of headache in workdays was 14.6%. Lost productivity to headache was 27.7%, considering 2h of absenteeism and 37.5% of productivity decrease over 50%; 60% employees believed to be able to compensate for lost work, but not family/ social time. 84.4% of headache suffering employees considered headache to impact their your personal, social or familiar life while only 22.7% in their academic or professional life. Direct healt-care resourse utilization in the previous year was 16.216€. Total cost of headache was 289.384 € per year, 94% of wage-loss cost.

Conclusion: Point-prevalence of headache was overestimated due to participation bias. Conservatively, total

yearly wage-loss cost for headache was 941.364€ in this company, 475.783.202€ in total Portuguese workforce.

Disclosure of Interest: None Declared

IHC-PO-065

Economic burden of episodic migraine in Singapore among full-time employees

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Objective: Migraine is disabling neurological disorder. Despite being highly prevalent in Asia, few studies have examined its economic impact on society. We aim to quantify the per capita and aggregate economic cost of episodic migraine (EM; ≤ 14 migraine monthly days) without aura among full-time employees in Singapore.

Methods: We fielded a cross-sectional web survey to full-time employees in Singapore who met the International Classification of Headache Disorders (3rdEdition, 2018) criteria for EM without aura. Subjects were segregated into two groups according to the frequency of monthly migraine days (MMDs) – ≤ 3 MMDs and 4–14 MMDs. The survey captured per capita healthcare resource utilisation and lost productivity (absenteeism and presenteeism) using the Work Productivity and Activity Impairment Questionnaire. We multiplied the unit costs for each group by prevalence data from Taipei, adapted for use in Singapore, to quantify the burden in Singapore.

Results: 606 participants completed survey. 81% experienced ≤ 3 MMDs. Total annual per capita costs were USD 3,740 (95% CI: 3,350- 4,130) and USD 11,030 (95% CI: 8,980- 13,070) for subjects with ≤ 3 MMDs and 4–14 MMDs respectively. Healthcare costs accounted for 20% of per capita costs. The single largest contributor was investigations (41%), followed by alternative medications (18%), consultations (16%), hospitalisations (13%), and medications (11%). Lost productivity accounted for 80% of costs on average, but was mainly driven by absenteeism costs for the group ≤ 3 MMDs (68%) and presenteeism costs (57%) for the group 4–14 MMDs. The total cost to Singapore for EM in 2018 was USD 762.3 million. 42% of the overall cost came from 19% of subjects having 4–14 MMDs.

Conclusion: EM imposes a substantial burden on society in Singapore, especially for those experiencing more MMDs. These costs were driven by missed workdays

and lost work productivity. Future research should investigate if acute and/or preventive treatments would improve productivity and reduce costs.

Disclosure of Interest: None Declared

IHC-PO-066

Prevalence and medical-social aspects of primary headaches in adolescents in the Republic of Moldova: descriptive epidemiological study

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Objective: The aims of this study were to estimate overall prevalence of primary headaches, prevalence of migraine (MG), tension-type headache (TTH) and to study medico-social characteristics of headaches in adolescents in the Republic of Moldova.

Methods: This school-based study was conducted during the study year 2015–2016. In total there were 3389 adolescents, whose age ranged from 10 to 19 years, recruited from urban and rural areas of the country. The information was collected with the use of self-administered questionnaire based on ICHD–2 (2004) and ICHD–3 (2013) criteria. Primary headaches were classified according to the type of headache and to the frequency of headache attacks/month. The statistical analysis was performed by applying IBM SPSS Statistics for Windows version 22.

Results: The overall prevalence of primary headaches in Moldavian adolescents is 38.75% (girls–49.7%, boys–27.8%), and it is higher in urban (48.23%) than in rural (30.05%) area. The prevalence of MG is 19.7%. The prevalence of MG is higher in girls (27.5%) than in boys (12.1%) and it is higher in urban adolescents 27.1% compared to rural ones 13.0%. The prevalence of TTH is 7.9% and it is almost equal in both sexes (8.0% in girls and 7.7% in boys). In urban adolescents, the prevalence of TTH is 10.2% and is more than 1.7 times the recorded level in rural areas 5.8%. Adolescents living with both parents suffer less often from headache (31.1%) compared to those living without parents (51.3%). In adolescents who practice extracurricular activity MG (23.7%) is more frequent than TTH (11.9%). Sleep disturbances were present in an equal proportion in adolescents with both types of headache (MG–57.9%, TTH–53.7%). Pain comorbidity was more common in adolescents with MG (65.9%) than with TTH (58.3%). Anxiety disorder was found more frequently in adolescents diagnosed with MG (54.6%), compared with adolescents diagnosed with TTH (46.3%). From all adolescents diagnosed with headache, who mentioned the presence of

headache in relatives, 61.1% were diagnosed with MG and 47.4% with TTH.

Conclusion: The present research is the first Moldavian survey on epidemiology of primary headaches in adolescents.

Disclosure of Interest: None Declared

IHC-PO-067

Annual Indirect Costs Secondary to Headache Disability in Brazil

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Objective: To estimate indirect costs from absenteeism and presenteeism due to headache disorders in Brazil.

Methods: We performed a secondary, descriptive analysis of two nationwide database (a headache prevalence survey and a national health survey) to estimate indirect costs based on headache-related disability and socioeconomic data.

Results: In the first database analysed, 5.1% of employed population with headache disorders missed at least 1 day of work in the last 3 months [mean, 95% CI = 4.7 days (3.6–4.7)]. Based on income data, the extrapolation to current Brazilian population resulted in R\$ 18.2 billion (US\$ 4.8 billion) lost due to headache-related absenteeism annually, with R\$ 14.2 billion (US\$ 3.7 billion) from migraine and R\$ 3 billion (US\$ 0.8 billion) from tension-type headache). For presenteeism cost estimate, 10.6% of employed population with headache disorders worked at least 1 day in the last 3 months with 50% reduced productivity [mean, 95% CI = 5.7 days (5.3–6.2)], amounting R\$ 25.8 billion (US\$ 6.8 billion) annually. Migraine and tension-type headache accounted for R\$ 9.1 billion (US\$ 2.4 billion), and R\$ 7.7 (US\$ 2 billion), respectively. In the other database analysed (n = 205,546), 14,052 (6.8%) respondents missed work/school or household duties in the past 2 weeks due to some disease. Of these, 4.7% attributed their days lost to headaches disorders, which ranked 4th among the main causes of days of habitual activities lost due to disease (among 23 diseases) in the economically active population.

Conclusion: The economic burden of headache disorders in Brazil, mostly due to migraine, may reach up to R\$ 44 billion (US\$ 11.6 billion) annually, and headache disorders represent a leading cause of absenteeism due to disease.

Disclosure of Interest: None Declared

IHC-PO-068**Observational study about epidemiological and clinical factors associated with the higher frequency of headache in Chronic Migraine in a series of 985 patients**

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Objective: Chronic migraine (CM) criteria require the presence of pain at least 15 days per month during at least 3 months, being at least 8 of these days with migraine-like phenotype. We aim to evaluate if the CM sufferers exhibit any epidemiological difference when comparing patients with 15–22 headache days per months and those with 23–31.

Methods: Observational transversal study including all consecutive patients fulfilling ICHD-3beta and IHCD-3 criteria for CM evaluated in our 3rd level headache clinic at the moment of CM diagnosis. We compared the group of less frequent (LF) sufferers (15–22 days) and very frequent (VF) patients (23–31 days) in terms of epidemiological and clinical variables. We analyzed data with parametrical tests and validated with regression tests, considering a significant p-value if <0.003 after Bonferroni correction.

Results: We included 985 patients between 2013 and 2019. We found statistically significant differences in the following items: age at diagnosis, chronic migraine duration, mean number of migraine days per month, symptomatic treatment days per month and frequency of concomitant medication overuse headache (MOH). (Table 1). Linear regression showed that the higher the chronic migraine duration, the higher frequency of headache days per month ($p < 0.001$). We did not found differences when comparing prior preventive efficacy between groups.

Abstract number: IHC-PO-068

Less frequent (n = 394)	Item	Very frequent (n = 591)	p-value
37.8 (13.2)	Age at diagnosis (years)	41.5 (14.0)	<0.001
18.6 (9.1)	Age of onset (years)	19.3 (10.0)	0.23
27.9 (37.3)	Chronic migraine duration before diagnosis (months)	40.6 (70.0)	<0.001
84.0	Gender (% female)	87.5	0.12
11.9 (5.4)	Migraine days per month	8.1 (15.7)	<0.001
13.1 (7.0)	Symptomatic treatment days	18.8 (9.7)	<0.001
60.4	Medication overuse headache (%)	73.9	<0.001
16.1	Allodynia (%)	15.1	0.86
52.5	Prior use of preventive treatment (%)	52.6	0.97

Conclusion: We found that in CM sufferers, patients with a higher frequency of headache per month showed a more prolonged CM before diagnosis and a higher frequency of MOH, but we did not found differences in prior preventive frequency.

Disclosure of Interest: None Declared

IHC-PO-069**Depression and Anxiety Are Associated With Increased Headache-Related Disability in Episodic and Chronic Migraine: Results From the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study**

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Objective: To examine influences of depression and anxiety on headache-related disability in people with episodic (EM) and chronic migraine (CM).

Methods: This cross-sectional analysis of sociodemographic and headache features, headache-related disability, migraine symptom severity, and cutaneous allodynia used data from CaMEO. Depression or anxiety alone, both, or neither subgroups were defined by scores denoting \geq moderate severity on validated depression (PHQ-9) and anxiety (GAD-7) screeners. A negative binomial

regression model investigated predictors of disability (Migraine Disability Assessment Scale [MIDAS]) score.

Results: Respondents (N = 16,788; mean age, 41.1 years) were mainly female (74.4%) and white (84.0%); 39.5% had depression and/or anxiety. Those with CM (n = 1476) had more headache days/month and greater headache-related disability, migraine symptom severity, and likelihood of cutaneous allodynia than those with EM (n = 15,312). They also had significantly higher rates of depression (56.6% vs 30.0%; $P < 0.001$) and anxiety (48.4% vs 28.1%; $P < 0.001$) and were more likely to have both comorbidities than those with EM. After adjusting for sociodemographic and headache features, respondents with both depression and anxiety (22.7% of respondents) had the highest risk of disability (rate ratio: 1.79; 95% confidence interval [CI], 1.71–1.87; $P < 0.001$), followed by those with depression alone (9.5%; rate ratio: 1.56; 95% CI, 1.46–1.66; $P < 0.001$) and anxiety alone (7.0%; rate ratio: 1.39; 95% CI, 1.30–1.50; $P < 0.001$).

Conclusion: Migraine with depression and/or anxiety was common (39.5%), especially in those with CM, and associated with greater headache-related disability in those with both than those with neither. A greater proportion of respondents with CM than EM had depression and anxiety. Although a cross-sectional analysis cannot determine causality, treating depression and anxiety may improve headache-related disability in those with migraine.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland

Richard B. Lipton, MD, serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta.

Min Kyung Chu has received honoraria from Allergan Korea and YuYu Pharma.

Elizabeth K. Seng, PhD, has received research support from the National Institutes of Health and the International Headache Academy. She has served as a consultant for GlaxoSmithKline.

Michael L. Reed, PhD, is managing director of Vedanta Research, which has received research funding from Allergan, Amgen, Eli Lilly, GlaxoSmithKline, Merck, and Promius via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study.

Kristina Fanning, PhD, is an employee of Vedanta Research, which has received research funding from Allergan, Amgen, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Promius via grants to the National Headache Foundation. Vedanta has received funding directly from Allergan for work on the CaMEO Study.

Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc, and owns stock in the company.

Dawn C. Buse, PhD, has received grant support and honoraria from Allergan, Amgen, Avanir, Eli Lilly and Company, and Promius Pharma. She is on the editorial board of Current Pain and Headache Reports.

IHC-PO-070

Recurrent visits to the Emergency Department (ED) due to Headache: economic burden and epidemiological profile

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Objective: To present data of health resource utilization of patients admitted due to headache in the ED of a Tertiary Centre in Brazil.

Methods: We conducted a retrospective review of records from patients admitted in the ED with headache from January to December 2018. Clinical and economical aspects of recurrent patients, defined as those who had more than one visit within the same year, were compared to non-recurrent ones.

Results: In 2018 a total of 66,808 patients were admitted in the ED, accounting for 117,004 visits. Headache was the 6th most frequent diagnosis with 3,943 (3.4%) visits from 3,308 patients. A total of 424 (12%) patients had more than one visit with the same diagnosis in the period and accounted for 1,059 (26%) visits due to headache. The mean cost of ED visit was US\$ 185.27 and the mean cost of inpatient treatment was US\$ 2,181.08. Neither the costs per visit nor admissions differed between recurrent and non-recurrent patients. However, recurrent patients were more prone to inpatient admission (OR 3.06, IC 95%: 3.25–5.32, $p < 0.001$), which cost is 1177% higher than the ED visit.

Conclusion: Our data demonstrate that headache is frequent in the ED and accounts for high costs to the healthcare system, especially for patients with recurrent visits. It supports the importance for healthcare providers and insurance companies to build a patient-centered headache care and improve cost-effectiveness. The identification of patients who seek ED due to headache complain more than once a year can be a sensitive tool to find eligible patients.

Disclosure of Interest: None Declared

IHC-PO-071

Characteristics of Migraine Patients Visiting the European Headache Specialist Centres: Real-World Evidence from the Multinational BECOME Study

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Objective: Real-world evidence on the characteristics of patients with migraine from Europe is limited. The current study provides real-world evidence on the characteristics of patients visiting European headache specialist centres.

Methods: BECOME was a prospective, multicentre, non-interventional study in adult patients (18–65 years) with migraine consisting of two parts, conducted across Europe and Israel. In Part 1, all patients visiting the participating headache specialist centres over a 3-month prospective period were screened for frequency of prior prophylactic treatment failure (PPTF), monthly migraine days (MMD), and other characteristics (**Table**). Patients identified by study investigators with ≥ 1 PPTF and ≥ 4 MMD were enrolled in Part 2 of the study, which examined the burden of disease and healthcare resource utilisation (results presented separately).

Characteristics of the BECOME study population in Part 1

	Part 1 (N = 20,837), n (%)
No prior prophylactic treatment failure	7880 (37.8)
≥ 1 prior prophylactic treatment failures	12,957 (62.2)
<4 monthly migraine days	5358 (25.7)
≥ 4 monthly migraine days	15,479 (74.3)
First visit	5621 (27.0)
Follow-up visit	15,216 (73.0)
Any medication overuse	3706 (17.8)
Any suspected medication overuse headache	2464 (11.8)
Outpatient visits	19,700 (94.5)

Results: Of the 163 centres participating in the study, 156 had data available for Part 1. As shown in the **Table**, 20,837 patients with migraine visited the headache centres during screening period, of which 62.2% reported ≥ 1 PPTF and 74.3% reported ≥ 4 MMD. Furthermore, 16.9% of patients reported ≥ 4 PPTF and 22.9% reported ≥ 15 headache days with ≥ 8 MMD. Approximately a quarter (27.0%) of patients with migraine visited the centres for the first time.

Conclusion: The BECOME study represents real-world characteristics of the migraine patient population visiting headache specialist centres in Europe and Israel. Nearly 17% of the study population reported ≥ 4 prior prophylactic treatment failures and more than 20% reported ≥ 15 headache days per month, demonstrating the high burden of disease, and a high-unmet need with current prophylactic migraine therapy.

Disclosure of Interests: This study was funded by Novartis Pharma AG, Basel, Switzerland.

Patricia Pozo-Rosich – received honoraria as a consultant and speaker during the last 5 years for: Allergan, Almirall, Chiesi, Eli Lilly, Novartis and Teva. Her research group has received research grants from Allergan and has received funding for clinical trials from Alder, Boehringer Ingelheim, MSD, electroCore, Eli Lilly, Janssen Cilag, and Novartis. She is a trustee member of the board of the International Headache Society and a Member of the Council of the European Headache Federation. She is on the editorial board of *Revista de Neurologia*. She is an editor for *Frontiers of Neurology* and *Journal of Headache and Pain*. She is a member of the Clinical Trials Guidelines Committee of the International Headache Society. She has edited the Guidelines for the Diagnosis and Treatment of Headache of the Spanish Neurological Society. She does not own stocks from any pharmaceutical company. Christian Lucas – collaboration as an expert, investigator or coordinator of clinical trials with Novartis, Teva, Sanofi, Grünenthal, Eli Lilly, Biogen, and Ethypharm. David Watson – received honoraria from Novartis, Teva and Allergan in the last 12 months for consultancy and educational work. Charly Gaul – received honoraria for consulting and lectures within the past 3 years from Allergan Pharma, Ratiopharm, Boehringer Ingelheim Pharma, Eli Lilly, Novartis Pharma, Desitin Arzneimittel, Cerbotec, Bayer Vital, Hormosan Pharma, electroCore, Grünenthal, Reckitt Benckiser, and Teva. He does not hold any stocks of pharmaceutical companies or medical device companies. Emma Ramsden – provides services to Novartis Pharma AG. Paolo Martelletti – Section Editor, *Medicine*, Springer Nature Comprehensive Clinical Medicine; Editor-in-Chief, *The Journal of Headache and Pain*; Headache Books Series Editor, Springer; EU Expert, European Medicine Agency. Past-President of European Federation, Chairman of School of Advanced Studies of European Headache

Federation. He does not hold any stocks of any pharmaceutical companies or medical device companies. Shannon Ritter and Josefin Snellman – employees and stocks: Novartis.

IHC-PO-072

Data mapping to understand local, regional and provincial patterns of headache diagnosis, treatment and health resource utilization in Children and Adults in Alberta, Canada

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Objective: Develop case definitions of headache disorders and apply to multiple administrative health databases in Alberta, Canada to understand headache prevalence and impact in Alberta.

Methods: Observational population based study with retrospective review of 8 health administrative databases for the province of Alberta (4.29 million) in pediatric and adult patients with a headache diagnosis ({ICD} 9/10) from April 2012 – March 2018. Data analyzed by biostatisticians, crosslinked by the anonymous PHN (provincial healthcare number).

Results: From **Apr 1, 2012 – March 31, 2018:**

7671 inpatient hospitalizations for 7083 patients (63% female, mean 49.5 years SD 22.2) for one of (ICD-10): G43 Migraine without aura; G43.1 Migraine with aura, G 44.2 Tension-type headache, R51 Other headache, G44.3 Post-traumatic headache.

166,198 emergency department visits made by **125,992 patients** (63% female, mean 39 years SD 20.0). **1,149, 577 prescriptions** for WHO ATC code **N02C** "anti-migraine medications" in **114, 990 patients** (mean 39.8 years SD 14.2, 78% female).

In total, **304,031 unique patients** in Alberta from April 2012-March 2018 received at least one headache diagnosis either by an ambulatory care physician, emergency physician or during inpatient hospitalization.

Of these unique patients, **40,517** were pediatric (<18 years) representing 13.3% of the total patients who received at least one headache diagnosis in this time frame. The average age at first visit was 37.5 years (SD 16.4) and 74% female.

Conclusion: First population based study in Alberta, Canada regarding prevalence, patterns of care and prescription dispensations for headache including migraine in

children and adults using multiple administrative health databases in Alberta.

A significant proportion (over 10%) of cases are children; need for appropriate assessment/treatment of pediatric headache.

Future data extractions will examine prescription analyses (opioid dispensation), general practitioner vs. specialist diagnoses and the rural vs. urban spread of patients. Future data mapping will geographically target populations in Alberta requiring headache education/treatment.

Disclosure of Interest: None Declared

IHC-PO-073

Clinical characteristics of headache in patients with migraine with typical aura according to the presence of aura

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Objective: The previous studies reported that the age of onset of migraine with aura is earlier than that of migraine without aura (MO) and the headaches are less severe compared with those of MO. However, it is unclear whether these findings could apply to patients who have both types of migraine. This study examined clinical characteristics of headache in patients who had both types of headache, migraine with typical aura (MTA) and MO according to the presence of aura.

Methods: Total of 138 subjects with a diagnosis of MTA were consecutively screened for the study. Among them, 47 patients were excluded because of the absence of headache: 5 patients had aura without headache only and 42 patients did not have MO. Ninety-one patients (16 men and 75 women, mean age 30.12 (SD 11.32)) were analyzed. We investigated the age of onset of MTA and MO, types of headache, severity of headache according to the presence aura.

Results: The mean age of onset of MTA was 24.12 (SD 11.11) and MO was 16.64 (SD8.62) respectively. MO had earlier age of onset than MTA ($p < 0.001$) in patients with both types of migraine. Five patients (5.5%) had non-migraine headache during the MA attack. The mean numeric rating scales (NRS) of headache severity was 7.59 (SD 1.54) in MTA and 5.27 (SD 1.76) in MO patients, which showed significant difference ($p < 0.001$).

Conclusion: Our results indicate that in patients who have both MTA and MO, MO episodes usually start earlier than MTA episodes. Headaches accompanied by aura usually are more severe those of without aura.

Disclosure of Interest: None Declared

IHC-PO-074**Increased Burden of Headache in Patients with Migraine Complicated by Medication Overuse Headache: Sub-group Analysis of the BECOME Study**

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Objective: To evaluate the burden of headache in patients with chronic migraine complicated by medication overuse headache (CM+MO) using patient-reported outcomes (PRO) and healthcare resource utilisation (HRU) questionnaires.

Methods: BECOME was a prospective, non-interventional study conducted in 2 concurrent parts over 3 months across Europe and Israel. Part 1 assessed clinical characteristics of all patients with migraine visiting headache specialist centres over 3 months. Part 2 examined burden of disease in patients with ≥ 1 prior prophylactic treatment failure (PPTF), ≥ 4 monthly migraine days (MMD). We assessed quality of life (QoL) in patients in

Part 2 using PRO questionnaires Euro QoL5 dimensions 5 levels (EQ-5D-5L), modified Migraine Disability Assessment (mMIDAS), Headache Impact Test (HIT-6) in the previous 3 months. HRU was assessed based on number of patients consulting physicians in the previous 3 months, visits to emergency department (ED), computed tomography (CT) or magnetic resonance imaging (MRI) scans of head, and hospital admissions over the previous 12 months.

Results: Of the 2419 patients (86.9% females; mean[SD] age 43.0[11.56] years) analysed in Part 2, 571 (23.6%) reported CM+MO. Patients with CM+MO reported lower functioning (mean[SD] EQ-5D utility scores 0.67[0.24] vs 0.78[0.21]), lower health status (EQ VAS scores 59.3[20.94] vs 69.8[19.48]), higher disability (mMIDAS score 35.5[21.98] vs 21.9[17.39]) and greater proportion had grade IV disability (88.1% vs 80.1%) than those without MO (**Table**). A higher proportion of patients with CM+MO consulted physicians, visited ED, received MRI and CT scans, and were hospitalised than those without MO.

Conclusion: Patients with ≥ 1 PPTF reported severe burden of migraine irrespective of MO, but patients with MO had lower functioning and health status, greater severity in disability, and greater use of HRU than those without MO. This indicates a higher burden of disease and unmet need in patients with MO.

Disclosure of Interests: This study was funded by Novartis Pharma AG, Basel, Switzerland. Patricia Pozo-Rosich – received honoraria as a consultant and speaker during the last 5 years for: Allergan, Almirall, Chiesi, Eli Lilly, Novartis and Teva. Her research group has received research grants from Allergan and has received funding for clinical trials from Alder, Boehringer Ingelheim, MSD,

Abstract number: IHC-PO-074 PRO and HRU of patients in Part2, by MO

PRO	CM+MO, N=571	No CM+MO, N=1844	HRU	CM+MO, N=571	No CM+MO, N=1844
EQ-5D-5L utility index score, mean (SD)	0.67 (0.24)	0.78 (0.21)	GP consultation	233 (40.8)	540 (29.2)
EQ-5D-5L VAS score, mean (SD)	59.3 (20.94)	69.8 (19.48)	Neurologist consultation	371 (65.0)	1032 (55.9)
HIT-6 total score, mean (SD)	66.9 (5.20)	64.7 (5.62)	Other specialist consultation	119 (20.8)	318 (17.2)
Modified MIDAS total score ^a , mean (SD)	35.5 (21.98)	21.9 (17.39)	Other office-based practitioner consultation	173 (30.3)	493 (26.7)
MIDAS disability grade I ^b (score 0–5)	37 (6.5)	123 (6.7)	ED visit	167 (29.2)	347 (18.8)
MIDAS disability grade II ^b (score 6–10)	6 (1.1)	70 (3.8)	MRI scan	125 (21.9)	368 (19.9)
MIDAS disability grade III ^b (score 11–20)	15 (2.6)	147 (8.0)	CT scan	84 (14.7)	197 (10.7)
MIDAS disability grade IV ^b (score ≥ 21)	503 (88.1)	1479 (80.1)	Hospitalisation for migraine	92 (16.1)	111 (6.0)

All values are n (%) of patients unless specified. ^aModified MIDAS total scores were assessed for previous 1 month. ^bMIDAS disability grades were assigned by multiplying modified MIDAS score by 3. CM+MO, patients with chronic migraine complicated by medication overuse headache; ED, emergency department; EQ-5D-5L, EuroQoL 5 dimensions 5 levels; GP, general practitioner; HIT-6, Headache Impact Test; HRU, healthcare resource utilisation; MIDAS, Migraine Disability Assessment scale; MO, medication overuse headache; N, number of patients in the group; PRO, patient-reported outcomes; SD, standard deviation; VAS, visual analogue scale.

electroCore, Eli Lilly, Janssen Cilag, and Novartis. She is a trustee member of the board of the International Headache Society and a Member of the Council of the European Headache Federation. She is on the editorial board of *Revista de Neurologia*. She is an editor for *Frontiers of Neurology* and *Journal of Headache and Pain*. She is a member of the Clinical Trials Guidelines Committee of the International Headache Society. She has edited the Guidelines for the Diagnosis and Treatment of Headache of the Spanish Neurological Society. She does not own stocks from any pharmaceutical company. Christian Lucas – collaboration as an expert, investigator or coordinator of clinical trials with Novartis, Teva, Sanofi, Grunenthal, Eli Lilly, Biogen, and Ethypharm. David Watson — received honoraria from Novartis, Teva and Allergan in the last 12 months for consultancy and educational work. Charly Gaul – received honoraria for consulting and lectures within the past 3 years from Allergan Pharma, Ratiopharm, Boehringer Ingelheim Pharma, Eli Lilly, Novartis Pharma, Desitin Arzneimittel, Cerbotec, Bayer Vital, Hormosan Pharma, electroCore, Grünenthal, Reckitt Benckiser, and Teva. He does not hold any stocks of pharmaceutical companies or medical device companies. Emma Ramsden – provides services to Novartis Pharma AG. Paolo Martelletti – Section Editor, Medicine, SpringerNature Comprehensive Clinical Medicine; Editor-in-Chief, The Journal of Headache and Pain; Headache Books Series Editor, Springer; EU Expert, European Medicine Agency. Past-President of European Federation, Chairman of School of Advanced Studies of European Headache Federation. He does not hold any stocks of any pharmaceutical companies or medical device companies. Shannon Ritter and Josefin Snellman – employees and stocks: Novartis.

IHC-PO-075

Prevalences of migraine and other types of primary headache in China: a systematic review and meta-analysis

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Objective: Migraine and other types of primary headache are highly prevalent, and may be associated with a significant global economic burden. However, previous studies have reported inconsistent results regarding the precise prevalences of primary headaches in China. This meta-analysis aimed to determine the prevalence of migraine and other types of primary headache in China.

Methods: We searched the CNKI, Wanfang, Weipu, and PubMed databases for articles published between 1988 and 2015, in either English or Chinese, that reported

prevalence estimates for migraine and other types of primary headache in China. The studies' quality was evaluated using the STROBE guidelines. Prevalence estimates were summarized using a random effects mode, and we explored the potential sources of heterogeneity using meta-regression analysis.

Results: We included 15 studies (8,316,844 individuals), and only one study described the epidemiology of cluster headache. The prevalence of migraine ranged from 0.24% to 10.53%, and the prevalence of tension headache ranged from 1.96% to 35%. The pooled prevalence of migraine among Chinese individuals was 2.9% (95% confidence interval [CI]: 2.6–3.3%) and the pooled prevalence of tension-type headache was 14.24% (95% CI: 3.47–30.61%). Substantial heterogeneity was observed among the included studies.

Conclusion: Although the prevalence of primary headache in China is relatively low, compared to that in other countries, our findings indicate that migraine is associated with a significant burden in China. Our findings also indicate that there is a shortage of related high-quality epidemiological studies in China.

Disclosure of Interest: None Declared

IHC-PO-076

Transcultural adaptation and psychometric properties of the Brazilian version of the Headache Disability Inventory (HDI-Brasil)

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Objective: To translate and perform the transcultural adaptation of the Headache Disability Inventory (HDI) questionnaire into Brazilian Portuguese and to analyze its psychometric properties.

Methods: Patients with primary and secondary headaches were screened from a tertiary headache outpatient clinic and diagnosed by neurologists with expertise in headaches. It was included patients between 18 and 65 years old, with headache at least one day in the last month. Illiterate individuals were excluded. The translation process was conducted according to the Guideline for Transcultural Adaptations to Self-reported Measures, and 30 patients (age 34.9; SD 11.5) were asked to answer the questionnaire pre-final version in a self-administered form, reporting any doubts during filling. The assessment of its psychometric proprieties was performed according to the COSMIN Guidelines. It was included 80 women and 32 men (age 39.0; SD 12.8) and 38 women and 11 men (age 35.0; SD 12.4) to test the validity and reliability of the HDI-Brasil, respectively. The internal consistence of the

HDI-Brasil was assessed through the Cronbach's alpha coefficient. Pearson's correlation test was used to analyse the questionnaire construct validity, and Intraclass Correlation Coefficient (ICC) was used to assess its reliability with significance level of 5%.

Results: For the transcultural adaptation of the HDI-Brasil, only 20% of the patients had doubts regarding the understanding and meaning of the words. The internal consistency was 0.84, considered an optimal correlation among the questionnaire items. Since the limit of individuals with doubts was not exceeded, the final version of the questionnaire was defined. For construct validity assessment, the HDI-Brasil was compared to the Headache Impact Test (HIT-6™) and to the SF-12 quality of life questionnaire, resulting in moderate ($r=0.62$; $p<0.001$) and strong ($r=-0.73$; $p<0.001$) Pearson's correlation, respectively. The test-retest reliability, performed with one-week interval resulted in excellent reliability (ICC: 0.94, CI 95%: 0.90–0.96).

Conclusion: The Brazilian version of the HDI was successfully adapted to the Brazilian population, and exhibited adequate validity to measure headache impact, with excellent reliability.

Disclosure of Interest: None Declared

IHC-PO-077

The IRON Registry (The Italian chRONic migrainE registry): an update on 637 patients

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Objective: To update the findings of the Italian IRON Registry, the first chronic migraine (CM) registry worldwide, which is aimed to disentangle the diverse endophenotypes of CM, optimize its ascertainment, favor a shared clinical management strategy and rationalize healthcare resource use.

Methods: All consecutive CM patients seen at 22 Italian headache centers were enrolled. 406 items on socio-demographic factors, life-style, migraine features before and after chronicization, comorbidities and healthcare resource use were gathered by specifically-trained

neurologists via face-to-face interviews and shared a web-based platform.

Results: 774 CM patients were enrolled, the interim analysis was conducted on 637 individuals. The majority of patients were females (83.1%), mean age of 46.8 ± 12.9 yrs and a mean monthly headache frequency of 26.9 ± 16.4 days. Migraine started at 17.6 ± 9.3 yrs, chronicization at 27.6 ± 7.4 yrs and the first headache specialist consultation at 36.3 ± 13.0 yrs. 70% of patients were on migraine prophylaxis, only 20.6% of them when migraine was episodic. The mean n. of preventive treatments per patient was 1.84 ± 1.9 . Analgesic overuse was present in 57.9% of cases, detoxification in 33.1% of patients, effective only in 17.6%. Symptoms of peripheral trigeminal sensitization were common: unilateral headache (48.4%), pulsating (55.0%), associated with vegetative symptoms (73.8%) and unilateral cranial autonomic symptoms (31.1%). Almost 80% had consulted ≥ 2 headache centers. 77.2% of patients underwent >1 investigation-frequently inappropriate (48%) and generally (57.8%) charged to the national health system (NHS). During the previous year, 18.7% of patients were admitted to the ED; lifetime hospitalization for migraine was 18.5%, for DH 16.8%, mean n. of specialists consultations was 9.22 ± 16.86 per patient.

Conclusion: The IRON registry shows the presence of symptoms of peripheral trigeminal sensitization in CM; a substantial delay between age at migraine chronicization and headache center consultation; a relatively low n. of prophylaxis tried by patients; a large number of inappropriate diagnostic procedures, mostly charged at the NHS

Disclosure of Interest: None Declared

IHC-PO-078

Economic Burden of Migraine Patients with Eight or More Headache Days per Month: A Cross-Sectional Analysis of Survey Data in the EU5 (France, Germany, Italy, Spain, and the United Kingdom)

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Objective: Migraine is among the top contributors of disability amongst people aged 15–49 years. We aimed to characterise the incremental burden of migraine of patients suffering from ≥ 8 Monthly headache days (MHDs), in terms of Healthcare Resource Use (HRU) and Work and Activity Impairment in the EU5 (France, Germany, Italy, Spain, and the United Kingdom).

Abstract number: IHC-PO-078 Work impairment and HRU amongst patients with ≥ 8 MHDs compared to propensity matched healthy controls: Results from NHWS 2017 EU5 sample

	No migraine	4–7 MHDs	≥ 8 MHDs
Work productivity and activity impairment			
Absenteeism, Mean % (SD)*	8.47% _a (22.29)	11.28% _b (23.91)	15.57% _c (27.96)
Presenteeism, Mean % (SD)*	20.54% _a (26.91)	32.11% _b (28.18)	37.43% _c (27.26)
Total Work Productivity Impairment, Mean % (SD)*	22.62% _a (29.06)	34.77% _b (30.24)	40.85% _c (29.81)
Activity Impairment, Mean % (SD)*	25.69% _a (28.16)	39.23% _b (29.32)	47.37% _c (28.85)
Healthcare resource use in past 6 months amongst those who had ≥ 1 HCP visit			
HCP visits, Mean (SD), % Patients with ≥ 1 visit	5.46 _a (6.4), 85.1% _a	8.30 _b (9.34), 96% _b	9.26 _c (9.28), 94.9% _b
Hospitalizations, Mean (SD), % Patients with ≥ 1 visit	1.66 _a (1.67), 7.8% _a	1.59 _a (1.30), 11.9% _b	1.66 _a (1.67), 15.1% _b
ER visits, Mean (SD), % Patients with ≥ 1 visit	1.52 _a (0.97), 11.9% _a	1.82 _a (1.33), 23% _b	2.17 _b (2.26), 24.4% _b
GP visits, Mean (SD), % Patients with ≥ 1 visit	2.69 _a (2.91), 65.1% _a	3.45 _b (3.54), 79.4% _b	4.03 _c (3.85), 81.9% _b
Neurologist visits, Mean (SD), % Patients with ≥ 1 visit	1.88 _a (1.34), 4.2% _a	1.68 _a (1.28), 12.4% _b	1.82 _a (1.34), 19% _c

Values in the same row not sharing the same subscript are significantly different at $p < .05$ in the two-sided test of equality for column means or proportions. *Includes only those respondents who were employed at the time of the survey. HCP: Healthcare provider, ER: Emergency room, GP: General practitioner.

Methods: A retrospective analysis was conducted using EU5 data from the 2017 National Health and Wellness Survey. A total of 1,569 patients who self-reported a physician diagnosis of migraine and ≥ 4 MHDs were 1:1 propensity score matched to non-migraine controls on socio-demographic characteristics and health variables that could affect the outcomes. HRU was estimated through standard questions, while work and activity impairment was calculated using the Work Productivity and Activity Impairment (WPAI) questionnaire. Bivariate analyses were conducted after matching to compare those with 4–7 MHDs ($N=783$) and ≥ 8 MHDs ($N=786$) with those without migraine using independent-samples t-tests and Chi-square tests depending on the nature of variables.

Results: WPAI scores amongst the ≥ 8 MHDs sub-group were almost twice that of their non-migraine counterparts (15.57% vs 8.47% [absenteeism], 37.43% vs 20.54% [presenteeism], 40.85% vs 22.62% [total work productivity impairment] and 47.37% vs 25.69% [total activity impairment], all $p < 0.05$). HRU for the ≥ 8 MHDs sub-group was significantly higher than that of non-migraine controls; the largest difference was observed for mean number of visits to any healthcare practitioner (HCP) (9.26 vs 5.46, $p < .001$) and general practitioners (GP) (4.03 vs 2.69,

$p < .001$). The proportion of patients with ≥ 8 MHDs with ≥ 1 HCP visit was approximately twice as much for hospitalizations and ER visits and almost 5 times more for neurologist visits when compared to non-migraine controls.

Conclusion: Patients with ≥ 8 MHDs have significantly higher HRU and work impairment when compared to non-migraine controls. In addition, a substantially higher proportion amongst them have ≥ 1 visits to HCPs when compared to non-migraine controls.

Disclosure of Interests: This study was funded by Novartis Pharma AG, Basel, Switzerland.

IHC-PO-079

Characterization of a continuous daily headache in children, adolescents and young adults

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Objective: To characterize clinical headache features observed in a large population of patients with continuous daily headaches, including patients with New Daily Persistent Headaches (NDPH), and continuous Chronic Migraine (CM).

Methods: Participants included all patients presenting to a specialty headache center between August 1997 and March 2019 who reported continuous or “always” headache at the time of their initial visit. Diagnoses included CM, NDPH, chronic tension-type headache (CTTH), and probable-NDPH and probable-CM in patients with less than 3-month duration of daily headache. Data were collected using semi-structured interviews employing a standard intake questionnaire. Diagnoses were by ICHD criteria corresponding to the time of enrollment with retrospective assessment to ICHD-3.

Results: A total of 1695 patient visits were analyzed. Of these, 1337 patients (79%) were female and 357 (21%) were male. Median age was 15 years old (range 3–25 years; only 46 were older than 18 years). Duration of continuous headache ranged from 5 days to 12 years. 1351 patients (80%) reported throbbing headache, 1391 (82%) reported photophobia, 1377 (81%) reported phonophobia, 1105 (65%) reported nausea, and 412 (24%) reported vomiting as associated symptoms. Median PedMIDAS score was 54. Additional analyses will sub-categorize this group of continuous headache patients by diagnosis and look at the prevalence of features including the presence or absence of medication overuse, degree of disability, and presence or absence of family history of migraine.

Conclusion: This is the largest cohort of pediatric, adolescent and young adult patients with continuous headache to be described to date. Continuous headache is more common in female than in male patients in this population, and most have migrainous features to their headaches. Their headache typically results in moderate to severe disability as measured by PedMIDAS. Future studies are planned to evaluate the clinical trajectory of these patients, as well as to further characterize this patient group including analysis of lifestyle habits, history of psychological comorbidities, and presence of clinical hypermobility.

Disclosure of Interest: None Declared

IHC-PO-080

Symptomatic headache in the neurological emergency department – a retrospective study

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Objective: The aim of this study was to examine profiles of patients presenting with headache in a university

emergency department and to record clinical, epidemiological and diagnostic data.

Methods: 11210 patients who presented to the Department of Neurology at Rostock University Hospital between 11/2013–11/2016 were included in this retrospective cross-sectional study. 1020 had the cardinal symptom of headache. For these patients, 63 variables including headache characteristics and data on diagnostic procedures were collected from the medical records.

Results: The prevalence of headache in the neurological emergency room amounts to 9.1% with a female preponderance (64%) and an average age of 46 years. Primary headaches were the most frequent headache type (40.1%) with migraine as the most frequent subtype (73.4%), followed by tension-type headache (17.2%) and trigeminal neuralgia (7.7%) as the most frequent facial pain. The second largest group (28.9%) were patients with symptomatic headache. 17.3% were due to infection, 17.3% to disorders of homeostasis, 15.9% to vascular disease, 5.8% to trauma, 7.1% to intoxication or withdrawal, and 11.2% to psychiatric disorders. Of the headache in vascular disease, 20.8% were present in patients with cerebral ischemia, 12.5% in subarachnoid hemorrhage, 14.6% to subdural hematoma, and 6.3% to arterial dissection. Age ($p = 0.001$) and male sex ($p = 0.011$) correlated positively with a diagnosis of symptomatic headache. Patients with cardiovascular disease were significantly more likely to have symptomatic headache ($p > 0.001$).

67.8% of all patients received cerebral imaging, which showed abnormalities in 53% of patients diagnosed with symptomatic headache. In addition, 43.6% of all patients who presented to the emergency room with an emergency doctor suffered from a symptomatic headache.

Conclusion: With a prevalence of 9.1% headache as main symptom is slightly below the published data. With a rate of 30%, symptomatic headaches represent a relevant group that need a timely diagnosis, especially in elderly or male patients and those with cardiovascular co-morbidity.

Disclosure of Interest: None Declared

IHC-PO-081

Frequency of diagnoses in a specialized headache clinic in Buenos Aires

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Objective: Headache is one of the most frequent reason for consultations in neurology. The global prevalence

among adults with migraine is >10%, 40% for tension-type headache (TTH) and 3% for chronic daily headache.

The purpose of this study is to analyze the prevalence of the diagnoses of headache and craniofacial pain among patients evaluated in a specialized headache clinic of Buenos Aires during 2017.

Methods: Retrospective, descriptive study. We reviewed the electronic medical records of patients who consulted for headaches or craniofacial pain from January 1st to December 31st, 2017. Diagnoses were made according to the criteria of the International Classification of Headache Disorders (ICHD-3).

Results: We reviewed 3254 electronic medical records and documented 3941 diagnoses: headache (93.03%), craniofacial pain (3.62%) and undefined (3.35%). The average age was 43.14 years. 80.7% were women.

Primary headaches were the most frequent diagnoses (78.54%). Migraine represented the main diagnosis (87.42%). Episodic migraine without aura was the most prevalent diagnosis (48%). Tension-type headache (TTH) was found in 8.74% of cases of primary headaches and Trigeminal autonomic cephalalgias (TACs) in 2.89%. Medication-overuse headache (MOH) represented 77.93% of the secondary headaches, and the majority fulfilled criteria of chronic migraine.

Primary trigeminal neuralgia represented 50% of craniofacial pain and 27% were secondary trigeminal neuralgia, mostly postherpetic or posterior to dental procedures. 33.58% of the patients had chronic headache.

Conclusion: In our section, migraine is the most frequent diagnosis followed by medication-overuse headache. The percentage of chronic headache is higher than the prevalence in the general population, probably because it is a tertiary center.

Disclosure of Interest: None Declared

IHC-PO-082

Primary headache in elderly

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Objective: The diagnosis of primary headache in the elderly is increasing lastly including both the recurrent and new onset cases. Our aim was the study the prevalence of primary headaches in the elderly adults and to see the correlation between the age and some other variables as gender, other concomitant diseases, the headache form etc.

Methods: We interviewed 160 persons over 50 years old using a specific questionnaire on the form of headache, age at onset, if the headache was stopped or not, the familiar

history, imaging data, other concomitant diseases as arterial hypertension, the age of onset of other diseases, the frequency of headache, the severity of headaches, etc. The questionnaires are filled out by residents of neurology in a 10 days period. The diagnosis of primary headache is done according to the International Classification of Headache Disorders, 3rd edition (2018).

Results: We interviewed 160 persons: 28 (17.5%) were inpatients of Neurology ward. The others were persons randomly chosen, as patient's familiars and medical staff. The mean age of the interviewed people is 62.5 years old (50–89 years). There are 85 (53%) females. 21 patients had primary headache during their life, just stopped at the time of the study. We identified 67 (41.8%) patients suffering of primary headache, 67.1% of them were female. The mean age of headache male patients is 60.9 years old and 61.2 for the females. According to headache form there were: 24 patients suffering of tension headache (16- 66% female), 25 patients fulfilling the migraine criteria (19–76% females), and 4 with hypnotic headache (2 –50% females), 14 with other forms of headache. 52 headache patients had high arterial pressure. There were 13 (19%) cases with onset on or over 50 years old. The mean frequency is from once a month to daily headache. The mean severity is 6.37 (1–10 scale), slightly higher in males. No significant correlation with imaging data is found. The familiar history was present in 42% of cases.

Conclusion: Primary headache is not a rare finding in elderly people. According to recent publications the diagnosis of onset or ongoing primary headache in elderly people must be important. The management of headache is more complicated because of other concomitant diseases.

Disclosure of Interest: None Declared

IHC-PO-299

Impact and Burden of Episodic, Acute Migraine (I-BEAM): A Patient Experience Study

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Objective: The objectives of this patient survey were to better understand: 1) the experiences of episodicmigraineurs and the effect of migraine on daily life; 2) the typical pathway and barriers to diagnosis and treatment; and 3) satisfaction levels with current treatments and to identify unmet needs.

Methods: Participants were recruited via social media and referrals. A preliminary 15-minute online survey was conducted with current migraine sufferers to determine history, past and current treatments, and overall experience with migraine treatments. One-hour individual-depth

interviews (IDIs) were conducted with respondents in three major U.S. cities, and 1-hour web-enabled telephone-depth interviews (TDIs) were conducted with others throughout the United States.

Results: Of study participants ($n = 50$), 75% were female, 64% were aged 30–49 years, and 56% suffered from 3–5 migraines or 4–8 migraine-days a month. The two most common types of migraines reported were rapid-onset migraine (34%) and early morning migraines (30%). Although 96% took a prescription medication for migraines, only 30% were satisfied with their medication. Incomplete, unreliable and short lasting relief were cited as the biggest problems. Lack of speed to onset of effect was also a point of dissatisfaction with >50% reporting inability to resume normal activities within 4 hours after medicating. Up to 68% reported headache relief lasting less than 12 hours and pain returning or worsening afterwards. Further, 30% respondents had to seek emergency migraine care in the past year despite access to standard of care. Thus, the social, societal and economic burden of episodic migraine significantly impacts the daily lives and livelihoods of patients with migraine.

Conclusion: This study further demonstrates the unmet needs of current episodic migraineurs. Patients described their ideal medication to be: (1) fast acting (15–30 mins) (2) long-lasting (12–24 h) (3) providing complete or near complete relief (4) can be taken any time during the migraine and (5) with few or no side effects. Many are willing to accept minor side effects as a tradeoff for increased speed and efficacy. A product is being developed by Impel NeuroPharma to address all 5 of these requirements.

Disclosure of Interests: Drs Ray and Shrewsbury are both full time employees of Impel NeuroPharma

IHC-PO-300

Is pediatric headache increasing in emergency department? An Italian experience

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Objective: The aim of this study was to analyze the change in the prevalence of children with headache presenting to the emergency department over a period of ten years.

Methods: The total number of accesses to the emergency department of the Children's Hospital G. Cristina in Palermo was retrospectively analyzed in the two-year period 2009–2010 and in the two-year period 2017–2018 in order to examine the differences over a period of 10 years. The percentage of accesses for headache and the number of specialistic assessments and of imaging procedures (computed tomography) have been analyzed in the two periods examined.

Results: The total accesses to the emergency department have decreased from 55616 to 50096 (–10%) between the two-year periods considered while the number of accesses for headache has increased by around 63.56% ($p < 0.0001$). The highest increase occurred in the age groups of 7–13 and 14–17 (respectively 69.23% and 52.12%). The increase is mainly due to the entry of probably primary headaches or not classifiable headaches (about 67% of the total increase), especially for the age group 7–13 and for the group 14–17. At the same time the number of child neuropsychiatric assessments and the number of computed tomography have remarkably increased.

Conclusion: The significant increase of accesses for pediatric headaches is probably due to the limited efficacy of the Italian and international guidelines and of the educational strategies, underlying the existing connection difficulties between the primary care network and hospitals. It is also important to reflect on the use of red flags because many of them probably have poor sensitivity and specificity. This results in an avoidable overcrowding of the emergency department for useless accesses, in an increase of unnecessary assessments and procedures and, in the end, in an increase of health costs.

Disclosure of Interest: None Declared

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Anesthetic blocks for the treatment of headaches in elderly people

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Objective: The possibility of anesthetic blocks would be an interesting option for elderly patients, as treatment options are limited, considering the presence of comorbidities and daily medications in use. This study aimed to describe and analyze, in a single center, elderly patients who were treated with anesthetic blocks for headache. The main types of headache, indications of peripheral

blocks, blocked points and, adverse effects response to treatment were also assessed.

Methods: The study was conducted from the review of medical records in a Neurological Clinic. Patients with headache diagnosis, with 50 years old and older, who received anesthetic blocks were included. Diagnosis of headache, characteristics, intensity and frequency, associated comorbidities, instituted treatments, including anesthetic blocks and botulinum toxin application, as well as therapeutic response and presence of adverse effects were described.

Results: Medical records from 2013 to 2017 were reviewed ($n = 4,106$). Of these, 785 patients were treated for chronic pain with anesthetic blocks and 82 patients were elderly with headache, treated with anesthetic blocks. The mean age of the patients was 57.7 years (SD 7.89) and 65 (79.3%) were women. The main diagnosis of headache was migraine (41, 50%), cervicogenic headache (33, 40.2%), temporomandibular dysfunction (11, 13.4%), trigeminal-autonomic headache (4, 4.8%) and tension-type headache (2, 2.4%). The frequency of pain was 24.3 days/month (SD 9.2) and mean pain intensity was 9.3 (0–10). The abusive use of analgesic medications was described in 17 (20.7%) patients. The main anesthetic blocks were major and minor occipital nerves (62, 75.6%) and muscular trigger points (19, 23.2%). Botulinum toxin application was performed in 6 patients (7.3%). The average number of blocks was 2.74 (SD 2.38) per patient. There was a total improvement of the symptoms in 52 (63.4%) and partial improvement in 22 (26.83%). The mean frequency of pain after treatment was 4.3 days/month (SD 6.09). There were no adverse events related to the procedures.

Conclusion: The use of anesthetic blocks in the elderly in the treatment of headache was considered safe and effective as a therapeutic option.

Disclosure of Interest: None Declared

IHC-PO-302

Medication overuse headache in Bihar, India

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Objective: Medication overuse Headache (MOH) is a well-known cause of chronic headache worldwide. The prevalence of MOH is about 2% in women and about 1% in men in industrialized countries. There are very few studies from India and none from the state of Bihar with a population of 104 million. The aim of the study was to document the findings and observations in MOH patients seen in Bihar, India.

Methods: A questionnaire based, prospective study including consecutive patients at Headache clinic in the

department of Neurology at a tertiary referral center in India. The patients were diagnosed based on the International Classification of Headache Disorders 3rd edition (ICHD 3) criteria. Patients above 18 years and with more than 1 year of headache were included and details on demographics, history, clinical pattern and treatment were recorded.

Results: Of the 1356 patients presenting to headache clinic from January 2018 to February 2019, 32 patients fulfilled the criteria for MOH. Females comprised 91% of the study group, with an average age of 33.89 years. Ergotamine in combination with caffeine, paracetamol and prochlorperazine contributed the most (65.62%) followed by combination analgesics (31.25%) and Ibuprofen (3.12%). There was no instance of triptan, barbiturate or opioid over-use. All the patients had episodic migraine to begin with, none had tension-type headache or any other headache. The average intake was 21.5 months for ergots and 18 months for combination analgesics. 4/32 had depression and 6/32 had associated anxiety. None of the patients developed vascular complications with ergotamine or were aware about the difference between prophylactic and abortive medications.

Conclusion: MOH is an under-diagnosed condition in India, but the prevalence is lower than the western countries. The general fear of kidney damage, practice of applying local pain balms, delaying taking painkillers and alternative treatment options probably is the reason. Ergotamine was the main culprit due to easy availability, cost and popularity amongst non-neurologists. Cost is a major factor limiting factor for triptans and other medications are not used routinely for pain relief in India. Raising awareness regarding MOH, prophylactic medications in primary physicians and developing treatment strategies is the need of the hour.

Disclosure of Interest: None Declared

IHC-PO-303

Disease management quality indicators for two high burden, high prevalent conditions: Is migraine neglected in comparison to diabetes?

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Objective: Diseases with comparably high associated disability are managed with very different levels of direct healthcare spending across the United States, Canada,

Germany, and the Netherlands. Health expenditure in migraine was consistently and by far the lowest, in diabetes (another high prevalent and high disability condition), it was 7 to 37-fold of migraine. Here, we aimed to compare the real-world management standards in migraine with those in diabetes across the four countries.

Methods: A targeted literature review was conducted using Embase[®], Medline[®], and Google Scholar to identify studies (published in English in past 5 years) providing data for disease quality care indicators in migraine and diabetes.

Results: Twenty studies were identified. In migraine, numerous poor-quality indicators for disease management were observed: diagnosis rates (25% to 46%), headache specialist/neurologist consultation rates (3% to 33%), and limited use of migraine preventive medications (2% to 56%). Contrary to this, diagnosis rates for diabetes were almost 2-fold of migraine (56% to 90%). Furthermore, real-world diabetes care was associated with varied disease management indicators, including HbA1c over-testing vs. under-testing (61% vs. 26%) and potential over-treatment (11% to ~60%) vs. under-treatment (7% to 28%) with anti-diabetic drugs.

Conclusion: This study indicates strong disparities in the management standards and healthcare spending for diabetes and migraine despite comparable associated disability, though different long-term risks. Highly different levels of healthcare spending seem to be correlated with different healthcare quality indicators for patients: migraine was consistently associated with insufficient/under-management, while diabetes was observed to be associated with more effective management standards. Increased focus on migraine may help overcome the insufficient management and decrease the high level of avoidable disability burden among its patients.

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IHC-PO-304

My Migraine Voice Survey: How is living with migraine in Argentina?

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Objective: The objective of this worldwide study was to better understand what it is like to live with migraine. We included respondents' from Argentina to reflect our country situation.

Methods: My Migraine Voice was an online survey, cross-sectional, in 31 countries. Participants were adult migraine patients, who reported ≥ 4 migraine days/month in the 3 preceding months. Pre-specified screener criteria were applied as 90% of participants had taken at least one preventive treatment, and 80% switched preventive at least once.

Results: From 11,266 participants worldwide, we included 227 from Argentina. 85% women, average age 34 y/o. 70% were employed. Average days per month with headache was 9.8/month.

Burden of migraine: 62% reported being extremely limited during migraine. 36% headache lasted over 24 hours. 94% had sleep difficulties. 81% had to stay long periods in the dark isolated (average 17.9 hours/month). Most of them reported impact on their personal (68%), social (81%), or laboral (86%) life. 56% missed at least a day at work (average 3.9 lost days/month). They missed 12% of working time and 51% of productivity due to migraine. Average monthly expenses due to migraine are AR\$6401. 21% reported limitation in access to treatment.

Barriers in diagnosis and treatment: diagnosis was performed by neurologist in 67% and by general practitioner in 23%. They were evaluated by 2.8 professionals in 5.4 medical visits prior to diagnosis, 33% took more than a year being diagnosed. A diagnostic imaging was made in 72%, with 13% with more than 5 images made. 67% of participants took medication in acute crisis. 67% was prescribed, 55% over-the-counter medication, 29% used alternative therapies. Most of participants were on preventive treatment (88%).

Conclusion: This study describes the burden that migraine exerts on individuals with migraine living across the world, particularly in Argentina.

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IHC-PO-305

Analysis of the work of headache outpatient office

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Objective: World Health organization (WHO) ranked headache among the ten most disabling conditions worldwide. Patients who consult doctors have different clinical features. Aim of study to analyze of the work of the headache outpatient office.

Table 1. Classification of headache among patients.

ICHD 3d edition diagnosis		Number of patients
Primary headaches		47
Migraine		17
Tension headache		22
Cluster headache		3
New daily persistent headache		2
Headache attributed to external application of a cold stimulus		2
Primary headache associated with sexual activity		1
Secondary headaches		26
Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure	-Cervicogenic headache	5
	-Headache attributed to disorder of the eyes	3
	- Headache associated with pathology of ENT organs	6
Chronic post-traumatic headache		3
Headache attributed to hypertensive encephalopathy		5
Headache caused by a pituitary adenoma		1
Trigeminal neuralgia		3

Abstract number: IHC-PO-305

Table 2. Main clinical characteristics of the migraine attacks.

Indicator	Episodic migraine without aura	Episodic migraine with aura	Possible episodic migraine	Chronic migraine	Menstrual migraine
Number of patients	9 (53%)	1 (5,9%)	3 (17,6%)	3 (17,6%)	1 (5,9%)
The frequency of migraine attacks (per month)	3,5	2	2,8	6,7	4
The duration of the attack (hours)	22,2	8	15,1	7,2	6
Intensity VAS	6,4	8	5,3	7	6
MIDAS	II	I	I	II	I

Methods: At the headache outpatient office based on neurology and clinical genetics department of Kyrgyz State Medical Academy for the period of 6-months (October 2018- March 2019) were consulted 73 patients with headache. All patients were filled special questionnaires for revealing a main headache characteristic. During the initial consultation a headache diary was

issued to all patients with instructions on how to complete it. Clinical diagnosis was made according to the criteria of the International Classification of Headache Disorders (ICHD) 3 edition. Visual Analogue Scale (VAS) and MIDAS scale was used. Additional laboratory tests and visualization methods were used to identify secondary type of headaches.

Results: Primary headaches were observed in 47 (64.4%) patients, secondary headaches in 26 (35.6%). Table 1 shows the structure of the diagnoses of patients who complained of headache. In primary headache group 17 (36.1%) patient has a migraine. Sex differentiation – 15 females, 2 males; average age 32.3 ± 2.4 years. The results of the analysis of provoking factors showed that emotional stress was the most frequent factor causing a migraine attack. Also, attacks were often caused by alcohol, weather changes, smells, and lack of sleep. Table 2 shows the main clinical characteristics of the migraine attacks. Most of the patients for the relief of headache took drugs of the NSAID group, codeine containing and combination drugs. Preventive therapy has not previously been conducted.

Conclusion:

- low awareness of the population and doctors about migraines (for 85% diagnose migraine was putting the first time)
- excessive use of drugs of the NSAID group, codeine containing drugs for the relief of a headache attack, which can result in abuse headache and complications from other systems (eg gastric and duodenal ulcer, reduction of blood pressure when taking NSAIDs)
- not a serious attitude in keeping a diary headache.

These problems that have arisen during the study can be solved through active information work among specialists and patients by the help of brochures, lectures.

Disclosure of Interest: None Declared

IHC-PO-306

Migraine-related healthcare resource use in the emergency department setting: a panel-based chart review in France, Germany, Italy, and Spain

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Objective: To evaluate migraine-related healthcare resource use (HRU) in the emergency room (ER)/ Accident & Emergency (A&E) setting for patients with four or more monthly migraine days (≥ 4 MMDs).

Methods: A retrospective, non-interventional, panel-based chart review was conducted among physicians who had treated patients with ≥ 4 MMDs in the ER/A&E setting in France, Germany, Italy, and Spain. Data for physician and ER/A&E characteristics, patient/disease characteristics, treatment history, and migraine-related HRU during the ER/A&E visit were collected. Descriptive analyses were conducted in the pooled population and by country.

Abstract number: IHC-PO-306 Migraine-related HRU amongst patients with ≥ 4 MMDs during the ER/A&E visit

	Overall (N = 467)	France (N = 120)	Germany (N = 120)	Italy (N = 107)	Spain (N = 120)
Length of ER/A&E visit in hours, mean (SD)	7.9 (8.7)	8.6 (6.3)	5.4 (5.7)	10.3 (12.7)	7.5 (8.4)
Hospital admission, n (%); inpatient days [mean (SD)]	99 (21.2%); 3.4 (2.7)	45 (37.5%); 2.9 (2.2)	27 (22.5%); 2.7 (1.5)	17 (15.9%); 4.6 (2.2)	10 (8.3%); 5.6 (5.9)
Referral to a neurologist or HA specialist, n (%)	273 (58.5%)	69 (57.5%)	60 (50.0%)	86 (80.4%)	58 (48.3%)
Any acute/preventive pharmacologic treatment administration, n (%)	452 (96.8%)	115 (95.8%)	118 (98.3%)	104 (97.2%)	115 (95.8%)
Blood tests, n (%)	382 (81.8%)	87 (72.5%)	108 (90.0%)	95 (88.8%)	92 (76.7%)
Cranial computerized tomography scan, n (%)	214 (45.8%)	63 (52.5%)	43 (35.8%)	68 (63.6%)	40 (33.3%)
Electrocardiography, n (%)	291 (62.3%)	69 (57.5%)	95 (79.2%)	71 (66.4%)	56 (46.7%)
Fundoscopy, n (%)	131 (28.1%)	21 (17.5%)	19 (15.8%)	43 (40.2%)	48 (40.0%)
Urinalysis, n (%)	176 (37.7%)	26 (21.7%)	62 (51.7%)	41 (38.3%)	47 (39.2%)

Results: A total of 467 patients were included in the analysis (64% female, mean age 39 years, average disease duration 6.7 years). Migraine-related HRU in the ER/A&E setting was high. Overall, 21% of the patients were hospitalized (mean: 3.4 days), 58% were referred to a neurologist/headache (HA) specialist, and >95% were administered migraine treatment (acute/prophylactic) during their visit. On average, patients spent almost eight hours in the ER/A&E. The most commonly used procedures were blood tests (82%), electrocardiography (62%), and cranial computerized tomography scans (46%). The HRU varied across different countries, and no consistent trend was observed (Table).

Conclusion: This study highlights that migraine is associated with a substantial HRU burden in the ER/A&E setting. The burden further extends past the ER/A&E, as many of the patients are hospitalized or referred to specialists.

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Pamela Vo: Employee of Novartis Pharma AG, Switzerland; Elyse Swallow, Eric Wu, Wei Gao, Miriam Zichlin, Eleanore Fuqua: Employees of Analysis Group, United States; Thais Tarancon and Marta Aguirre Vasquez: Employees of Novartis Farmaceutica, S.A., Spain; Monika Maier-Peuschel: Employee of Novartis Pharma GmbH, Germany; Marianonietta Naclerio, Daniela Ritrovato, and Silvia Rossi: Employees of Novartis Farma S.p.A., Italy; Nicolas Mahieu: Employee of Novartis Pharma S.A.S. France.

IHC-PO-307

Impact of Anxiety and Depression on Patients with Migraine. Results from the Atlas of Migraine in Spain 2018

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Objective: To identify anxiety and depression and their impact on patients with chronic (CM) and episodic (EM) migraine.

Methods: The *Atlas of Migraine in Spain* is an online survey promoted by the Spanish Patient Association of Headache and Migraine (AEMICE), and developed by the HTR of the University of Seville, with the support of the Headache Study Group of the Spanish Neurological Society (GECSN). From the 124 surveyed items, the following

were used for this analysis: sociodemographic, clinical characteristics and comorbidity data, as well as the MIDAS, Headache Needs Assessment (HANA) questionnaire and, the Hospital Anxiety and Depression Scale (HADS).

Mean (Kruskal-Wallis test), distribution (χ^2 test), and correlation analyses were performed to assess the association of HADS levels with sociodemographic and health outcome variables.

Results: Among patients who completed the survey ($n = 1283$), 65.6% had EM and 34.4% CM. The prevalence of anxiety was 59.5% in EM and 77.4% in CM, whereas depression was 28.2% in EM and 55.4% in CM. Having university education was associated with lower levels of anxiety and depression. MIDAS and HANA were higher in patients with anxiety and/or depression, but especially high in those with CM. The total HADS score was associated with both MIDAS ($r = 0.28$; $p < 0.001$; $n = 606$) and HANA ($r = 0.50$; $p < 0.001$; $n = 619$). Anxiety and/or depression were associated with greater presence of comorbidities, specifically with arthritis, chronic pain, hypertension, and fibromyalgia. For CM, they were also associated with obesity, sinusitis, and heart problems.

Conclusion: The prevalence of anxiety and depression in patients with migraine is high, particularly in those with CM, and contributes to a decrease of health-related quality of life and disability. Our findings highlight the importance of addressing these affective disorders when treating migraine patients.

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IHC-PO-308

Proportion of Migraine Patients in Migraine Frequency Sub-Groups: A Cross-Sectional Analysis of Survey Data in France, Germany, Italy, Spain, and the United Kingdom

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Objective: Migraine is a debilitating disorder that affects over 10% of the world's adult population. However, there are limited data on prevalence of migraine by its frequency sub-groups. We aimed to estimate and stratify the proportion of migraine patients by frequency sub-groups, in the EU5 countries, and compare their healthcare resource use (HRU) using baseline data from the 2017 National Health and Wellness Survey (NHWS).

Abstract number: IHC-PO-308 NHWS 2017 participants in EU5 and their HRU, stratified by country and migraine frequency

Migraine Sub-Group	UK (N = 624)	France (N = 695)	Germany (N = 621)	Italy (N = 663)	Spain (N = 289)	EU5 Total (N = 2,892)
1–3 MHDs	% (N)	39.9% (249)	50.5% (351)	34.1% (212)	52.6% (349)	45.8% (1323)
% Patients with ≥ 1 HCP visit	ER: 19.3% Hosp: 12.9% Neur: 5.2%	ER: 13.4% Hosp: 9.4% Neur: 4.3%	ER: 11.3% Hosp: 11.3% Neur: 12.3%	ER: 16.0% Hosp: 8.6% Neur: 7.4%	ER: 39.5% Hosp: 8.6% Neur: 5.6%	ER: 18.1% Hosp: 10.1% Neur: 6.7%
4–7 MHDs	% (N)	21.2% (132)	27.9% (194)	30.3% (188)	28.7% (190)	27.1% (783)
% Patients with ≥ 1 HCP visit	ER: 17.4% Hosp: 12.1% Neurologist: 5.3%	ER: 21.1% Hosp: 17.5% Neur: 9.3%	ER: 19.7% Hosp: 11.2% Neur: 19.1%	ER: 22.1% Hosp: 8.4% Neur: 10.5%	ER: 46.8% Hosp: 7.6% Neur: 20.3%	ER: 23.0% Hosp: 11.9% Neur: 12.4%
8–14 MHDs	% (N)	15.4% (96)	14% (97)	21.6% (134)	11.3% (75)	14.8% (429)
% Patients with ≥ 1 HCP visit	ER: 18.8% Hosp: 14.6% Neur: 7.3%	ER: 18.6% Hosp: 14.4% Neur: 15.5%	ER: 20.1% Hosp: 20.1% Neur: 17.2%	ER: 18.7% Hosp: 10.7% Neur: 16%	ER: 59.3% Hosp: 3.7% Neur: 18.5%	ER: 21.7% Hosp: 14.9% Neur: 14.5%
≥ 15 MHDs	% (N)	23.6% (147)	7.6% (53)	14% (87)	7.4% (49)	12.3% (357)
% Patients with ≥ 1 HCP visit	ER: 27.2% Hosp: 15.6% Neur: 24.5%	ER: 30.2% Hosp: 20.8% Neur: 11.3%	ER: 25.3% Hosp: 19.5% Neur: 33.3%	ER: 14.3% Hosp: 0% Neur: 16.3%	ER: 66.7% Hosp: 19.0% Neur: 38.1%	ER: 27.7% Hosp: 15.4% Neur: 24.4%

MHDs: Monthly headache days, ER: Emergency room, Hosp: Hospital, Neur: Neurologist.

Methods: We conducted this retrospective analysis using the 2017 NHWS EU5 sample. All respondents had a medical diagnosis of migraine and were stratified by frequency of monthly headache days (MHDs); 1–3, 4–7, 8–14 and ≥ 15 MHDs. HRU was estimated through standard questions including visits to healthcare practitioners (HCPs).

Results: Amongst respondents with migraine, 45.8% of the population suffered from 1–3 MHDs while 54.3% suffered from ≥ 4 MHDs (4–7 MHDs: 27.1%, 8–14 MHDs: 14.8% and ≥ 15 MHDs: 12.3%). Overall, in comparison to patients with 1–3 MHDs, the HRU amongst patients with ≥ 4 MHDs was much higher. For example, in the past 6 months, 12.4% of patients with 4–7 MHDs, 14.5% with 8–14 MHDs and 24.4% with ≥ 15 MHDs had visited a neurologist, compared to only 6.7% of patients with 1–3 MHDs. Similarly, 11.9% of patients with 4–7 MHDs, 14.9% with 8–14 MHDs and 15.4% with ≥ 15 MHDs had been hospitalized due to migraine, compared to 10.1% of patients with 1–3 MHDs (Table).

Conclusion: This analysis estimated the proportion of migraine patients according to migraine frequency, using data from the 2017 NHWS. Since the NHWS sample is representative of adults across the EU5 countries, this analysis could further be used to estimate the prevalence of migraine by frequency sub-groups in these countries. Furthermore, this study demonstrates that, while the proportions of patients in the 1–3 MHDs and ≥ 4 MHDs sub-groups are almost equal, the economic burden through HRU is mainly contributed by patients suffering from ≥ 4 MHDs.

Disclosure of Interests: This study was funded by Novartis Pharma AG, Basel, Switzerland.

IHC-PO-309

Health-related Quality of Life of Migraine Patients with Eight or More Headache Days per Month: A Cross-Sectional Analysis of Survey Data in the EU5 (France, Germany, Italy, Spain, and the United Kingdom)

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Objective: We aimed to characterize the incremental burden of migraine in terms of health-related quality of life (HRQoL) of patients suffering from ≥ 8 Monthly Headache Days (MHDs), in the EU5 (France, Germany, Italy, Spain, and the United Kingdom).

Methods: A retrospective analysis was conducted using data from the EU5 sample of the 2017 National Health and Wellness Survey. A total of 1,569 patients who self-reported a physician diagnosis of migraine and ≥ 4 MHDs were 1:1 propensity score matched to non-migraine controls on socio-demographic characteristics and health variables that could affect the outcomes. The HRQoL estimates for 786 patients with ≥ 8 MHDs are presented here, using scores from the Short-Form 12-Item Survey Instrument version 2 (SF-12v2) physical and mental component

summary (PCS and MCS), Short form-6D (SF-6D) and EuroQoL-5D (EQ-5D). Bivariate analyses were conducted after matching to compare those with 4–7 MHDs (N = 783) and ≥ 8 MHDs (N = 786) with those with and without migraine using independent-samples t-tests and Chi-square tests depending on the nature of variables.

HRQoL of patients with ≥ 8 MHDs compared to propensity matched healthy controls: Results from NHWS 2017 EU5 sample

	No Migraine controls (N = 1569)	Patients with migraine (N = 1569)	
		4–7 MHDs (N = 783)	≥ 8 MHDs (N = 786)
SF-12v2 MCS, Mean (SD)	45.17 _a (10.08)	41.02 _b (10.75)	38.44 _c (10.9)
SF-12v2 PCS, Mean (SD)	50.87 _a (8.94)	48.11 _b (9.07)	45.12 _c (10.45)
SF-6D Utility Score, Mean (SD)	0.70 _a (0.13)	0.64 _b (0.11)	0.61 _c (0.12)
EQ-5D Index Score, Mean (SD)	0.83 _a (0.2)	0.75 _b (0.23)	0.66 _c (0.28)

Values in the same rows not sharing the same subscript are significantly different at $p < 0.05$. Tests assume equal variances. MHD: Monthly headache days, SF-12v2: Short-Form 12-Item survey instrument version 2, PCS: Physical component summary, MCS: Mental component summary, EQ-VAS: EuroQoL- visual analogue scale, SF-6D: Short form-6D and, (EQ-5D: EuroQoL-5D. The minimally important difference (MID) for SF MCS and PCS is 3.0, the MID for SF-6D Utility Score is 0.041 and the MID for the EQ-5D Index Score is 0.074.

Results: Patients with ≥ 8 MHDs reported significantly lower scores on SF-12v2 MCS and PCS compared to patients with 4–7 MHDs and matched non-migraine controls ($p < 0.05$ for all, Table). This suggests that the physical and mental functioning of patients with ≥ 8 MHDs is further compromised due to migraine when compared to patients with 4–7 MHDs and individuals without migraine. Similarly, the Health State Utility Values (HSUVs [SF-6D, EQ-5D]) of patients with ≥ 8 MHDs were also significantly lower to those of patients with 4–7 MHDs and matched non-migraine controls ($p < 0.05$ for all, Table). All mean scores of ≥ 8 MHDs patients reached minimal clinical differences on all scales when compared to both, non-migraine controls and 4–7 MHDs patients.

Conclusion: HRQoL scores and HSUVs of the ≥ 8 MHDs patients were statistically lower and clinically meaningful when compared to both non-migraine controls and to 4–7 MHDs patients, thus indicating a worse off HRQoL compared to both these groups.

Disclosure of Interests: This study was funded by Novartis Pharma AG, Basel, Switzerland.

IHC-PO-310

Headache-Free Days among Migraine Patients and its Association with Burden: A Cross-Sectional Analysis of 2017 Survey Data in France, Germany, Italy, Spain, and the United Kingdom

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Objective: Migraine affects multiple domains of patients' lives. We aimed to assess the incremental association between the number of headache-free days and health-related quality of life (HRQoL), work productivity, and healthcare resource use (HRU), from the patients' perspective using data from the 2017 National Health and Wellness Survey (NHWS).

Methods: Data of 1,569 migraine patients were taken from the NHWS EU5 sample. HRQoL was measured via Short Form survey-version 2 (SF-12v2) physical and mental component summary (PCS and MCS), the EuroQoL- visual analogue scale (EQ-VAS), the Short form-6D (SF-6D) and the EuroQoL-5D (EQ-5D). Economic burden was calculated through Work Productivity and Activity Impairment questionnaire-general health (WPAI-GH), and HRU via visits to healthcare providers (HCPs), the emergency room (ER), and hospitals in the preceding six months. The number of HFDs in the past 30 days was defined as the following: 30 days – number of headache days in the past 30 days. Generalized linear models (GLMs) were used to explore associations, and regression coefficients, p-values, and confidence intervals were calculated for each outcome adjusted for potential confounds. GLMs were used to specify the appropriate distribution for each outcome of interest.

Results: An increase in 5 headache-free days was associated with a mean increase of 0.0153 points in SF-6D utility scores and 0.04 in EQ-5D Index scores (both $p < 0.001$), 0.855 in MCS, 1.53 in PCS and 3.79 in EQ-VAS. Amongst employed respondents, a 5-day increase in headache-free days was associated with an expected decrease in absenteeism (days missed at work) by 18.2% and in presenteeism (days present at work while sick) by 10.3%. Similarly, a 5-day increase in headache-free days was associated with an expected decrease in HCP visits by 4.7%, GP by 6.9%, hospitalizations by 10.7%, and ER visits by 9.6% (Table).

Abstract number: IHC-PO-310 Regression results between economic burden (productivity and HRU) and number of headache-free days

	Rate Ratio (95%CI)	2 Days	3 Days	4 Days	5 Days
Absenteeism [#]	0.961 (0.95 to 0.971)	0.0772	0.1135	0.1484	0.1819
Presenteeism [#]	0.979 (0.968 to 0.99)	0.0424	0.0629	0.083	0.1026
Total Work Productivity [#]	0.979 (0.968 to 0.99)	0.0416	0.0617	0.0814	0.1007
Activity Impairment [#]	0.982 (0.975 to 0.989)	0.0355	0.0528	0.0698	0.0865
No. of HCP Visits in past 6 months	0.99 (0.983 to 0.998)	0.0192	0.0286	0.038	0.0473
No. of Hospitalizations in past 6 months	0.978 (0.962 to 0.993)	0.0442	0.0656	0.0865	0.1069
No. of ER Visits in past 6 months	0.98 (0.968 to 0.993)	0.0394	0.0585	0.0772	0.0955
No. of General/Family Practitioner Visits in past 6 months	0.986 (0.977 to 0.994)	0.0283	0.0422	0.0558	0.0693
No. of Neurologist Visits in past 6 months	0.954 (0.94 to 0.968)	0.0898	0.1317	0.1716	0.2096

N = 1,569, #Assessed only for respondents employed at the time of survey (N = 938), p < 0.05. Covariates = Sex (female = reference), Country (UK = reference), BMI (normal weight = reference), employment status (employed = reference; only for Activity Impairment), marital status (not married = reference), household income (low = reference), education (not completed University = reference), Alcohol (none = reference), exercise (no = reference), age (years), and CCI.

Conclusion: Increase in headache-free days among migraine patients is highly associated with increase in their HRQoL, and decrease in their work productivity and activity impairments and HRU.

Disclosure of Interests: This study was funded by Novartis Pharma AG, Basel, Switzerland.

IHC-PO-311

Migraine in children under 6 years of age: a long-term follow-up study

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Objective: Migraine received poor attention in very young children, specially under the age of 6. Early starting of migraine is frequently associated with higher frequency of attacks and worse clinical picture with respect to later onset, and seems predictive for less favorable outcome in later ages. We report here the longest follow-up study in a population of children presenting with migraine under the age of 6.

Methods: We followed-up 74 children under the age of 6, originally referred for headache to our department between 1997 and 2003 (T0). The study was carried out

between October 2016 and March 2018 and consisted of 2 steps: patients' search and clinical interview. Step 1 was achieved through a phone contact directly with the patient or with family doctors to find the subjects of the original cohort and to know basics about the clinical outcome. Then, subjects willing to participate, underwent a clinical interview to evaluate more in detail their actual headache condition (T1). Headache diagnoses were made according to the IHS criteria.

Results: 23/74 patients, 31% of the original cohort, were found at follow-up in a period ranging between 15 to 21 years after the first visit. Seven of them were headache free. The remaining 16 patients had migraine. 13 of these showed persistent migraine disease since T0, while the remaining 3, previously affected by other headaches had changed to migraine. In the migraine group, the localization of pain changed in 75% of the subjects, 11/16 (68.7%) had allodynia and 9/16 (56.25%) had cranial autonomic symptoms

Conclusion: Our results suggest that the onset of migraine at very young age represents a bad prognostic factor for persistence of the disease at later ages. Some clinical features may change during clinical course, and the active persistence of the disorder may lead to an increase in allodynia. Moreover, the occurrence of cranial autonomic symptoms in preschooler migraineurs may be predictive of disease persistence.

Disclosure of Interest: None Declared

IHC-PO-312**My Migraine Voice: Burden of Migraine and its management in an Australian cohort**

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Objective: Migraine is the greatest cause of disability under the age of 50. The estimated cost of migraine in Australia is \$35.7 billion per annum¹. This survey aimed to assess the impact of migraine and its management.

Methods: This cross-sectional study was a survey of patients with ≥ 4 monthly migraine days and at least one preventive treatment for migraine previously. Data from the Australian cohort was compared to the data of the overall global cohort².

Results: 68% of the 320 Australian patients were women, mean age 41 years, similar to the global cohort. On average, diagnosis of migraine took 2.4 medical professionals and 4.1 appointments. Depression (41%) and anxiety (40%) were higher in Australian responders, compared to 23% and 27% of the global responders, respectively. Depressed and anxious patients had the lowest rates of being on current preventive management for their migraine. Most (60%) reported fear of the next attack, hopelessness and difficulty thinking clearly during attacks. Preventive therapies had limited retention of use (43%) and satisfaction (53%), with reasons for switching preventives including lack of efficacy (54%) and too many side effects (36%). 69% of employers were aware of the migraines, with only 24% offering support for the migraines. In the Australian cohort, there was higher absenteeism (17% Australian; 13% global) and reduction in productivity (53% Australian; 48% global). 13% of the Australian cohort were on a disability pension due to migraine. Employers were often (69%) aware of the migraines, but only 24% offered any support.

Conclusion: The My Migraine Voice Survey adds weight to understanding the burden of migraine in Australia, as well as giving insights into the patient journey and limitations of current management options. Self-reported rates of anxiety, depression and absenteeism from work were reported in the Australian cohort, compared to the global cohort. Awareness of the burden of disease to patients, physicians and employers is still required for improved outcomes in this disabling condition.

Disclosure of Interests: Dr Jenkins, A/Prof Stark and Dr Hutton have received fees for lectures and advisory boards for Allergan, Eli Lilly, Novartis and Teva; Dr Hutton has also received fees for lecture and advisory board for Sanofi-Genzyme. Rebeca Quintana and Veruska Carboni have no financial relationship. Dania Yaghoobian, Guillaume Wieliczko and Pamela Vo are Novartis employees.

IHC-PO-313**Workplace strategies for management of headache among employees**

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Objective: Headache is a disabling disorder with severe consequences for quality of life as well as labor market-related outcomes such as ability to work, absence due to sickness, turnover, and unemployment. Furthermore, people suffering from headaches are at risk of not fulfilling their expected social roles and of stigmatization.

Previous studies have primarily focused on individual headache-management strategies. However, introducing headache-management strategies at the workplace level has the potential of providing a structural rather than an individual approach to headache management.

The aim of this study is to investigate what strategies Danish workplaces use to reduce negative consequences of headache on quality of life, ability to work, and absence due to sickness among employees suffering from headache.

Methods: The study will collect data through structured interviews. Information will be obtained through direct contact with the workplaces' human resource departments. The interview will include questions on what management strategies the workplace has in place, specifically on what the workplaces offer the employees regarding terms of employment, education, flexibility, and the workplaces' attitude towards headache. The overall focus will be on what the workplace offers to reduce the negative outcome of headache.

Up to 20 workplaces will be selected to represent the public and private sector and across fields. Furthermore, workplaces with best practice strategies will be included.

Results: The results will demonstrate examples of applied strategies and initiatives that are used by Danish workplaces to manage headache and headache-related outcomes among employees.

Conclusion: Based on knowledge about headache-management strategies used at Danish workplaces, non-pharmaceutical interventions can be suggested with the aim of

reducing consequences of headache among occupationally active individuals.

Disclosure of Interest: None Declared

IHC-PO-314

What matters in the treatment of migraine? A transversal study on general practitioners-reported outcomes:

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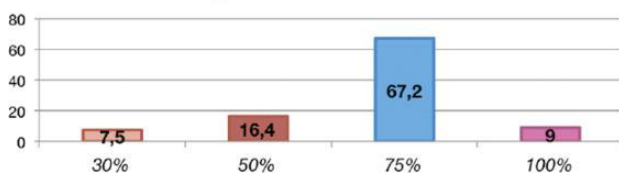
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Objective: Patient-reported outcomes are gaining attention in the headache field and the International Headache Society (IHS) recommends their use. Most of the studies employ endpoints considered relevant by headache physicians. We aim to evaluate what General Practitioners (GPs) consider most important in the treatment of migraine.

Methods: Transversal descriptive study. All GPs from our healthcare area were invited. We administered an online survey addressing demography and preferences in the acute and preventive treatment. Participants rated in a 0–10 scale the following aspects: time to effect onset, tolerability, interaction profile, cost, effectiveness, sustained response, lack of tachyphylaxis, and effect on other migraine symptoms. We also asked about the desirable time to effect, the optimal duration of preventive treatment and the desirable percentage of headache reduction compared with baseline.

Desired % reduction of headache days in preventive treatment



Results: We included 67 GPs, aged 52.3 (9.5), 76.1% female. 38.8% of them suffered headache, with a mean frequency of 2.29 (2.01) days per month. Concerning acute treatment, the best-rated characteristic was effectiveness (9.31), followed by sustained pain free response (8.99) and short onset of action (8.94). The least scored was cost (7.1). 90.5% of responders considered that pain should be relief within 30 minutes and only 1 responder considered acceptable 120 minutes.

In the case of preventive treatment, the most rated characteristic was effectiveness (9.18), followed by tolerability and sustained effect (8.93 both). Cost was the least rated (6.86). The percentage of improvement in terms of headache days per month compared with baseline is represented in table 1. The desirable time until the effect onset was 14.0 days in mean (9.3) and the mean duration of treatment was 6.28 months (2.1).

We did not find any differences between headache and non-headache sufferers.

Conclusion: GPs consider effectiveness, short onset of action and tolerability as the most important factors. Both the desirable time to effect and the percentage of headache-days reduction differ from the usually employed in clinical trials.

Disclosure of Interest: None Declared

IHC-PO-315

Primary Headaches at the Emergency Center in a Third Level Hospital in Buenos Aires – Argentina

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Objective: eadaches are among the frequent causes for emergency department (ED) visits worldwide. They are thought to be 1–4% of appointments. It is the objective of this research to describe the characteristics of primary headaches of patients that attended a tertiary care hospital center during 2017.

Headaches are among the frequent causes for emergency department (ED) visits worldwide. The objective of this research is to describe the characteristics of primary headaches of patients that attended a tertiary care hospital center during 2017.

Methods: Observational retrospective study of all primary headaches consultations presented by +18 year-old patients in ED of a third level hospital center in Buenos Aires during 2017. Secondary headaches were excluded.

Results: A total of 3554 consults from 3120 patients have been included in the present study. Of those, only 9.2% (n=252) concurred to hospital 2 or more times. The average age of patients was 42 years old (IIQ 30–59) and 70.7% (n=2205) were women. A history of headaches was found in 93% (n=2905) of patients. ER consultations

comprised 70.6% (n = 2509) of cases. The health insurance more commonly used by patients was the one provided by the institution's own HMO (55%, n = 1954). Administration of medication was not required in 52% (n = 1873) of consultations. In 1681 episodes, 3832 drug dosages were administered (2.3 treatment/episode). The most common route of administration was intravenous (71.5%, n = 2739). Complementary studies were carried out in 22% (n = 766) of cases. Patients stayed in the ED an average of 139 minutes (IIQ 87–217). 1% (n = 35) was hospitalized after ED evaluation.

Conclusion: Although our results are comparable to those found in other studies, this is the first one carried out on our context. The choice of medication seems to be appropriate, with the exception of high usage of corticosteroids. There might also be a percentage of unnecessary studies. Finally, a high percentage of consults could be done through outpatients.

Disclosure of Interest: None Declared

IHC-PO-316

The real-world burden of migraine treatment failure: a panel-based chart review in France, Germany, Italy, and Spain

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Objective: To evaluate the six-month migraine-related healthcare resource use (HRU) among patients who had ≥ 4 monthly migraine days (≥ 4 MMDs) and had failed ≥ 2 prior prophylactic treatments (2+TFs).

Methods: A retrospective, non-interventional, online panel-based chart review was conducted among neurologists and headache/pain specialists who treated patients with migraine in France, Germany, Italy, and Spain. Data for migraine-related HRU were collected during the six-month study period following the index date (date of the most recent prophylactic treatment initiation), and analysed for patients with ≥ 4 MMDs and 2+TFs. Descriptive analyses were conducted for the pooled population and by country.

Abstract number: IHC-PO-316 Six-month migraine-related HRU among patients with ≥ 4 MMDs and 2+ TFs

Number of patients with at least one* (%)	Overall (N = 168)	France (N = 51)	Germany (N = 28)	Italy (N = 44)	Spain (N = 45)
Sick days, n (%); mean (SD) [#]	47 (32.2%); 7.9 (8.3)	8 (20.5%); 5.3 (6.5)	20 (74.1%); 5.2 (4.2)	13 (31.7%); 7.8 (6.3)	6 (15.4%); 20.8 (12.7)
Outpatient visits at physician's office, n (%)	140 (83.3%)	33 (64.7%)	28 (100%)	38 (86.4%)	41 (91.1%)
ER/A&E visits, n (%)	44 (27.2%)	16 (32.0%)	3 (12.5%)	10 (22.7%)	15 (34.1%)
Hospitalizations, n (%)	9 (5.5%)	3 (6.0%)	6 (23.1%)	0 (0%)	0 (0%)
Blood tests, n (%)	66 (39.3%)	9 (17.7%)	17 (60.7%)	29 (65.9%)	11 (24.4%)
Cranial and cranio-cervical MRI scans, n (%)	37 (22.0%)	12 (23.5%)	11 (39.3%)	10 (22.7%)	4 (8.9%)
EEGs, n (%)	29 (17.3%)	6 (11.8%)	9 (32.1%)	9 (20.5%)	5 (11.1%)
Cranial CT scans, n (%)	22 (13.1%)	7 (13.7%)	3 (10.7%)	7 (15.9%)	5 (11.1%)

*All numbers reported at physician's office. The evaluable N differs for different outcomes and the overall N reported is the total number of patients from individual countries.

[#]Data for mean days is among patients with one or more sick days.

Abbreviations: CT: Computerized tomography; EEG: Electroencephalogram; ER/A&E: Emergency room/accident & emergency department; MRI: Magnetic resonance imaging scans; TF: Treatment failure.

Results: A total of 168 patient charts were analysed (mean age 37.6 years, 63% female). On an average, patients had failed 2.3 prior prophylactic treatments (median [range]: 2.0 [2.0, 9.0]). During the six-months, 83% of patients had at least one migraine-related outpatient visit in the participating physician's office (mean visits: 2.6), 27% had visited emergency departments (mean visits: 2.8), 5% were hospitalized (mean: 3.3 days), and 32% were prescribed at least one sick day (mean: 7.9 days). Most commonly used procedures were blood-tests (39%), magnetic resonance imaging scans (22%), electroencephalograms (17%), and cranial computerized tomography scans (13%). Country-specific HRU results are presented in the Table.

Conclusion: This real-world analysis suggests that migraine imposes a significant economic burden in terms of HRU among patients who have failed ≥ 2 prior prophylactic treatments.

Disclosure of Interests: This study was funded by Novartis Pharma AG, Basel, Switzerland.

Pamela Vo: Employee of Novartis Pharma AG, Switzerland; Elyse Swallow, Eric Wu, Wei Gao, Miriam Zichlin, Eleanore Fuqua: Employees of Analysis Group, United States; Thais Tarancon and Marta Aguirre Vasquez: Employees of Novartis Farmaceutica, S.A., Spain; Monika Maier-Puschel: Employee of Novartis Pharma GmbH, Germany; Marianonietta Naclerio, Daniela Ritrovato, and Silvia Rossi: Employees of Novartis Farma S.p.A., Italy; Nicolas Mahieu: Employee of Novartis Pharma S.A.S. France.

IHC-PO-317

Idiopathic Intracranial Hypertension – A study of incidence and demographics in Northern Ireland

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Objective: Idiopathic Intracranial Hypertension (IIH) is a common neurological condition which often initially presents to acute services. Incidence is normally reported at 1–2 per 100,000 however in practice the number often feels larger than this. We set out to look at the incidence of IIH in Northern Ireland a population well suited to incidence studies due to low levels of migration. We also recorded patient demographics when available from clinical notes and electronic care records to look at key demographics including patient BMI, imaging findings and initial ophthalmological examination.

Methods: We made use networked imaging systems as the main information source cross referenced with clinical coding data from admissions units and eye casualty. We

sampled the time period March 2017 to February 2019 inclusive and used National Office of Statistics population estimates to calculate incidence.

Results: We have demonstrated an incidence of IIH within the Northern Irish population which is much higher than is commonly reported in the literature but which is in line with similar studies published by our colleagues in the North West of Ireland. Demographic data shows the condition to affect a predominantly female population who are overweight and between the ages of 15 to 45. This is in keeping with the published body of literature.

Conclusion: Is IIH a Northern Irish problem or one systematically under reported in the literature? We postulate that the previously published literature on incidence is out of date and does not reflect current incidence. The increasing obesity epidemic is likely a major contributing factor to increasing incidence.

Disclosure of Interest: None Declared

IHC-PO-318

New daily persistent headache in a pediatric cohort

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Objective: Our aim was to investigate the clinical features of NDPH Primary new daily persistent headache (NDPH in a cohort of pediatric patients).

Methods: We retrospectively reviewed the charts of patients attending the Headache Centre of Bambino Gesù Children from the last ten years with history of NDPH (ICHD-3). Statistical analysis was conducted to study correlations between: – NDPH and population features (age and sex); – NDPH and headache qualitative features; – NDPH and response to prophylactic therapies.

Results: We included 377 patients with CPH (66.4% female, 33.6% male, age between 0 and 18 years). The frequency of NADPH was 13%. We did not find significant differences in frequency between males (42.9%) and females (57.1%). We found that NDPH is less common in the age group of 7–10 years ($p < 0.05$). Regarding the features of the pain we did not find significant differences compared to the other forms of chronic headache for the quality of pain (throbbing or grating), and the presence of photophobia (59.2% vs 60.7%, $p > 0.05$) and phonophobia (63.3% vs 70.1%, $p > 0.05$). However we found a low frequency of nausea and vomiting in the NADPH population (28.6% vs 48.2%, $p < 0.05$). We found that 75% of

patients have an onset of the symptoms in the winter months (November-February), respect the remaining months of the year when the incidence is very low ($p < 0.05$). Our results show that 29 (30.6%) out of 49 NADPH CPH received a prophylactic therapy. Among them, 26 patients received amitriptyline, 4 patients topiramate, one patient L-5 hydroxytryptophan, and one patient flunarizine. Positive response to therapy (reduction of attacks by at least 50% in a month) was detected in 30.6% of patients, while no outcome data were obtained from 63.3% of cases. Amitriptyline showed the highest efficacy ($p < 0.05$).

Conclusion: Our results show that the incidence of NADPH in children with daily headache is 13%. In general, the onset occurs in the winter months and this is probably related to the increase in requests for school activities. Qualitative characteristics as for adults are variable, migrainous or tension type. The most effective drug is amitriptyline.

Disclosure of Interest: None Declared

IHC-PO-319

Direct Headache Care: Patient Outcomes Using A Membership Based, Multidisciplinary Model

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Objective: To measure outcomes in patients with headache treated using an integrative “direct care”, membership model

Methods: International Headache Center pioneered a monthly fee, membership based clinic October 2018, which includes direct communication (texting) with physician, as well as unlimited in-office or telemedicine visits. 7 charts from all new memberships starting December 2018 were retrospectively reviewed. 1 patient was excluded, since she was an established patient.

Demographics and standardized scales were recorded on initial visit. Headache burden is measured using monthly frequency and intensity on a scale of mild (0–4/10), moderate (5–7/10), severe (8–10/10) during maximal pain of attack. These values are observed at onset of treatment and for 3 subsequent months. Most recent headache burden, March 2019 was also included.

Results: Data were collected from 1 male and 5 females. The male member was age 19 with diagnoses of chronic migraine and spontaneous intracranial hypotension. Standardized scales were recorded as follows: MIDAS 90, Allodynia Questionnaire 4, PHQ9 22, GAD7 12. At initial consult headache frequency was 30 days in

a month, with severe headache intensity. March 2019 burden was decreased to 1 mild headache per 6 weeks. The women in the study were ages 27–37, with primary headache diagnoses of chronic migraine, episodic migraine with aura, new daily persistent headache and primary headache associated with sexual activity. Standardized scale ranges: MIDAS 29–90, Allodynia Questionnaire 0–6, PHQ9 3–18, GAD7 5–10. At initial consult headache burden ranged from 10–30/30 days for frequency, and moderate to severe for intensity. March 2019 headache burden ranged from 1–11/30 days for frequency, and varied from mild, moderate to severe for intensity.

Conclusion: Although this quality improvement project was limited by a small number of patients, decreased headache burden was achieved and at a steady pace despite significant burden and standardized measurements of disability from headache at the time of initial visit.

The multidisciplinary, direct headache care clinic model conforms to the expected norms, and by speculation, may be able to achieve a decreased headache burden at a faster pace, perhaps due to real-time patient-provider communications. A formal research study would be helpful in following outcomes.

Disclosure of Interest: None Declared

Age/ Gender at Presentation	Headache Type	Month #1 Headache Frequency/ Intensity	Month #2 Headache Frequency/ Intensity	Month #3 Headache Frequency/ Intensity	March 2019 Headache Frequency/ Intensity
19/M	Chronic Migraine, SIH	30/ severe	8/ moderate	6/ mild	0/ mild
27/F	Chronic Migraine, MOH	30/ moderate to severe	28/ mild to moderate	30/ mild	11/ mild to moderate
29/F	Episodic Migraine w Aura	10/ severe	6/ severe	3/ moderate	1/ severe
32/F	Chronic Migraine, SIH	30/ severe	20/ moderate	10/ moderate	5/ moderate to severe
37/F	NDPH, Primary headache associated with sexual activity	30/ moderate to severe	23/ moderate	4/ mild	4/ mild
38/F	Chronic Migraine	26/ severe	30/ severe	14/ moderate	3/ moderate to severe

Abstract number: IHC-PO-319

IHC-PO-320

Misdiagnosis and changes in the clinical characteristics of patients with transformed migraine

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Objective: To determine the misdiagnosis of the migraine and to compare the clinical characteristics of current and initial headache in patients with migraine,

Methods: We reviewed the clinical files of patients of the service of neurology of the National Medical Center "20 de Noviembre" attended between September and December 2018.

We determined the diagnosis of the current headache according to the criteria of the ICHD-3 and we compared with the diagnosis of ICHD-3 of the initial headache. We established as "transformed migraine" those patients in whom the initial headache met criteria of migraine but the current headache does not.

In patients diagnosed with migraine, we compared the initial semiology with the current headache using chi square

to find significant differences, considering significant $p < 0.01$

Results: We reviewed files of 114 adult patients, aged between 18 and 86 years. Applying the criteria of the ICHD3 to the current headache we found that 19 patients had a migraine, 55 tension headache, 20 medication-overuse headache and 20 other headaches. In the initial headache we found that 41 patients had migraine, 54 tension headache and 19 other headache. Comparing the clinical findings of the initial headache with the current one, we found that in the initial headache: 27 had unilateral pain, 35 pulsatile, 32 nausea, 31 photo /sonophobia, 19 had frequency > 14 days per month. Currently: 15 had unilateral pain, 25 pulsatile, 24 nausea, 14 photo /sonophobia, 33 had frequency > 14 days per month. Applying chi square we found very significant differences in the frequency of headache and in the migraine companions of photo and sonophobia ($p < 0.001$). Significant differences in the type and location of pain ($p < 0.05$) and there are no significant differences in the presence of nausea or aura.

Conclusion: Of the patients who arrive at our headache unit, 35% started their headache as migraine but currently only 16% meets ICHD3 criteria for migraine. Changes in the clinical characteristics of migraine (transformed migraine), mainly the increase in frequency, the absence of photo/sonophobia, could cause erroneous diagnoses. An adequate anamnesis of the initial headache of the patients is necessary for an adequate diagnosis and thus establish the appropriate treatment for the type of headache

Disclosure of Interest: None Declared

IHC-PO-321

Assessing the burden of migraine on acute and emergency services in a London teaching hospital

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Objective: There is a lack of data on the burden of primary headache disorders such as migraine on emergency and acute services in the UK. Existing data relies on a coding of "headache" which encompasses both primary headache and secondary headache of all causes e.g sub-arachnoid haemorrhage or infection. Guy's and St Thomas' NHS Trust in London is one of the UK's busiest accident and emergency services with 150,000 attendances per year. It is teaching hospital with a headache service. We aim to assess the burden of primary headaches, in particular migraine, on acute and emergency services with the aim of redirecting resources to more appropriate

pathways and avoiding unnecessary, often invasive investigations.

Methods: We conducted an audit of all adult presentations to the emergency department and urgent care centre of St Thomas' Hospital which were coded as "headache" over the first six months of 2018. We reviewed the initial diagnosis at presentation and also the diagnosis at discharge, number of investigations (imaging/lumbar puncture) and outcome.

Results: Out of 78311 attendances to A and E there were 1435 adult presentations to the emergency department with "headache" as their primary complaint. "Migraine" was the most frequent of all diagnoses at presentation and also at discharge. The data will be presented in detail.

Conclusion: The data demonstrates the significant impact of migraine and other primary headaches on health resources and also informs us about the need to develop better care pathways for migraine and to improve headache education for physicians. These findings will enable us improve the management for patients with primary headache disorders.

Disclosure of Interest: None Declared

IHC-PO-322

Practice Trends in the Multidisciplinary Treatment of Migraine: A Cross-Sectional Pilot Survey

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Objective: Limited research has been conducted characterizing treatment components used across multidisciplinary headache centers. The aim of this study is to describe variation and practice pattern characteristics for the multidisciplinary management of migraine across headache centers in the United States.

Methods: We developed an 18 item questionnaire using Qualtrics[®], a web based survey and data analytics tool. The survey consisted of single select, multiple choice, sliders, numerical scales, and free text fields. Validation criteria and quality checks were also added to the survey design.

All known headache centers and clinics in the United States were eligible for inclusion. Sites were located using a combination of hand searching by region and state, through professional society and foundation website resources, and by snowball sampling.

The questionnaire solicited information regarding treatment team staff, frequency of team meetings, use of non-pharmacological and behavioral interventions, estimates of

principal headache diagnoses, utilization of infusion therapy, participation in clinical trials, etc.

A pilot survey was distributed via email to 20% (n = 16) of total headache centers identified (N = 82). Pilot centers were divided by region and randomly selected using a number generator. Weekly reminders were sent and feedback was solicited regarding clarity of survey questions. There were no financial incentives offered to participate in the study.

Results: Data collection is ongoing. Preliminary results of the pilot study will be presented at the meeting.

Conclusion: The results from this descriptive survey will provide insight into current practices and variation amongst headache centers in the United States. Findings from this study can be used by academic and private headache centers to implement or improve current multidisciplinary treatment approaches for the management of migraine.

Disclosure of Interest: None Declared

Headache in History and Arts

IHC-PO-323

A History of Dihydroergotamine in Migraine

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Objective: Ergot use in obstetrics dates back to 1100 BC in China, 370 BC by Hippocrates and 1808 in the US. However, it was not until 1918 that ergotamine was isolated, subsequently modified to DHE and approved in 1946 for the treatment of migraine. For the next 40 years, DHE was available as the most specific, acute anti-migraine therapy until the advent of the Triptans. DHE is still used today, available in multiple formulations and remains a dependable choice for Neurologists and Headache specialists for acute migraine, status migrainosus and cluster headache. This work provides a history of dihydroergotamine (DHE) treatment from its synthesis in 1943 from ergotamine to modern day formulations and routes of administration.

Methods: A primary literature review was conducted of the PubMed database for the study period (1946–2018) and seminal studies identified following methods similar to Tfelt-Hansen and Koehler, 2011. Market research data was also analyzed.

Results: A timeline of major landmarks in the development and clinical use of DHE was identified and is presented. Despite sophisticated biologic treatments for migraines, DHE remains a leading treatment in migraine clinics for intractable migraines via the intravenous route

of administration. The supportive body of clinical evidence for DHE is vast and impressive and suggests a risk profile that some consider as good as the triptans. Recent research and development efforts to provide improved bioavailability and consistency of DHE via the novel upper nasal cavity route may at last bring the benefits of IV DHE to patients and physicians via self-administered, in-home treatment.

Conclusion: DHE has accumulated over 70 years of clinical practice data showing that it is a safe and reliable treatment when delivered consistently at adequate dose levels for acute migraines providing rapid and sustained relief, even when other options have failed.

Disclosure of Interests: Impel employee

Headache Pathophysiology – Basic Science

IHC-PO-083

CSDs evoked in either awake or asleep mice show different patterns of vascular activity

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Objective: Cortical spreading depolarization (CSD) is believed to underlie the migraine aura and has been used extensively as a translational model for migraine. Thus far, the majority of CSD measurements have been done in animals under anesthesia, while a small number of studies of involving awake animals have been limited because of the requirement for implantation of electrodes and lasted only for a few hours. With a novel approach we are able to trigger CSD in animals that are not under anesthesia and measure their cortical blood flow continuously for prolonged periods of time (weeks). Using this technique our objective was to determine if the threshold for evoking CSD and the characteristics of the blood flow changes associated with CSD differ when CSD is triggered during sleep vs. wakefulness.

Methods: We use skull-mounted microelectronics in mice that express channelrhodopsin in cortical pyramidal cells to trigger and record spontaneous and CSD-associated neurovascular activity without compromising the skull. Under anesthesia, a microchip to measure optical reflectance and ultra small LEDs to illuminate the cortex (571 nm) and stimulate channelrhodopsin (470 nm) were mounted on the skull of the mice. The mice were allowed to recover for 3–4 day after which the animals were connected to a setup for tethered recordings. At least two CSD were evoked several days apart in each mouse, one

during the awake phase of the day and one during the sleep phase.

Results: The threshold to induce CSD was not different during the awake or sleep state of the animals. However, the characteristics of the prolonged (~1 hr) vasoconstriction seen after CSD were significantly different when the CSD was evoked during the awake vs. sleep state. The amplitude of the vasoconstriction was greater with CSD's evoked during sleep compared with wakefulness, as was the duration of vasoconstriction. CSD evoked during sleep also resulted in a characteristic delayed awakening that occurred at the end of the prolonged vasoconstrictory phase 45–90 minutes after the initial CSD event.

Conclusion: Differences in CSD-associated changes in cortical blood flow could play a role in difference in migraine attacks starting at different times of the day.

Disclosure of Interest: None Declared

IHC-PO-084

Female-specific prolactin contributions in migraine-like facial hypersensitivity

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Objective: Migraine is one of the most complex and prevalent neurovascular disorders that afflict approximately 1 in 10 people worldwide. The involvement of sex hormones is well accepted in the field as migraine is predominantly a female disorder. Reports suggest that prolactin, a luteotropic hormone that is mostly released by the pituitary, may be a worsening factor in migraine. Under normal conditions prolactin levels are low in both men and women, however levels can surge during stages of the menstrual cycle, or pregnancy, and even stress, the most common trigger for migraine. Moreover, prolactin is controlled by dopamine and dopamine agonist/prolactin antagonist bromocriptine has been shown to be an effective treatment in a subset of migraine patients. The objective of the study is to determine whether prolactin plays a role in stress-induced facial hypersensitivity, our preclinical migraine model.

Methods: Both male and female ICR mice were administered either 2 mg/kg bromocriptine or 10 ml/g b.w. vehicle for five days and subjected to our stress paradigm for two hours per day for a total of three days. Mice were tested for facial hypersensitivity until they returned to baseline which is approximately 14 days after stress. Following their return to baseline, mice were administered a non-noxious dose (0.15 mg/kg) of sodium nitroprusside (SNP) to determine if the animals would be primed to respond to a low dose NO-donor.

We have generated a mouse model in which the prolactin receptor gene is excised from sensory neurons. These mice are herein referred to as Nav1.8/Prlr-lox. Both male and female Nav1.8/Prlr-lox and their control littermates were subjected to our stress paradigm and tested for facial hypersensitivity.

Results: Female ICR mice that were stressed and treated with bromocriptine exhibited significantly higher thresholds than female mice that were stressed and received vehicle. Conversely, male ICR mice that were stress and received bromocriptine displayed thresholds similar to male mice that were stressed and administered vehicle. Lack of the prolactin receptor in sensory neurons attenuated facial hypersensitivity in female, but not male, Nav1.8/Prlr-lox mice.

Conclusion: Together these data suggest that prolactin receptor activation in sensory neurons may play a role in stress-triggered migraine-like hypersensitivity.

Disclosure of Interest: None Declared

IHC-PO-085

Cephalic Allodynia and Cortical Spreading Depression results in decreased neuronal complexity, the restoration of which relieves migraine-associated symptoms

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Objective: Chronic migraine is an especially disabling disorder, which is 15 or more headache days a month. Some chronic pain states have been found to result in altered neuroplasticity. α and β tubulin heterodimers make up microtubules which comprise cell morphology. Tubulin dynamics are regulated through post-translation modifications, including α -tubulin acetylation. Acetylated tubulin results in stable microtubules that are more resistant to breakage, and is induced by α -tubulin N-acetyltransferase 1 (α TAT1). Deacetylated tubulin is associated with more fragile microtubules, and is induced by histone deacetylase 6 (HDAC6). The aim of this study was to determine if chronic migraine-associated pain altered neuronal cytoarchitecture, and if HDAC6 inhibition could reverse these changes and correspondingly produce pain relief

Methods: To induce chronic migraine-associated pain, the human migraine trigger nitroglycerin (NTG; 10 mg/kg, IP) or vehicle (VEH) was administered to C57BL6/J mice every other day for 9 days. Cephalic allodynia was

measured using von Frey hair stimulation of periorbital region. On day 10, 24 h after the final NTG/VEH injection, animals were tested with the HDAC6 inhibitor, ACY-738 (50 mg/kg, IP) or VEH. Mice were sacrificed, and neuronal architecture analyzed using Golgi stain. Migraine aura was modeled through cortical spreading depression (CSD), induced by 1 M KCl solution on the dura. Mice were pretreated with ACY-738/VEH before induction of CSD. A second cohort of mice were pretreated with ACY-738/VEH, underwent CSD or a sham surgery and had tissue collected for Golgi stain

Results: Following chronic NTG neurons in the trigeminal nucleus caudalis showed decreased neurite branching and complexity. HDAC6 inhibitor reversed these cytoarchitectural changes and significantly reduced chronic allodynia. CSD also resulted in decreased neurite growth in the cortex and ACY-738 decreased susceptibility to CSD and reversed cytoarchitectural changes

Conclusion: Our results demonstrate that migraine pathophysiology is associated with disrupted neuronal cytoarchitecture and that HDAC6 inhibitors could be a novel therapeutic target for this disorder

Disclosure of Interest: None Declared

IHC-PO-086

Long-term monitoring of intracranial pressure in freely-moving rats using telemetry system

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Objective: Headache is a major cause of morbidity in patients with raised intracranial pressure (ICP) disorders such as idiopathic intracranial hypertension (IIH). To understand the mechanisms underlying IIH, precise and valid ICP recordings are of crucial importance. The traditional intraventricular technique used in preclinical setting is highly invasive and causes severe complications, rendering it suitable only for short term and requiring use of anesthesia. Therefore, we investigated the use of telemetry probes for ICP recordings, which has number of advantages; it allows daily and long-term recordings in freely moving rats that can be co-housed with no use of anesthesia. The aim was to investigate the feasibility and stability of long-term recordings of ICP in rats implanted with telemetry device.

Methods: Telemetry device with a solid-state pressure sensor at the tip of the catheter was implanted in rats. The body of the telemeter was inserted into the abdominal cavity and the catheter was tunneled to the base of the skull and placed epidural. The telemeter was charged by an

inductive Smartpad placed under the home cage of the rat, which also acted as a receiver for the ICP signals. The received signals were sampled at 1 kHz. Data were collected continuously for at least 15–45 days.

Results: ICP measurements were started after surgery (day 0), and ranged from -2.56 to 6.99 mmHg. Validity of the ICP signal was confirmed by postural changes. The ICP signal decreased and increased in response to a head up and head down tilt respectively. The signal was also assessed by compressing the jugular veins, which gave a significant increase of ICP. No significant difference was observed between days 0, 7, 18 and 25 ($P > 0.05$). The signals were stable throughout the recording period with an average ICP value of 3.54 ± 0.66 mmHg. Significant light-dark difference was observed (0.22 ± 0.04 , $P = 0.0114$). Inspection of the brain post-mortem did not show any signs of tissue damage.

Conclusion: Long-term and stable ICP monitoring was performed in conscious rats in their home cage. This opens up opportunities to investigate how ICP may change under normal and during disease development such as IIH.

Disclosure of Interest: None Declared

IHC-PO-087

Expression of the CGRP family of peptides and their receptors in the rat retina

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Objective: The calcitonin gene-related peptide (CGRP) family of peptides includes CGRP itself, calcitonin, adrenomedullin and amylin. They are all related to each other vis-à-vis peptide sequence and receptor biology. Understanding expression of the peptides and their receptors lays the foundation for more deeply understanding their physiology and pathophysiology in eye diseases, and their plausible therapeutic possibility.

Methods: We have designed an in-depth study of the expression of the CGRP family of peptides and their receptors in rat retina using single and double immunohistochemistry with antibodies against: CGRP, calcitonin, adrenomedullin, amylin, CLR, RAMP1, RAMP2, RAMP3 and CTR.

Results: We observed that CGRP was mainly seen in Müller cell end feet, adrenomedullin and calcitonin were expressed in the blood vessels, while amylin was widely distributed within the retina. CGRP receptors consist of CLR/RAMP1. These two receptor components are

co-localized in the nerve fiber layer, RAMP2/3 are found in the nuclear layers, and CTR in the plexiform layers. The only co-localization ligand/ligand, receptor/receptor or ligand/receptor was CLR/RAMP1, and thereby suggesting a functional receptor. CTR is the only component that is needed for the calcitonin receptor.

Conclusion: We conclude that in the normal rat retina, functional CGRP receptors and also calcitonin receptors (consisting of only CTR) exist, but not adrenomedullin or amylin receptors.

Disclosure of Interest: None Declared

IHC-PO-088

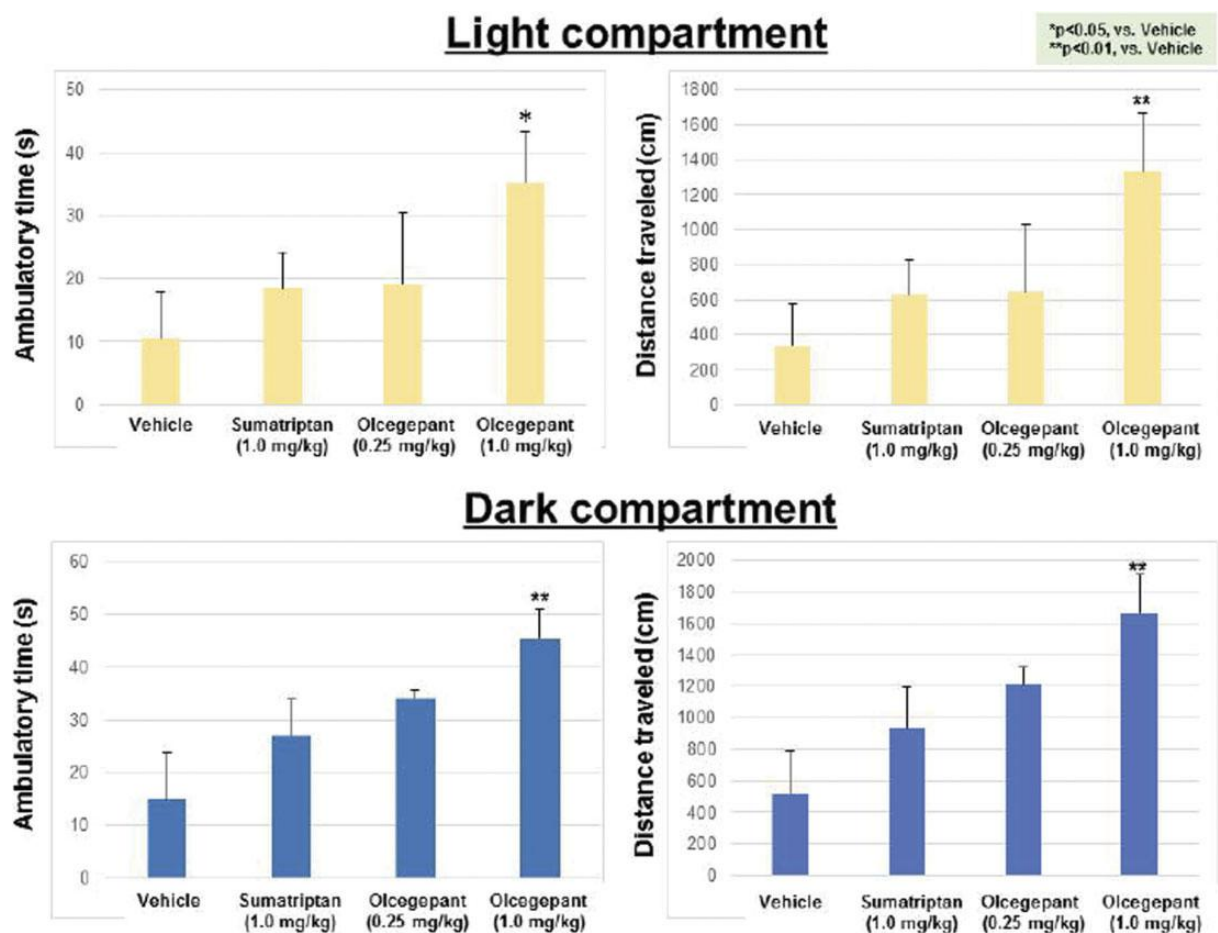
Effects of olcegepant and sumatriptan on locomotive activity after cortical spreading depolarization in mice

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Objective: Improvement of functional impairment due to headache is an important migraine-related therapeutic goal. CGRP receptor antagonists (gepants) are now being developed as novel anti-migraine drugs. Because of lack of vasoconstrictive action, gepant are considered as a favorable therapeutic choice over triptans. Here, we explore the effects of olcegepant and sumatriptan on the locomotive activity after cortical spreading depolarization (CSD).

Methods: C57BL/6 mice were initially acclimatized to a test chamber environment. Under anesthesia with isoflurane, craniotomy and slight dural incision were performed,



Abstract number: IHC-PO-088

and a 5 μ l-aliquot of KCl solution was applied to the occipital cortex. Development of CSD (5–6 times) was confirmed by continuously recording of DC potentials. At 24 hours after CSD induction, olcegepant, sumatriptan or vehicle was injected intraperitoneally. At 10 minutes after the drug administration, quantitative analysis of locomotive activity (duration: 30 min) was initiated in the test chamber with light and dark compartments by employing an infrared beam tracking system. In parallel, we evaluated motor activity of mice treated with each drug without CSD. Numerical data were expressed as mean \pm SD. Statistical analysis was performed by the Kruskal-Wallis test.

Results: After CSD, mice treated with olcegepant (1.0 mg/kg [high-dose], N=4) exhibited significantly greater ambulatory time and distance in both light and dark compartments, as compared to those treated with vehicle (N=4) (Light/Ambulatory time: 35.2 ± 8.1 s vs. 10.5 ± 7.4 s, $p=0.0149$; Light/Distance: 1335 ± 329 cm s vs. 340 ± 239 cm, $p=0.0069$; Dark/Ambulatory time: 45.4 ± 5.6 s vs. 14.8 ± 9.0 s, $p=0.008$; Dark/Distance: 1663 ± 243 cm vs. 518 ± 273 cm, $p=0.0027$). There were no significant differences in motor activity between vehicle-treated and olcegepant (0.25 mg/kg [low-dose])-treated mice. Neither olcegepant nor sumatriptan affected motor activity in mice without CSD.

Conclusion: Olcegepant is efficacious in ameliorating CSD-induced locomotive impairment in a dose-dependent manner, and its efficacy is observed in the condition that causes photophobia. Our results support the tenet that CGRP blockade leads to the improvement of migraine-associated functional disability.

Disclosure of Interest: None Declared

IHC-PO-089

Systemic injection of CGRP prolongs a nausea-like state in mice

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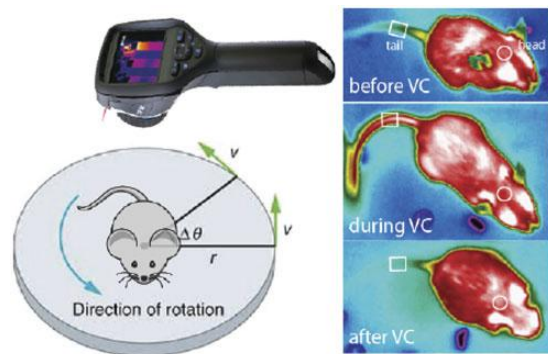
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Objective: Nausea is a prominent symptom and major cause of complaint for patients with migraine and specifically vestibular migraine (VM). As a readout of a nausea-like state present in migraine and VM, we will assess hypothermic responses to provocative motion. Recent studies have demonstrated that provocative motion causes robust and prominent hypothermic responses in rats, humans, house musk shrews, and mice that there is a clear parallel in hypothermic responses between animals and humans in

underlying physiological mechanism – cutaneous vasodilation that favors heat loss. Additionally, because systemic CGRP injection has been shown to cause light-aversion (photosensitivity) in mice, we wondered what effect systemic CGRP injection would have on these nausea-like states in wildtype mice.

Methods: We carried out these studies on 20 wildtype C57BL/6J (JAX 664) mice (10F/10M). Head and tail temperatures were measured using an FLIR E60 IR camera before, during, and after a 20 min orbital rotation (0.75 Hz to 4 cm displacement). One week later, the same mice were injected systemically with 0.1 mg/kg rat α -CGRP (Sigma), and were retested.



Results: We confirmed in both female and male C57BL/6J mice during provocative motion there is a decrease in head temperature (hypothermia) of ~ 1.5 degree C which recovers and is associated with a short-lasting tail-skin vasodilation (tail skin temperature increase of ~ 4 degrees C). Interestingly, systemic CGRP injection caused a similar reduction in head temperature, yet the hypothermia did not recover. Moreover, there was no associated tail-skin vasodilation in CGRP-injected mice.

Conclusion: In conclusion, provocative motion in wildtype mice is accompanied by hypothermia that involves both autonomic and thermo-effector mechanisms. Moreover, a systemic CGRP injection prolongs the hypothermia and eliminates the tail-skin vasodilation. Experiments are underway to determine what effects CGRP antagonists and triptans may have on these physiological correlates of nausea.

Disclosure of Interests: Research supported by NIH R01 (AEL) and grants from the Kearns Center and Discovery grants (University of Rochester)

IHC-PO-090**Investigating the migraine premonitory phase: orexinergic networks regulating migraine initiation**

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Objective: Here we sought to investigate potential neural mechanisms underlying premonitory symptoms in migraine, most commonly presenting as marked fatigue. Given their prominent role in arousal promotion and link to trigeminal nociceptive processing, we hypothesized that disrupted orexinergic-mediated hypothalamic signalling may be a potential mediator for migraine-related fatigue and abnormal sensory processing.

Methods: Twelve adult mice (6 orexin Cre⁺, 6 Wild-type) underwent targeted ablation of hypothalamic orexinergic neurons via stereotaxic injection of a cre-dependent diphtheria toxin (dtA) or dummy injection into the lateral hypothalamus. Orofacial mechanical withdrawal thresholds were assessed in conjunction with general locomotor activity (open arena) as a surrogate marker of a generalised fatigue phenotype. Orofacial thresholds and locomotor activity were assessed between groups using independent t-tests. Following behavioural analysis mice were transcardially perfused and processed for standard immunohistochemical analysis of orexinergic cell body and fibre density, assessed via the Mann-Whitney U test.

Results: Stereotaxic injection of a cre-dependent dTA or dummy injection into the hypothalamus resulted in a significant reduction in orexinergic cell bodies in orexin-cre mice compared to WT controls. Further analysis identified a significant reduction of orexinergic fibre density in the locus coeruleus (LC; $p=0.0079$) and Periaqueductal Gray (PAG; $p=0.0087$). Mice lacking orexinergic neurons demonstrated a significant reduction in orofacial mechanical withdrawal thresholds ($p=0.0264$) combined with a significant reduction in locomotor activity ($p=0.0001$). There was no change in melanin-concentrating hormone cell density highlighting a specificity for orexin ablation.

Conclusion: Loss of orexinergic-mediated hypothalamic signalling results in increased periorbital mechanical sensitivity and reduced locomotion, potentially via reduced innervation of the PAG and LC. As such, orexinergic signalling and its dysregulation may play an important role in the occurrence of migraine-related premonitory symptoms, such as fatigue, and subsequent headache.

Disclosure of Interest: None Declared

IHC-PO-091**Multiple cortical spreading depression-induced calcitonin gene-related peptide gene expression in amygdala of rats is regulated by NMDA receptors**

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Objective: Calcitonin gene-related peptide (CGRP) is a key target for migraine prevention; however, the mechanism by which CGRP function in migraine is not fully elucidated. This study aims to investigate whether repetitive cortical spreading depression (CSD) could induce CGRP gene expression in rat amygdala, hippocampus and thalamus, key subcortical regions related to migraine and whether such changes in CGRP mRNA are associated with activation of NMDA receptors.

Methods: CSD was induced by KCl and monitored using electrophysiological methods. Quantitative PCR was used to measure CGRP mRNA levels in ipsilateral and contralateral subcortical regions of the rat following a single and repetitive CSD and compared to respective sham treatments. Drugs was perfused into contralateral intracerebral ventricle.

Results: Repetitive CSD events do not alter CGRP gene expression at 3 h post-CSD in all the three subcortical regions. Elevation in CGRP mRNA levels in ipsilateral amygdala is seen at 24 h post repetitive CSD. Whilst such increase is not seen in hippocampus and thalamus at all tested time points after a single and repetitive CSD. Interestingly, elevation of CGRP mRNA in amygdala was reduced after NR2A-containing NMDA receptor antagonism by NVP-AAM077, which correlates with a reduced cortical susceptibility to CSD.

Conclusion: Multiple CSD induces CGRP mRNA in amygdala, which can be regulated by NR2A-containing receptors. This data suggest an important mechanism involving amygdala CGRP by which repetitive episodes of CSD lead to the development of migraine.

Disclosure of Interest: None Declared

IHC-PO-092

Characterisation of PACAP and VIP receptor pharmacology and signaling reveals distinct profiles that provide insights into therapeutic targeting for migraine

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Objective: Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide hormone, which is hypothesised to play a pathophysiological role in migraine. PACAP activates three related receptors; VPAC₁, VPAC₂ and PAC₁. The PAC₁ receptor is believed to mediate the effects of PACAP in migraine. However, the PAC₁ receptor has several known splice variants in the N-terminal domain, which is important for neuropeptide recognition. In order to effectively target the PACAP system it is essential to determine which PACAP-responsive receptor mediates PACAP activity in sensory neurons.

Methods: The pharmacology of PACAP38, PACAP27, VIP, Maxadilan, PHM and antagonists was profiled at PAC_{1n}, PAC_{1s}, VPAC₁ and VPAC₂ receptors in transfected Cos7 cells using cAMP assays. This was compared to pharmacological profiles generated in sensory neuron cultures.

Results: The signaling profiles observed at PACAP receptors in Cos7 cells suggested the PACAP does not display agonist bias. However, the profiles displayed marked differences between the PAC_{1n} and PAC_{1s} splice variants. The agonist profiles observed in sensory neuron cultures were similar to those observed at transfected PAC_{1n} receptors. Probe dependent-antagonism was observed in both transfected cells and sensory neurons.

Conclusion: The pharmacology of sensory neuron cultures is consistent with a PAC₁ receptor and suggests that this is a potential site for PACAP to induce migraine and pain. However, differences between the pharmacology of the PAC_{1n} and PAC_{1s} splice variants suggests that these receptors may be functionally distinct. Blocking the PAC₁ receptor is a potential therapeutic strategy for migraine, however, the precise splice variant and agonist targeted should be considered in drug development efforts.

Disclosure of Interest: None Declared

IHC-PO-093

Parenchymal neuroinflammation in familial hemiplegic migraine type I transgenic mice after cortical spreading depolarization

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Objective: Cortical spreading depolarization (CSD) is the likely cause of the migraine aura. CSD activates a signaling pathway between stressed neurons and trigeminal afferents via the opening of neuronal Pannexin-1 channels followed by high mobility group box 1 (HMGB1) release from neurons and nuclear factor kappa B (NF-κB) relocation in astrocytes (Karatas et al. Science 2013). Familial hemiplegic migraine type I (FHMI) is a rare monogenic subtype of migraine with aura caused by missense mutations in the CACNA1A gene. Here, we investigated basal and CSD-induced parenchymal neuroinflammation in female mutant and wild-type (WT) mice and studied whether CSD-induced inflammation shows a particular (regional) pattern.

Methods: CSD was induced by pinprick in urethane-anesthetized mice followed by transcardial perfusion 30 minutes after CSD. Naïve mice were perfused after intraperitoneal injection of chloral hydrate to investigate basal neuroinflammation. Brains were extracted for molecular analysis.

Results: We found a basal parenchymal neuroinflammatory state in R192Q mutant mice as revealed by higher neuronal HMGB1 release and NF-κB activation in astrocytes. HMGB1 release and NF-κB translocation were more pronounced in subcortical regions including the thalamus in mutants compared to WT, in line with the enhanced spread of SD to subcortical areas in R192Q and S218L mutant mice (Eikermann-Haerter et al. J Neurosci 2011); parenchymal neuroinflammation was bilateral in the mutant.

Conclusion: These findings suggest that an enhanced inflammatory response to noxious stimuli, induced by mutations affecting Ca_v2.1 Ca²⁺ channels, may contribute to unfavorable outcome in the context of (repeated) CSD, stroke and brain trauma in knock-in mice, which gives new insights into the pathophysiology of FHM.

Disclosure of Interest: None Declared

IHC-PO-094**Shared neuropeptide changes between chronic migraine and opioid induced hyperalgesia**

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Objective: Chronic opioid use can result in opioid induced hyperalgesia (OIH), where pain spreads beyond the initial injury and is refractory to treatment. Opioids are commonly prescribed for migraine, and can worsen this disorder resulting in medication overuse headache and migraine chronicity. Dysfunction in individual neuropeptides have been implicated in chronic migraine and OIH. Considering the interplay between these two disorders, we hypothesized that overlapping mechanisms between them could occur at the level of neuropeptide dysregulation.

Methods: To model chronic migraine, mice were injected every other day for 9 days with the known human migraine trigger nitroglycerin (NTG, 10 mg/kg IP) or vehicle. To model OIH a separate group of mice were injected with vehicle or morphine twice daily for 4 days (20 mg/kg days 1–3, 40 mg/kg day 4, SC). Tissue was collected 18–24 h after the final injection, and analyzed with a non-biased liquid chromatography mass spectrometry approach to identify and measure changes in levels of more than fifteen hundred different brain peptides.

Results: Only 16 neuropeptides were significantly altered between chronic migraine and OIH groups. Among the 7 peptides associated with chronic migraine, calcitonin-gene related peptide (CGRP), a well-established pro-migraine molecule was significantly altered. Further, endogenous opioids and other pain processing neuropeptides were among the 9 peptides affected in OIH. In addition to individual peptide level changes, composite peptide complements for vasoactive intestinal peptide (VIP) and pituitary adenylate cyclase-activating polypeptide (PACAP) showed significant changes in both chronic migraine and OIH groups. To confirm our findings, we tested the PAC1 antagonist, M65 in our chronic migraine and OIH models; and found that it attenuated allodynia in both conditions.

Conclusion: Our mass spectrometry approach revealed both known and novel neuropeptide changes in models of chronic migraine and OIH. Furthermore, we identified PACAP as a mechanistic link between these two disorders. Although PACAP has been previously associated with migraine, our work suggests that it could be particularly important in OIH or medication overuse headache as well.

Disclosure of Interest: None Declared

IHC-PO-095**PACAP-induced cephalic allodynia is inhibited by delta opioid receptor activation**

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Objective: Pituitary adenylate cyclase activating polypeptide (PACAP) is a known human migraine trigger; and antibodies against the peptide and its receptor (PAC1) are being tested for the treatment of migraine. We have previously identified the delta opioid receptor (DOR) as a novel therapeutic target for headache disorders. However, it is still unclear how DORs regulate migraine-associated symptoms. The aim of this study was to determine if DORs interact with the pro-migraine peptide PACAP and the PAC1 receptor. A further goal was to develop a mouse model of PACAP-induced headache.

Methods: Male and female C57BL/6J and DOR-eGFP mice were used in this study. To investigate if PACAP could induce chronic cephalic allodynia mice were injected with PACAP (0.91 microg/kg, SC) or vehicle every other day for 9 days. Cephalic allodynia was assessed using von Frey hair stimulation of the periorbital region. The effect of sumatriptan (0.6 mg/kg IP) or the DOR agonist SNC80 (10 mg/kg IP) was tested in this model. Immunohistochemistry for DOR-eGFP was used to determine if PACAP treatment altered DOR expression. RNAScope in situ hybridization was used to investigate the co-expression of DOR with PACAP and the PAC1 receptor.

Results: Systemic injection of PACAP produced significant acute cephalic allodynia, and chronic intermittent administration resulted in long-term cephalic hypersensitivity which was blocked by both sumatriptan and SNC80. Concurrent treatment of PACAP with SNC80 also prevented the development of PACAP-induced chronic cephalic allodynia. Further, chronic administration of PACAP resulted in increased expression of DOR in the brain and trigeminovascular system. There was a high co-expression of DOR mRNA with PAC1, but not PACAP.

Conclusion: These results show that systemic administration of PACAP can be used to model PACAP-induced headache in mice. As in other headache models we observed an increase in DOR expression, which may act as a protective mechanism. Finally, DORs are co-expressed with PAC1 receptor. As DOR activation has an inhibitory effect, it likely prevents the propagation of PAC1 signaling; thus blocking pro-migraine effects of PACAP.

Disclosure of Interest: None Declared

IHC-PO-096**Exposure to flickering lights induces temporalis muscle sensitization in pain-free humans: an experimental study with 3 light colors**

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Objective: Abnormal sensitivity to light is often seen in migraine most likely as a result of trigeminal sensitization. Recently, it has been reported that green light has less of an intensifying effect on migraine headache compared with white, blue or red lights. We proposed that flickering light stimulation would sensitize the trigeminal system in healthy humans and induce pain and craniofacial muscle sensitivity and that color of light would influence the outcome.

Methods: After obtaining the ethical approval (N-20140088), 38 healthy participants (25.08 ± 4.44 years) were included in group 1 (white light, 5000 lux), and 30 (25.07 ± 4.35 years) in group 2 (red light, 3000 lux; blue light, 900 lux, crossover fashion). Participants received 2 min of flickering light exposure through a custom-made light chamber equipped with halogen lamp with a translucent plastic filter. Development of discomfort-head pain was measured. Pressure pain threshold (PPT) was recorded by hand held algometry on the temporalis muscles before and after the light exposures. Sex and eye color were taken into consideration for sub-analysis. $p < 0.05$ was considered significant.

Results: All participants developed a sense of discomfort in response to white light, but only 8 out of 30 to red light and 2 to blue light. Mean PPT values at right temporalis muscle decreased from the baseline after the light stimuli ($p < 0.05$). In response to white light, women had lower PPT values than men ($p = 0.022$). In response to red light, subjects with dark eyes had lower PPT values ($p = 0.001$). Subjects with dark eye colors had lower PPT values ($p = 0.027$) to blue light.

Conclusion: A short exposure to flickering light could provoke discomfort and temporalis muscle sensitization in healthy humans. White and red lights exerted the highest stimulating effect. Features of this short lived and safe model mimic some aspects of trigeminal sensitization in relation to photophobia and migraine and could offer a basic model for further investigation of trigeminal sensitization in humans.

Disclosure of Interest: None Declared

IHC-PO-097**Relationship between non-headache symptoms and dopamine and prolactin in migraineurs**

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Objective: Whether non-headache symptoms (NHS) were related to the abnormalities of dopamine (DA) and prolactin (PRL) has not been reported, the clinical features and NHS characteristics were investigated and the relationship with DA and PRL changes was analyzed in migraineurs.

Methods: One hundred and fifty nine migraineurs who were first admitted to the Out-patient Clinic of Shandong Provincial Hospital were enrolled between Jan and Dec 2017, and 103 sex – and age (± 3 years) – matched healthy subjects were chosen as control group. The clinical features and NHS characteristics of migraine were investigated. The content of PRL and DA was detected.

Results: The contents of PRL ($t = 4.160$, $P < 0.001$) and DA ($t = 3.129$, $P = 0.002$) in migraineurs were higher than those in controls. The content of PRL in chronic migraine (CM) subjects was higher than that of episodic migraineurs ($t = 3.849$, $P < 0.001$). There was a positive correlation between PRL and DA ($r = 0.404$, $P < 0.001$). The content of DA was positively correlated with HAMD scores ($r = 0.346$, $P < 0.001$). The content of DA was positively correlated with MIDAS scores in females ($r = 0.354$, $P < 0.001$), CM ($r = 0.442$, $P < 0.001$), migraine with aura ($r = 0.405$, $P = 0.022$) patients, respectively. There was a positive correlation between DA content and the numbers of NHS in headache phase (HP) ($r = 0.387$, $P < 0.001$) and resolution phase (RP) ($r = 0.307$, $P = 0.003$). There was a positive correlation between the amount of DA in episodic migraine ($r = 0.311$, $P = 0.001$), CM ($r = 0.425$, $P = 0.004$), migraine without aura ($r = 0.421$, $P < 0.001$) patients and the numbers of NHS in HP phase. In the RP phase, there was a positive correlation between the content of DA and the numbers of NHS in females ($r = 0.333$, $P = 0.005$), CM ($r = 0.380$, $P = 0.032$), migraine without aura ($r = 0.312$, $P = 0.008$) patients. There was no correlation between PRL content and clinical features and NHS characteristics.

Conclusion: The metabolism of DA and PRL were abnormal in migraineurs. DA and PRL may be risk factors for CM. The content of DA was associated with depression and disability in migraineurs. The content of DA is associated with the numbers of NHS in migraineurs. PRL may have nothing to do with the clinical features and NHS characteristics of migraineurs.

Disclosure of Interest: None Declared

IHC-PO-098

Erythrocyte health and the possible role of amyloidogenic blood clotting in the evolving haemodynamics of female migraine-with-aura pathophysiology: Results from a pilot study

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Objective: To critically evaluate viscoelastic profiles, erythrocyte morphology, fibrin network morphology, and presence of β -amyloidogenic alterations to fibrin through the phases of female migraine with aura.

Methods: Blood samples were obtained from the participants at 'baseline' (interictally) and during the headache phase. Viscoelasticity was evaluated using a TEG 5000 computer-controlled device (Haemonetics Corp., Niles, IL, USA). Peripheral blood smears were viewed using a Zeiss AXIO Imager M2 and analysed using Cellanalyzer software. Whole blood samples and fibrin networks were

viewed using a Zeiss Cryo CR-Beam Ultra-resolution SEM. Amyloid was detected by treatment of fibrinogen with thioflavin T and viewed using a Zeiss LSM 880 with Airyscan. All fibrin micrographs were analysed using the histogram function of FIJI. Statistical analyses were carried out using GraphPad Prism 6 with minimal significance defined as $P < 0.05$, CI = 95%.

Results: Analysis of PPP samples found clot reaction time and time to maximum rate of thrombus generation to be significantly decreased in female migraine-with-aura at baseline ($P < 0.05$). Erythrocyte circumferences were found to be significantly increased during the headache phase ($P < 0.0001$) while axial ratios were found to be increased both at baseline and during the headache phase of migraine compared to healthy controls ($P < 0.0001$). Analysis under light microscopy and SEM showed widespread aberrant erythrocyte morphology with increased presence of eryptotic cells in the cohort throughout the phases of migraine. Fibrin networks of female migraineurs at baseline were found to be significantly denser than those of healthy age-matched controls ($P < 0.0001$), with significantly higher numbers of β -amyloid fibrils at baseline than in healthy controls ($P < 0.001$). Changes in fibrin morphology have been shown in figure 1.

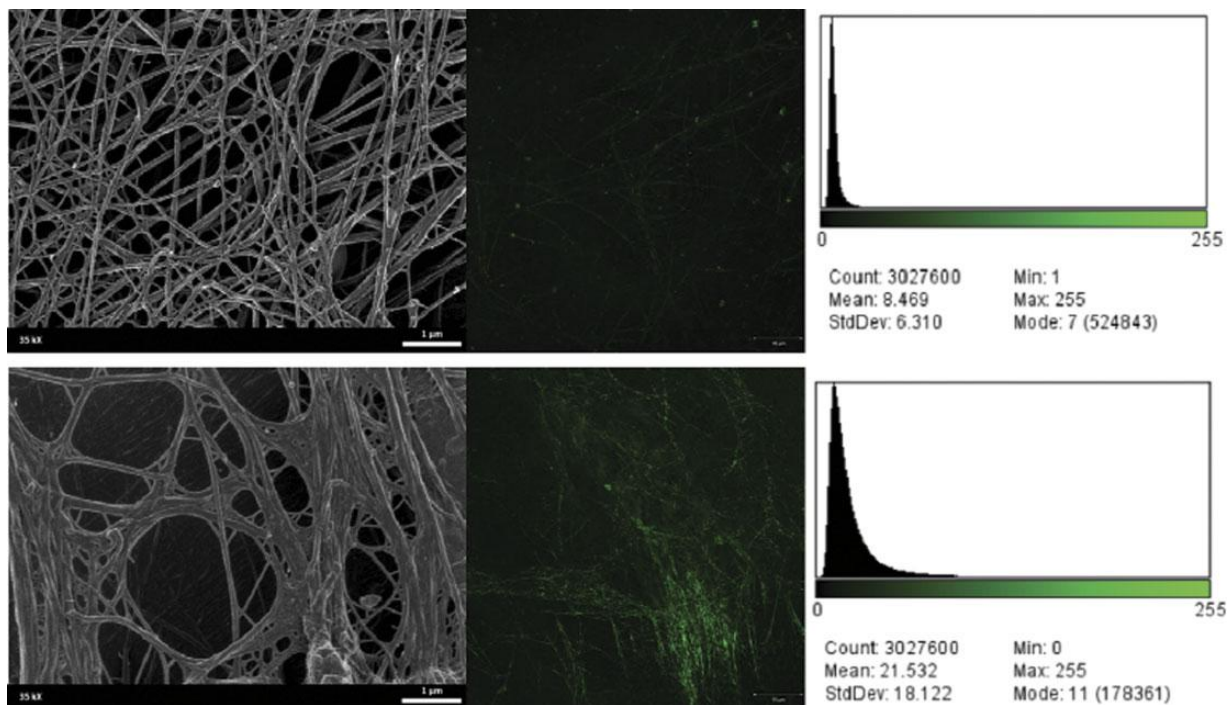


Figure 1: Thioflavin T was used as a marker of amyloid formation in PPP obtained from a female MA patient (A) at baseline and (B) during headache phase. Samples were analysed using a Zeiss LSM 880 with Airyscan at 63 kX under 488 nm laser and 458 nm excitation filter.

Conclusion: Morphological analysis of female migraineur erythrocytes indicates a high oxidative burden and as such a chronic systemic inflammatory state both at baseline and during the headache phase. Furthermore, a hypercoagulable state exists which likely results from aberrant fibrin polymerisation kinetics.

Disclosure of Interests: There are no conflicts of interest to disclose by any of the authors. Ethical clearance was obtained for this study from the University of Pretoria Research Ethics Committee (ethics protocol number 101/2015).

Disclosure of Interest: None Declared

IHC-PO-099

TRPA1 deactivation reduces the rapid induction of IL-1 β but not c-fos gene expression after cortical spreading depression

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Objective: The transient receptor potential ankyrin type-1 (TRPA1) channel plays a key role in migraine. However, the mechanisms underlying TRPA1 in migraine are still elusive. The aim of this study was to investigate whether TRPA1 deactivation could reduce the levels of mRNA encoding for both the proinflammatory cytokine, IL-1 β , and the pain marker, c-fos, induced by cortical spreading depression (CSD).

Methods: CSD was induced by K⁺-medium in the right cortices of rats and recorded by electrophysiological method. Quantitative PCR was used for gene expression analysis of IL-1 β and c-fos in the ipsilateral cortex, cerebral surface vasculature and associated meninges (MAV) and dura of rats.

Results: Pre-treatment of the anti-TRPA1 antibody into the intracerebral ventricle significantly suppressed CSD with a marked reduction of CSD number and magnitude and a significant prolongation of CSD latency. A pronounced induction of IL-1 β gene expression in the ipsilateral cortex, MAV and dura was observed immediate post-CSD. Similarly, elevation of c-fos gene expression was also seen in the ipsilateral cortex and MAV except in the dura. Interestingly, the induction of IL-1 β gene expression was markedly reduced by TRPA1 deactivation in the cortex and dura, but not in MAV; Whilst reduction of c-fos mRNA levels was not seen in all these brain regions.

Conclusion: CSD induces rapid induction of IL-1 β and c-fos gene expression in discrete brain regions of rat. TRPA1 deactivation reduces cortical susceptibility to CSD, which correlates with the reduced IL-1 β gene expression in the cortex and MAV. It is likely that TRPA1 deactivation for

migraine prevention is associated with the reduction of IL-1 β gene expression.

Disclosure of Interest: None Declared.

IHC-PO-324

Targeting CGRP via receptor antagonism and antibody neutralisation in two distinct rodent models of migraine-like pain

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Objective: Rodent disease models can play an indispensable role in drug development. Confirming that translationally relevant disease mechanisms are engaged in such models is a crucial facet of this process. Accordingly, we have validated the role of CGRP signaling in a mouse model of glyceryl trinitrate (GTN) provoked migraine-like pain and a spontaneous rat model (STA rats) of migraine-like pain by assessing their pharmacological responsiveness to the small molecule CGRP receptor antagonist olcegepant and the humanized monoclonal CGRP antibody ALD405.

Methods: Cutaneous sensitivity to hindpaw, and periorbital mechanical stimulation were used as surrogate markers of activation of relevant pain pathways in each respective model. Separate experiments were performed to identify the time-course of treatment response to olcegepant (1 mg/kg i.p.) and ALD405 (10 mg/kg i.p.).

Results: Olcegepant and ALD405 significantly alleviated cutaneous mechanical hypersensitivity in both models compared with corresponding control treatments (saline and IgG control antibody respectively). As expected, the duration of anti-nociceptive action obtained with ALD405 was considerably longer than that associated with olcegepant. Surprisingly, in the STA model the onset of action of ALD405 occurred within just 4 hours after administration.

Conclusion: The current data clearly show that CGRP-mediated signaling is critically involved in the manifestation of cutaneous hypersensitivity in distinct rodent models of migraine-like pain and emphasize their translational relevance. Moreover, the unexpected rapidity of onset observed for ALD405 supports (i) a probable site of action outside the blood brain barrier (ii) a potential clinical utility of specific monoclonal CGRP antibodies in the abortive treatment of migraine.

Disclosure of Interest: None Declared.

IHC-PO-325**De novo protein synthesis is necessary for priming in preclinical models of migraine**

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Objective: Despite its prevalence as the third most common disorder worldwide, the underlying pathophysiology of migraine is still poorly understood. Migraine headaches are often triggered by non-noxious stimuli. Similarly, in pre-clinical models of headache, mice exhibit hypersensitivity to innocuous stimuli after recovery from an initial pain-inducing stimulus, a model referred to as hyperalgesic priming. It has been shown in other pain models that this primed state is mediated by protein translation. The purpose of these studies was to determine whether protein synthesis is necessary for priming in a preclinical model of migraine.

Methods: Female wild-type (WT) mice were given a supradural co-injection of interleukin-6 (IL-6) in the absence or presence of the protein synthesis inhibitor anisomycin or the eIF4E/eIF4G inhibitor 4EGI-1 and were tested for facial hypersensitivity. Once mice returned to baseline, they were given a second supradural injection of innocuous pH 7.0 to test for priming. The role of translation in priming was also assessed using eIF4E knock-in (4EKI) mice. Male and female 4EKI and WT mice were subjected to repeated restraint stress and then tested for facial hypersensitivity. Once animals returned to baseline following stress, they were given a sub-threshold dose of the nitric oxide donor sodium nitroprusside (SNP, 0.1 mg/kg) and tested again.

Results: Mice that were co-injected with IL-6 and either anisomycin or 4EGI-1 exhibited acute hypersensitivity similar to those injected with IL-6 and vehicle; however, anisomycin and 4EGI-1 both blocked hyperalgesic priming to pH 7.0. Likewise, the normal hypersensitivity associated with priming to SNP following stress was not observed in 4EKI mice.

Conclusion: Using two different models of headache, these findings demonstrate that while local translation does not contribute to acute facial hypersensitivity with dural IL-6 or stress, it is indeed necessary for the development of a primed state. Our data suggest a role for *de novo* protein synthesis in events contributing to hypersensitivity in migraine patients.

Disclosure of Interest: None Declared.

IHC-PO-326**PACAP38 and PAC1 receptor in the brain – a widespread distribution**

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Objective: PACAP and its receptors are expressed in all mammals and have a evolutionary been conserved for 700 million years. The peptide is involved in numerous disorders both in brain diseases and in peripheral conditions. Hence it is not supprizing that PACAP has been found to be involved in primary headaches based on its release in migraine and cluster headache attacks. While many studies have shown focal distribution in the CNS, the more general picture is not clear. Our aim was to demonstrate the complex distribution pattern in the rat brain putatively linking it with migraine related structures. Our aim is to disclose the detailed localization of the PACAP38 and the PAC1 receptor in the CNS to provide a background to the functional studies in man.

Methods: With specific immunocytochemistry we have studied the detailed localization of PACAP38 and PAC1 receptor in different parts of the cerebrum, cerebellum and brainstem.

Results: PACAP38 positive fibres were seen in frontal and motor cortex, lamina II-IV, but not in the cell bodies. In central structures there were immunoreactive fibres in hippocampus and in Pyramidal cells of CA1 and CA2. Hypothalamus such as the paraventricular nucleus associated with stress, and in the thalamic habenular system, linked to reward function. In cerebellum we observed a dense network of PACAP38 fibres in the central pathway, and only minor in the granular layer. In the brainstem in areas linked with migraine pathophysiology like spinal trigeminal nucleus, locus coeruleus and inferior olive, PACAP38 expression was found.

PAC1 receptor immunoreactivity was observed in central parts of the brain such as the dentate gyrus, stria terminalis of the thalamus, septal nuclei and in the hippocampus and the paraventricular thalamic nucleus associated to stress responses. In the cerebellum we found PAC1 receptor positive fibres in the granular layer and in or close to the Purkinje cells. In the brainstem PAC1 immunoreactivity was observed in the reticular formation. The expression of other PACAP acting receptors such as VPAC1 and VPAC2 was very scant.

Conclusion: There is a rich supply of PACAP38 and PAC1 receptor expression in the brain, located in many regions associated with basic functional responses.

Disclosure of Interest: None Declared

IHC-PO-327**CGRP plasma levels in chronic migraine with medication-overuse: changes induced by detoxification**

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Objective: Chronic migraine (CM) is frequently associated to symptomatic medication overuse (MO) and this latter is considered one of the main causative factors for chronicification. Calcitonin gene related peptide (CGRP) is a key neuropeptide involved in the activation of the trigeminovascular system and it is likely involved in sensitization phenomena that are involved in migraine chronification. In this study, we assayed the plasma levels of CGRP before and after detoxification of subjects with CM and MO (CM-MO) to investigate the neuropeptide role in reduction of headache frequency.

Methods: Using a kit Elisa we assayed CGRP levels in the plasma of 21 subjects with episodic migraine (EM) and 19 subjects with CM-MO. Subjects in the CM-MO group were tested at baseline and 2 months after detoxification.

Results: Baseline CGRP levels were significantly higher in CM-MO subjects compared with EM patients (262.7 ± 74.8 pg/mL vs 173 ± 43.32 pg/mL, $p < 0.0004$), in agreement with previous studies. All the CM-MO subjects completed successfully the detoxification protocol and were overuse-free at 2 months. During the 2-month follow-up we recorded a 60% overall reduction in headache days/month reduction (25.42 ± 5.21 vs 10 ± 8.7). When stratifying the CM-MO population after detox in EM and CM based on the mean number of headache days during the 2-month follow-up (< 15 or ≥ 15), in the EM (n. 12) group we observed an obvious more marked reduction in headache days (24.6 ± 5.57 vs 6.13 ± 3.6) paired with a significant reduction in CGRP plasma levels (279.4 ± 74.63 pg/mL vs 137.5 ± 29.18 pg/mL). At variance, the CM group (n. 5) had a less marked reduction in headache days (28 ± 3.08 vs 21.6 ± 9.4), which was paralleled by a non-significant reduction in CGRP levels (209.5 ± 57.1 pg/mL vs 181 ± 38.72 pg/mL).

Conclusion: Altogether these findings confirm that increased CGRP plasma levels are a measure of migraine severity, and not a consequence of MO.

Disclosure of Interest: None Declared.

IHC-PO-328**Localization of 5-HT_{1B/1D} receptors in the trigeminal ganglion and dura mater**

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Objective: 5-hydroxytryptamine (5-HT) _{1B/1D} receptor agonists (triptans) are key molecules in aborting acute attacks of migraine but their detailed site(s) of action are still unknown. The present study was designed to examine the localization of 5-HT_{1B/1D} receptors in the trigeminal ganglion (TG) and dura mater in order to elucidate molecular site(s) of the receptors.

Methods: With specific immunohistochemistry we evaluated the localization of the 5-HT_{1B/1D} receptors in regards to the paranodal marker contactin associated protein 1 (CASPR) in both TG and dura mater.

Results: 5-HT_{1D} receptor immunoreactivity (IR) was observed in thicker TG nerve fibers with clear paranodal regions displayed by CASPR IR. The fibers were presumed to be A δ -fibers based on general paranodal diameter. We observed no clear co-localization of CASPR with 5-HT_{1D} receptor in A δ -fibers. In TG neurons 5-HT_{1D} receptor IR was observed in the cytoplasm and nucleus. IR for 5-HT_{1D} receptor was observed in the dura mater nerve fibers, but not in cell bodies.

In TG, IR for 5-HT_{1B} receptors revealed a similar expression as for 5-HT_{1D}. In addition, there was 5-HT_{1B} receptor IR in Schwann cells. In dura mater, 5-HT_{1B} receptor revealed positive IR mainly in mast cells.

Conclusion: The experiments suggest that the 5-HT_{1B/1D} receptors localize extensively but differentially in the TG and dura mater. The results indicate that the receptors are not expressed in the cell membrane of myelinated axons since there was no co-localization with CASPR. We therefore hypothesize that triptans may elicit their effect on these receptors on the neuronal soma but not the axons.

Disclosure of Interest: None Declared.

IHC-PO-329**Late sodium current blocker GS967 inhibits persistent currents induced by familial hemiplegic migraine type 3 mutations of the SCN1A gene**

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Objective: Familial hemiplegic migraine (FHM) is a group of autosomal dominant genetic diseases, whose major symptom is severe migraine, associated with hemiparesis and aura. Three different genes have been identified as causative for FHM-1,-2,-3, respectively. FHM3 is caused by mutations in SCN1A that encodes the voltage-gated Na channel, Nav1.1. 12 FHM3 causing SCN1A mutations have been found. Here we electrophysiologically characterized heterologously expressed the following so far functionally not studied mutations: Q1489H, I1498M, F1499L, M1500V, F1661L. In addition we tested in *Xenopus* oocytes the effect of the late Na current blocker GS967.

Methods: HEK cells were transiently transfected using an optimized SCN1A plasmid and Na currents were recorded using the patch clamp technique. For expression in *Xenopus* oocytes, cRNA was injected and two-electrode voltage-clamp measurements were performed.

Results: WT and mutant channels were characterized using standard electrophysiological protocols. In HEK cells, with the exception of I1498M, all mutants exhibited the same current density as WT. I1498M showed only very small functional expression, precluding a detailed analysis of gating parameters. All other mutants showed the following gating effects: a shift of the steady state inactivation to more positive voltages, accelerated recovery from inactivation, increase of the persistent current. Gating effects of mutants were similar in oocytes compared to HEK cells. The stability of the two-electrode voltage-clamp recording allowed to determine the pharmacological effect of 5 μ M GS967 using long voltage-clamp pulse protocols. GS967 inhibited the persistent current of all mutants and dramatically slowed recovery from inactivation of WT and mutants.

Conclusion: All mutants exhibit gating defects that can be considered a gain-of-function. Overall, this supports the hypothesis that FHM3 is caused by hyperactivity of the Nav1.1 due to a defect in the inactivation process. This behavior is expected to have a large effect on the neuronal firing properties. Since GS967 quite inhibits persistent currents, a preclinical testing of GS967 could be a valid approach to explore specific pharmacological treatment of FHM3.

Disclosure of Interest: None Declared

IHC-PO-330**The critical role of central delta opioid receptors in models of migraine and opioid-induced hyperalgesia**

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Objective: The delta opioid receptor (DOR) shows promise as a target for novel migraine medications as DOR agonists inhibit migraine-induced pain and negative affect in rodents without the abuse potential and hyperalgesia associated with μ opioid receptor agonists such as morphine. DORs are expressed in several peripheral and central regions important for pain processing and mood regulation, and it remains unclear which receptors are critical for regulating these anti-migraine effects. To this end, we examined the effects of the DOR agonist SNC80 in multiple headache models in conditional knockout mice with DORs missing from specific central or peripheral regions.

Methods: The DOR agonist, SNC80, was tested in multiple models of migraine and opioid induced hyperalgesia. Periorbital mechanical allodynia was measured following treatment with chronic nitroglycerin (NTG), a known migraine trigger. Periorbital and hindpaw allodynia was also measured following repeated treatment with morphine, a model of opioid-induced hyperalgesia. Migraine-associated negative affect was assessed using conditioned place aversion to NTG. We also evaluated the effects of SNC80 on KCl-evoked cortical spreading depression.

Results: Conditional knockout of DORs deleted from peripheral voltage-gated sodium channel Nav1.8-expressing neurons (Nav1.8-DOR) only inhibited the effects of SNC80 on opioid-induced hyperalgesia in the hindpaw. Loss of DORs in GABAergic forebrain neurons (Dlx-DOR) significantly diminished the effects of SNC80 in all observed outputs. NTG also enhanced DOR expression in multiple brain regions and measured by DOR-eGFP fluorescence.

Conclusion: Taken together, these data further support the potential of DOR agonists in the treatment of headache disorders and suggest that central delta opioid receptors are important mediators for the anti-migraine effects of DOR agonists.

Disclosure of Interest: None Declared.

IHC-PO-331**Expression and distribution of oxytocin and its receptor in rat trigeminal ganglion**

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Objective: Recently, oxytocin has been reported to inhibit migraine headache, which suggests an unexpected role of this neuropeptide in trigeminal pain signaling. To better understand how oxytocin may act, we determined the detailed expression and distribution of this peptide and its receptor in male rat trigeminal ganglion.

Methods: Single or double immunohistochemistry were applied on frozen sections of rat trigeminal ganglia using primary antibodies against oxytocin and oxytocin receptor, and molecular biological (RT-PCR) methods.

Results: Positive immunostaining showed oxytocin receptors (OTR) to be extensively localized in neurons throughout the ganglion. Many large soma as well as thick axonal fibers stained for OTR, consistent with expression of OTR in Ad sensory neurons. This pattern of OTR localization was similar to that of CGRP receptor expression, which we have reported previously. In addition, some small-medium sized soma stained for OTR, and in some cases, we could observe co-localization of OTR with CGRP immunostaining. These latter cells are characteristic of C-fiber neurons. We also detected immunostaining for oxytocin in glial satellite cells, indicating the presence of the peptide as well as its receptor in the ganglion. RT-PCR experiments confirmed a rich expression of mRNA for OTR in rat trigeminal ganglion, in which only little mRNA for oxytocin was measured.

Conclusion: These data suggest oxytocin has a major role in regulating both Ad- and C-fiber signaling in the trigeminal pain pathway. OTR appears to be promising target for novel anti-migraine drugs.

Disclosure of Interest: None Declared.

IHC-PO-332**Expression and distribution of Estrogen α and β receptors in rat trigeminal ganglion**

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Objective: Females have 2–3 times more migraine than males. The reason behind has been linked to female hormones, but the more detailed reason is not known. Here we aimed to analyze if Estrogen receptors are expressed in the trigeminal ganglion (TG) and in which cells.

Methods: Single immunohistochemistry were applied on frozen sections of rat TG using primary antibodies against Estrogen α and β receptors. In addition, double immunohistochemistry was performed using antibodies against Estrogen α or β receptor, and CGRP. The molecular qPCR method was used to identify expression of Estrogen α and β receptor.

Results: Estrogen α receptor immunoreactivity was found in neuronal nuclei, but not in the glial cell nuclei. In addition, neuronal processes of the seemingly A δ type showed Estrogen α receptor expression.

Estrogen β receptor expression was observed in the neuronal cytoplasm in a pattern resembling the Golgi apparatus.

Double immunohistochemistry revealed co-localization of Estrogen β receptor and CGRP in the Golgi apparatus. qPCR revealed mRNA for both Estrogen α and β receptors in the TG.

Conclusion: Estrogen exerts its effects through at least two different cellular mechanisms. One is the classical mechanism of estrogen receptor action, which involves binding of estradiol to Estrogen α or Estrogen β in the nucleus. The other is the “non-nuclear” mechanism of Estrogen action, which can activate rapid cytoplasmic signalling mediated by membrane-associated Estrogen receptors. In our study, we found proof of both mechanisms working in the trigeminal ganglion: nuclear Estrogen α receptor, and Estrogen β receptor in the Golgi apparatus. The results provide further in-depth understanding on how the female sex hormone Estrogen might act to modify the function of neurons in the TG.

Disclosure of Interest: None Declared.

IHC-PO-333**Expression of the CGRP family of neuropeptides and their receptors in the trigeminal ganglion**Karin N. Warfvinge¹ and Lars Edvinsson^{1,2,*}¹Department of Clinical Experimental Research, Glostrup Research Institute, Rigshospitalet, Glostrup, Denmark²Division of Experimental Vascular Research, Department of Clinical Sciences, Lund University, Lund, Sweden

Objective: The calcitonin gene-related peptide (CGRP) family of neuropeptides, besides CGRP, consists of adrenomedullin, amylin and calcitonin. The receptors consist of either calcitonin receptor like-receptor (CLR) or calcitonin receptor (CTR) which for function needs an accessory protein, receptor activity-modifying proteins (RAMPs). These define the receptor subtype and interact to produce different effects via signal transduction and receptor trafficking. CGRP has a pivotal role in primary headaches but the role of the other members of the CGRP family of peptides is not known. Here, we describe the expression of these molecules in the trigeminal ganglion to understand more on their role.

Methods: Single or double immunohistochemistry were applied on frozen sections of rat trigeminal ganglia using primary antibodies against CGRP, calcitonin, adrenomedullin, amylin, RAMP1/2/3, CLR and CTR.

Results: CGRP and calcitonin showed similar results with expression in small to medium-sized neurons in the TG. Immunoreactive fibers were also observed. Adrenomedullin immunoreactivity was found in the satellite glial cells and in fibers, probably processes of the myelinating glial cells. Amylin was found in the cytoplasm in many trigeminal ganglion neurons.

In addition to the well-known CGRP receptor (CLR/RAMP1) and the receptor for calcitonin – CTR, we propose that other receptors exist in the rat trigeminal ganglion: adrenomedullin receptor AM₂ (CLR/RAMP3) in mainly the satellite glial cells, amylin receptors AMY₁ (CTR/RAMP1) in mainly neurons and AMY₃ (CTR/RAMP3) in the satellite glial cells.

Conclusion: Several of the diverse biological actions of the CGRP family of peptides are clinically relevant. We demonstrate in the present study possible AM₂, AMY₁ and AMY₃ receptors in rat TG. Our findings demonstrate specific ligand and receptor sites in the rat trigeminal ganglion, highlighting recognition mechanisms to modulate TG function and possibly to facilitate drug development.

Disclosure of Interest: None Declared.

IHC-PO-334**PACAP-38 and PAC1 receptor in the trigeminal ganglion**Jacob Edvinsson^{1,*}, Kristian A. Haanes², Karin N. Warfvinge² and Lars Edvinsson^{2,3}¹Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, Copenhagen University, Copenhagen²Department of Clinical Experimental Research, Glostrup Research Institute, Rigshospitalet, Glostrup, Denmark³Division of Experimental Vascular Research, Department of Clinical Sciences, Lund University, Lund, Sweden

Objective: PACAP has been suggested to be involved in the pathophysiology of primary headaches based on (i) localization in trigeminal ganglion neurons that contain CGRP, (ii) PACAP is released in migraine and cluster headache attacks, and (iii) infusion induces migraine-like headache in migraine patients. Trigeminal ganglion (TG) contains 2 populations of neurons: (i) Neuronal cell bodies that contain calcitonin gene-related peptide (CGRP) and a subpopulation of these store PACAP-38. At present there are ongoing trials to examine if monoclonal antibodies towards PACAP-38 or PAC1 receptors can reduce migraine. However, little has been done to examine in detail the localization of the PACAP elements in the trigeminal system. Our aim is to map the detailed localization of the PACAP-38 and PAC1 receptor in the trigeminal system to provide a background to functional studies in man.

Methods: Using immunohistochemistry we have studied the detailed localization of PACAP-38 and PAC1 receptor in TG and the trigeminal fibers.

Results: (i) PACAP-38 was seen in the C-fibres that contain CGRP (ii) PAC1 receptors were found in the TG and in the distal parts of the trigeminal fibres. Notably PAC1 immunoreactivity was seen in some TG neurons and inside A δ -fibers. The study showed that PAC1 was found in the satellite glial cells that surround the different neurons in the trigeminal ganglion. PAC1 receptor antibodies bound to the outermost part of myelin that surrounds the A δ -fibers, demonstrating PAC1 receptors on the A δ -fibers.

Conclusion: PACAP-38 was found together with CGRP in neurons and fibers, while PAC1 was primarily related to SGCs and Schwann cells. Some PAC1 immunoreactivity was also seen in A δ -fibers and neurons, The role of PACAP-38 and PAC1 is multifaceted.

Disclosure of Interest: None Declared.

IHC-PO-335

An Investigation of Oxidant/Antioxidant Balance, Nitrosative Stress, and Inflammation in Migraine Patients Compared to Healthy Controls

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Objective: Due to inconclusive findings of previous researches, we aimed to investigate biomarkers of inflammatory and oxidative stress in chronic and episodic migraineurs (CM and EM patients) and controls.

Methods: Seventy-one migraine patients (44 EM, 27 CM subjects) and 19 age-sex-matched controls were enrolled. After collecting the data on demographic and headache characteristics, blood samples were collected and analyzed to detect the serum levels of C-reactive protein(CRP), Tumor Necrosis Factor(TNF)- α and interleukin(IL)-6, malondialdehyde (MDA), Catalase(CAT), Superoxide dismutase (SOD), Glutathione peroxidase (GPx-I), Trolox equivalent antioxidant capacity (TEAC) and nitric oxide(NO) in the studied subjects.

Results: Serum levels of CAT and SOD were significantly lower in CM group than EM and controls. However, serum GPx-I levels of CM group was slightly higher than EM and controls(P-value \leq 0.001). CM patients had lower TEAC levels than EM and controls(P-value \leq 0.001). Besides, serum levels of NO, MDA, IL6, CRP and TNF- α were significantly higher among subjects with CM than EM and controls. Pearson correlation analysis revealed negative correlations between frequency of headache days/month and serum concentrations of CAT ($r=-0.60$, P-value < 0.001) and SOD ($r=-0.50$, P-value < 0.001) and serum TEAC ($r=-0.61$, P-value < 0.001); while there were positive correlations between headache frequency and serum GPx-I levels ($r=0.46$, P-value < 0.001). Also, positive correlations were noted for headache frequency/month and serum NO ($r=0.62$, P-value < 0.001), MDA ($r=0.64$, P-value < 0.001), IL-6 ($r=0.53$ P-value < 0.001), CRP ($r=0.62$, P-value < 0.001) and TNF- α ($r=0.58$, P-value < 0.001).

Conclusion: Present findings highlighted that chronic migraineurs had lower antioxidant capacity than EM and control individuals. Moreover, a pro-inflammatory state was detected among EM and CM subject compared to controls. Although more studies needed to confirm these data, applying novel prophylactic medications or dietary supplements might be helpful in migraine therapy.

Disclosure of Interest: None Declared.

IHC-PO-336

Differential impact of different NSAID's in medication overuse headache

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Objective: Triptans and non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for acute migraine treatment. Medication overuse is a known risk factor for chronic migraine and can lead to medication overuse headache (MOH). Given the availability of NSAIDs, we sought to determine the impact of triptan and NSAIDs in isolation and when combined in a preclinical model of MOH.

Methods: Male C57BL/6J mice (N = 60) were separated into four equal groups receiving sumatriptan, ibuprofen, naproxen, sumatriptan and ibuprofen, sumatriptan and naproxen or vehicle respectively, daily for between 11 and 15 days. Mechanical hypersensitivity was evaluated every second day using von Frey filaments following habituation to the testing apparatus. The mechanical withdrawal threshold was calculated and analyzed over time using a two-way repeated measures ANOVA. At the conclusion of behavioural analysis, mice were processed for biochemical analysis of cyclooxygenase enzyme (COX-1 and COX-2) expression in the trigeminal cervical complex (TCC) and trigeminal ganglion (TG).

Results: Sumatriptan significantly reduced the mechanical withdrawal threshold compared to vehicle control maximally at day 15 by $94 \pm 4\%$; $F_{(1, 18)} = 54.23$, $P < 0.001$. Ibuprofen alone decreased the mechanical withdrawal threshold maximally at day 11 by $67 \pm 6\%$, $F_{(1, 18)} = 12.63$, $P < 0.001$; however, naproxen alone had no impact ($F_{(1, 18)} = 0.2633$, $P = 0.6141$). Sumatriptan and ibuprofen reduced mechanical withdrawal thresholds (maximally at day 13 by $71 \pm 4\%$; $F_{(1, 18)} = 12.45$, $P = 0.0024$); however, the thresholds were significantly greater than sumatriptan alone ($F_{(1, 18)} = 11.58$, $P = 0.0032$). In agreement with a lack of sensitization following naproxen alone, the combination of naproxen and sumatriptan significantly restored the reduction of mechanical withdrawal thresholds resulted from sumatriptan treatment alone ($F_{(1, 18)} = 30.6$, $P < 0.0001$). Ibuprofen further increased the

expression of COX-1 in the TCC and TG and COX-2 in the TCC only, an effect not observed following naproxen administration.

Conclusion: Our findings suggest that naproxen may be a potential therapeutic option in MOH and the differential response to ibuprofen and naproxen may be COX-dependent.

Disclosure of Interests: This study was supported by the MRC grant (MR/P006264/1) and PhD funding from the Development and Promotion of Science and Technology Talents Project (DPST), the Royal Thai Government.

IHC-PO-337

Trigeminovascular calcitonin gene-related peptide release in rapidly aging mice

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Objective: Migraine pathophysiology is associated with activation of the trigeminovascular system, calcitonin gene-related peptide (CGRP) release and cranial vasodilatation. Migraine prevalence is higher during the reproductive years, but decreases in the fifth or sixth decade of life, and about 40% of migraine patients stop having attacks. However, the mechanisms associated with this improvement are not understood.

Objective: To investigate trigeminal CGRP release in 2-month old wild-type and rapidly aging (*Ercc1*^{Δ/-}) mice, which phenocopy normal murine aging [4].

Methods: KCl-induced CGRP release from isolated preparations of mouse dura mater, trigeminal ganglion and trigeminal nucleus caudalis were compared between the two genotypes (n = 5–8). The release of CGRP was measured by enzyme-linked immunoassay and expressed as relative stimulated CGRP release, which was calculated as the ratio of KCl-induced CGRP release and basal CGRP release. Experiments were approved by the Erasmus University Medical Center's institutional ethics committee, in accordance with National Institute of Health guidelines.

Results: In comparison to baseline, KCl induced CGRP release ($p < 0.05$) in the dura mater, trigeminal ganglion, and trigeminal nucleus caudalis of mice of both genotypes. Interestingly, in *Ercc1*^{Δ/-} mice CGRP release was diminished ($p < 0.05$) in the dura mater (3.2 ± 3 vs 18.1 ± 9), trigeminal ganglion (2.8 ± 1 vs 8.0 ± 3), and trigeminal nucleus caudalis (3.2 ± 1 vs 15.9 ± 7) as compared to wild-type mice.

Conclusion: CGRP release from peripheral and central trigeminal nerve terminals is diminished in rapidly aging (*Ercc1*^{Δ/-}) mice. Further studies are needed to determine

the relationship between aging, nerve morphology and CGRP expression in trigeminal fibers.

Disclosure of Interest: None Declared.

IHC-PO-338

5-HT_{2B} receptor expression and function in primary dural endothelial cells with relation to a migraine mouse model

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Objective: The origin of migraine pain has been discussed to be located in meningeal afferents. Several external factors such as chronic stress or hormonal fluctuations can lead to a sensitized yet activated state of meninges known as neurogenic inflammation (NI). NI leads to a release of neuropeptides as Substance P or CGRP from trigeminal afferents resulting in vasodilation, mast cell degranulation and plasma protein extravasation (PPE). The latter is characterized as a transfer of blood-borne proteins into the vessel microenvironment and is a common indicator for migraine attacks in animal models.

In our hypoxic migraine mouse model, pharmacological examinations, including the application of 5-HT_{2B} partial receptor agonist mCPP lead to NI resulting in PPE in the dura mater of hypoxia-treated mice.

The established pathways for blood-borne proteins to extravasate blood vessels are across endothelial cells (transcellular) or between endothelial cells (paracellular). In our mouse model, electron microscopic experiments indicate that transcytosis is the main pathway for proteins to enter the perivascular tissue (Hunfeld et al., 2015).

For further investigations, regarding the underlying mechanisms of sensitization and transcytosis on a cellular level, we established a primary cell culture of murine dural endothelial cells (MDEC) in normoxic and hypoxic culture conditions. An enrichment of MDEC was achieved and further characterized using qPCR, single-cell PCR as well as immunocytochemical staining methods.

Methods: 1) Magnetic-activated cell sorting (MACS) and cultivation of MDEC. 2) qPCR and western blot (marker for transcytosis). 3) Receptor localization via ICC and single-cell PCR.

Results: The 5-HT_{2B} receptor is found to be located on MDEC and other cell types. The expression level of several markers for transcytosis and receptor expression in MDEC on RNA (qPCR) and protein (western blot) level show promising results for further pharmacological examinations of the 5-HT_{2B} receptor.

Conclusion: Hypoxia-induced regulation of transcytosis markers in MDEC show first indications for an altered vascular state under low oxygen conditions in vitro.

The location of the 5-HT_{2B} receptors on MDEC could be validated, which enables further experiments to discover the involvement of the 5-HT_{2B} receptor in NI and migraine pathophysiology.

Disclosure of Interest: None Declared.

IHC-PO-339

Oxytocin and Oxytocin receptor in the brain – a widespread distribution

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Objective: Oxytocin plays a central role in initiating the onset of maternal behavior. In addition to its involvement in uterine contraction, lactation and psychosocial processes, oxytocin has also been implicated in many central processes. A steadily increasing number of publications has appeared on the molecular, physiological, pharmacological, and behavioral significance of oxytocin. The underlying neuroanatomical and neurochemical basis have been studied to a much lesser extent. This is especially true for oxytocin projections within brain.

Methods: With specific immunocytochemistry we have studied the detailed localization of Oxytocin and Oxytocin receptor in different parts of the cerebrum, cerebellum and brainstem in sagittal sections of the rat brain (lateral 0.5–1.5 mm). In addition, we have compared the Oxytocin and Oxytocin receptor distribution pattern with the pattern of CGRP and CGRP receptor components.

Results: It is well known that oxytocin, together with vasopressin, are synthesized in magnocellular neurosecretory cells in the supraoptic and paraventricular nuclei of the hypothalamus. We identified strong oxytocin immunoreactivity in cell soma of both these nuclei. In addition, in almost the whole brain, such as cortex, cerebellum and brainstem, oxytocin immunoreactive fibers were visualized. It was especially true for cortex, where delicate networks of immunoreactive fibers were present. The oxytocin receptor immunoreactivity were not so abundant. The most striking immunoreactivity was found in hippocampal pyramidal cells and fibers.

Conclusion: We conclude that in the normal rat brain, we find oxytocin immunoreactive fibers in almost the whole brain. The most fascinating feature of the oxytocin neuron is the long-range axonal projections. However, the oxytocin receptor was not so abundant in the brain. To produce its actions in the brain, oxytocin must reach and activate its main target, the oxytocin receptor. This means

that it is not the distribution of oxytocin fibers in the brain that determines behavior, but the distribution of oxytocin receptors (Ludwig et al, *Nature Reviews Neuroscience* volume 7, pages 126–136, 2006).

Disclosure of Interest: None Declared.

IHC-PO-340

The evaluation of a role of the inconsistency of connective tissue in the development of pathological deformations of cerebral vessels in patients with primary headaches

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Objective: To analyze manifestations of connective tissue failure in patients with pathological deformations of cerebral vessels.

Methods: The study included 60 patients with primary headaches treated in 1st Republic Clinic in Tashkent between 2016–2018 years. The average age of the patients was 17–45 years (22.3 ± 2.5 years). Patients were divided into 2 groups: patients with (30 patients) and without (30 patients) abnormalities of cerebral vessels. The examination included a clinical neurologic examination, MRI with angiography and a duplex study of dysplasia on a questionnaire scan.

Results: The study showed that in the first group of patients, increased elongation, hyperelasticity of the skin were observed: the folded skin was easily pulled back by several centimeters, and then quickly returned to its original position. There was a slight vulnerability of the skin, even with minimal trauma, which slowly healed, leaving after themselves keloid scars, increased mobility and loose joints. Also, patients with anomalies in childhood often had joint dislocations, increased bleeding. At the time of the study, chronic arthralgia without signs of joint inflammation was found in 13.7% of patients. Scoliosis, kyphosis, their combination, as well as flat feet were noted. At the same time, in the observed patients, the breakdown in the strength of the internal organs tissues manifested itself in the form of hernia, 7.8% of cases, the lowering of the internal genitalia-9.7%, in 21.3% in the anamnesis, premature rupture of the membranes, premature birth and postpartum haemorrhage. A frequent complication in patients with connective tissue failure is the stratification of the extra- or intracranial segments of the vertebral arteries, which was verified in 5 patients diagnosed with basilar migraine.

Conclusion: Diffuse inconsistency of connective tissue was revealed in patients with deformations of cerebral vessels. Furthermore, it has been shown that systemic dysplasia of connective tissue is a risk factor for the

development of pathological deformations and to identify pathology from the connective tissue, it is necessary to include a screening of connective tissue in the primary headache examination.

Disclosure of Interest: None Declared.

Headache Pathophysiology – Imaging and Neurophysiology

IHC-PO-100

Revealing non-linear response characteristics of the migraine brain upon sum-of-sine visual stimulation

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Objective: In migraine, a neuronal excitation/inhibition imbalance is suggested to result in abnormal sensory (including visual) processing. Studies attempting to quantify this using flash or pattern visual stimuli and electroencephalography (EEG) to explore the direct linear response, yielded ambiguous results. Rather than studying the linear brain response, quantifying the nonlinear properties of sensory processing of the brain by using well designed sensory stimuli, e.g. a sum-of-sine paradigm, may provide more consistent results. In this study, we use sum-of-sinusoid visual flash stimulation combined with EEG to explore the brains' nonlinear visual processing features in migraine patients and headache-free participants.

Methods: Migraine patients with aura (MA; N = 19), without aura (MO; N = 20) and healthy participants (HC; N = 24) were recruited. Each participant received 320 s of red light (654 nm) flash stimulation using binocular LED goggles. All participants were tested during working hours and migraine patients >4 days after their last attack. The stimulation paradigm consisted of a sum of two sinusoids (13 & 23 Hz). EEG was recorded using both a 7-channel and high-density 128-channel (HD) EEG system. Nonlinear interactions were analysed using novel phase clustering – and amplitude spectral measures.

Results: The cortical response to visual stimulation was characterized by higher harmonics and intermodulation frequencies up to the 4th order. The 2nd order interactions revealed decreased phase locking in MA and MO

compared to HC. The time delay between visual input and the response at the occipital cortex was decreased for MA patients compared to HC and MO. HD-EEG revealed that different higher-order non-linearities are associated with distinct topographies that can be related to cortical and sub-cortical processing of visual input.

Conclusion: Migraine patients demonstrate an altered non-linear response to visual stimulation compared to healthy controls. Non-linear response characteristics of the visual system may provide a suitable electrophysiological biomarker of migraine phase and allow insight in temporal changes across the migraine cycle.

Disclosure of Interest: None Declared.

IHC-PO-101

PACAP27 induces migraine-like attacks in migraine patients

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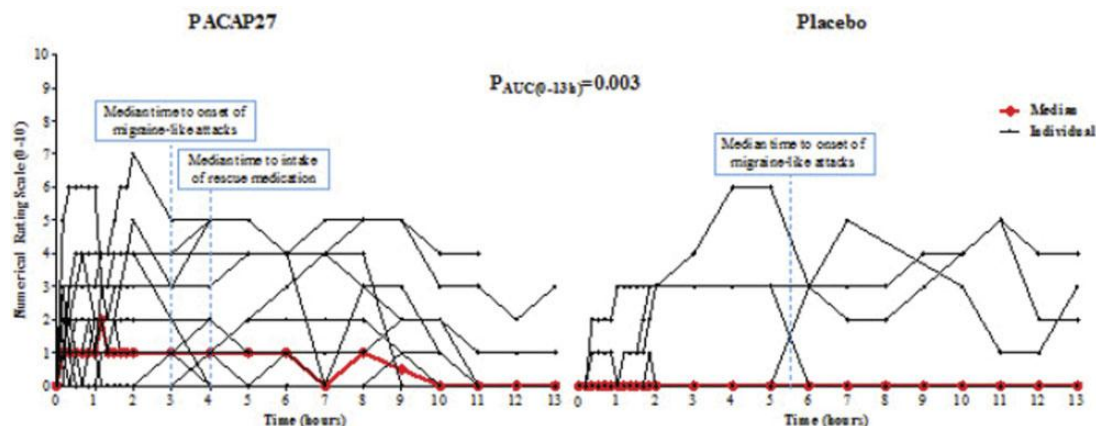
Objective: Pituitary adenylate cyclase-activating polypeptide (PACAP) is found in two functional isoforms namely; PACAP38 and PACAP27. The migraine inducing properties of PACAP38 is well studied. However, it is unknown whether the lesser known and understudied protein isoform, PACAP27 can also induce migraine attacks. Here, we studied the effect of human PACAP27 infusion in induction of migraine in a provocation model.

Methods: In a crossover study, twenty migraine without aura patients were randomly assigned to receive human PACAP27 (10 picomol/kg/min) or saline (placebo) infusion over 20 min. We recorded the migraine and associated symptoms.

Results: All patients completed the study. PACAP27 provoked migraine-like attacks in eleven patients (55%) and two developed after placebo (10%) ($p = 0.022$). The headache intensity and duration after PACAP27 was significantly greater compared to placebo ($p = 0.003$).

Conclusion: PACAP27 triggers migraine attacks without aura. These novel data strengthen the role of PACAP and its receptors in migraine pathogenesis.

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Abstract number: IHC-PO-101

IHC-PO-102

Sumatriptan binds to central 5-HT_{1B} receptors in migraine patients

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Objective: To determine to which extent sumatriptan enters the brain parenchyma and binds to central 5-HT_{1B} receptors and to investigate changes in brain serotonin levels during migraine.

Methods: Eight migraine patients underwent positron emission tomography scans after injection of the 5-HT_{1B} receptor specific radiotracer [¹¹C]AZ10419369, which is sensitive to competition at the binding site. All participants were scanned three times: 1) during an experimentally induced migraine attack, 2) after a subcutaneous injection of 6 mg sumatriptan, and 3) on an attack-free day.

Results: Sumatriptan significantly reduced cerebral 5-HT_{1B} receptor binding (mean BP_{ND} ± SD 1.20 ± 0.20 vs. 1.02 ± 0.22, $p = 0.0001$), corresponding to a mean occupancy ± SD of 16.0 ± 5.3%. Further, during migraine attacks 5-HT_{1B} receptor binding was significantly reduced in pain modulating regions as compared to outside of attacks (mean BP_{ND} ± SD 1.36 ± 0.22 vs. 1.20 ± 0.20, $p = 0.019$).

Conclusion: Sumatriptan crosses the blood-brain barrier and binds to central 5-HT_{1B} receptors. This may be an integral part of the antimigraine effect of sumatriptan. Further, the attack-related decrease in 5-HT_{1B} receptor binding indicates that brain serotonin levels increase during migraine attacks.

Disclosure of Interest: None Declared.

IHC-PO-103

Dynamic functional connectivity of migraine brain: a resting-state fMRI study

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Objective: Migraine is a chronic neurological disorder with distinct underlying brain characteristics (“migraine brain”). We aimed to find brain networks which characterize the migraine brain regardless of headache phase using dynamic functional connectivity analysis.

Methods: In this study, we prospectively recruited 50 patients with migraine and 50 age- and sex-matched controls. All subjects underwent a resting-state functional MRI. Significant networks were defined in a data-driven fashion from the interictal patients and matched controls (interictal dataset) and tested to ictal or peri-ictal patients and controls (ictal/peri-ictal dataset). Both static and dynamic analyses were used for the between-group comparison. Multiple comparisons were corrected with the false discovery rate correction.

Results: The static analysis did not reveal a network which was significant in both interictal and ictal/peri-ictal datasets. Dynamic analysis revealed significant between-group differences in seven brain networks in the interictal dataset, among which a frontoparietal network

(controls > patients, $p = 0.0467$), two brainstem networks (patients > controls, $p = 0.0467$ and < 0.001), and a cerebellar network (controls > patients, $p = 0.0408$ and < 0.001 in two states) remained significant in the ictal/peri-ictal dataset. Using these networks, migraine was classified with a sensitivity of 0.70 and specificity of 0.76 in the ictal/peri-ictal dataset.

Conclusion: In conclusion, the dynamic connectivity analysis revealed more functional networks related to migraine than the conventional static analysis, suggesting a substantial temporal fluctuation in functional characteristics. Our data also revealed migraine-related networks which show significant difference both in interictal and ictal/peri-ictal patients compared to normal controls.

Disclosure of Interest: None Declared.

IHC-PO-104

Neural correlates of visuospatial processing in migraine patients: does the pain network interfere?

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Objective: Previous clinical studies demonstrated impaired visuospatial abilities in migraine patients. Aim of this study was to explore functional and structural magnetic resonance imaging (MRI) correlates of visuospatial processing in migraine patients and their relation with visuospatial performance and patients' clinical characteristics.

Methods: A functional MRI visuospatial task, including an angle and a colour discrimination paradigm, was administered to 17 headache-free migraine patients and 16 controls. 3D T1-weighted scans and voxel-based morphometry were used to explore whether cortical areas activated during the visuospatial task had significant grey matter volume (GMV) alterations. The correlations between functional and structural MRI abnormalities and subjects' performance, clinical and neuropsychological variables were also investigated.

Results: The response accuracy and reaction times did not differ between migraineurs and controls. All study subjects activated frontal, parietal, occipital and cerebellar regions during both the angle and colour task. The comparison angle vs colour task revealed an increased activity of the right insula, middle frontal gyrus, bilateral

orbitofrontal cortex and middle cingulate cortex and decreased activity of the bilateral posterior cingulate cortex (PCC) in migraine patients compared to controls ($p < 0.05$, FWE corrected). No significant regional GMV differences were found between patients and controls. In migraineurs, a better performance in the angle task was associated with higher activation of the right insula ($r = 0.84$, $p < 0.001$, uncorrected) and orbitofrontal cortex ($r = 0.83$, $p < 0.001$, uncorrected). Decreased activity of the PCC correlated with shorter disease duration ($r = 0.92$, $p < 0.05$, FWE corrected).

Conclusion: Migraine patients experienced abnormal activation of visuospatial processing brain areas that are commonly involved also in nociception. The increased activity of the insula and frontal lobes and the decreased recruitment of the PCC might represent an adaptive response, strengthened by the recurrent activation of these regions during migraine attacks.

Disclosure of Interest: None Declared.

IHC-PO-105

Different gray matter volumes in high frequency migraine with different outcomes

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Objective: To identify the brain morphological changes related to headache persistence and chronification in patients with high frequency migraine.

Methods: We consecutive enrolled patients with high frequency migraine (HFM: ≥ 10 headache days/month) and longitudinally followed up their 2-year headache outcomes. Clinical data including demographics, headache profiles, scores of hospital anxiety and depression scale (HADS), and a brain MRI image were obtained at their first visit. Poor outcome was defined by headache frequency ≥ 10 days/month and less than 50% reduction of baseline headache days at the 2-year follow-up. Changes of gray matter volumes (GMV) on brain MRI associated with different outcomes were investigated using voxel-based morphometry. The correlation with headache profiles were also investigated for these GM changes.

Results: A total of 39 patients with HFM (28F/11M, 38.9 ± 10.3 years old, 17.8 ± 6.9 headache days/month) were included in the study. Among them, 23 had good outcome (3.1 ± 1.9 headache days/month at follow-up) and 16 had poor outcome (19.4 ± 7.6 headache days/month at follow-up). Patients with good and poor outcome were comparable in age, sex, baseline scores of

HADS and migraine disability assessment, but patients with poor outcome had a longer disease duration compared to those with good outcome (22.4 ± 12.8 vs. 14.6 ± 9.9 years, $p < 0.05$). After adjusting the confounding variables, patients with poor outcome had decreased GM volume over the left inferior temporal and precentral gyrus, the left insular cortex, the left cerebellum crus I, the right middle temporal gyrus, the right frontal and temporal pole, and the bilateral supramarginal gyrus compared to those with good outcome. All of the above brain structural volumes are correlated to headache frequencies at 2-year follow-up ($p < 0.05$).

Conclusion: Different brain structural volumes are corresponding to future headache frequencies.

Disclosure of Interest: None Declared.

IHC-PO-106

Chronic migraine patients show a different profile of the white matter fiber bundles compared to healthy subjects

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Objective: The migraine brain is characterized by an alteration of the intrinsic functional connectivity of different cortical networks. Little is known about the microstructural integrity of the fiber bundles that interconnect them. Here, we have investigated intracerebral fiber bundles using tract-based spatial statistics (TBSS) analysis of diffusion tensor imaging (DTI) data.

Methods: We enrolled 19 episodic migraineurs (EM) between attacks, 18 chronic migraineurs (CM) without overuse of symptomatic drugs and 18 healthy subjects (HS). All subjects underwent diffusion tensor imaging (DTI) scans using 3T MRI. We calculate diffusion metrics, including fractional anisotropy (FA), axial (AD), radial diffusion (RD) and mean diffusion (MD).

Results: TBSS showed no significant differences between EM patients and HC for FA, MD, RD and AD maps. In comparison to HS, CM exhibited widespread increased

RD (bilateral superior [SCR], anterior [ACR] and posterior corona radiata [PCR], right splenium of corpus callosum [SCC]; bilateral genu of CC, right anterior and posterior limb of internal capsule [IC], bilateral retrolenticular part of IC, bilateral external capsule, bilateral posterior thalamic radiation [PTR], bilateral sagittal stratum, bilateral fornix [cres]/stria terminalis) and MD values (left SCR and PCR, left superior LF, left splenium of CC). In comparison to EM, CM patients showed decreased FA (bilateral SCR and PCR, bilateral body of CC, bilateral superior LF, bilateral PTR, left sagittal stratum, bilateral retrolenticular part of IC) and increased MD values (bilateral SCR and PCR, bilateral body of CC, left superior LF, bilateral splenium of CC, left posterior limb of IC).

Conclusion: Our results provide evidence for microstructural alterations in brain white matter fiber bundles in CM patients that could be the underlining cause of the abnormalities previously observed in large-scale organization of the resting-state cortical functional networks.

Disclosure of Interest: None Declared.

IHC-PO-107

Pupil cycle time distinguishes migraineurs from subjects without headache

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Objective: Migraine is a neurological disorder characterized by paroxysms of head pain accompanied by trigemino-vascular system activation and autonomic dysfunction. Diagnosis is currently based on clinical diagnostic criteria. Though physiological differences exist between migraineurs and non-headache controls, true physiological biomarkers have been elusive, especially for the full clinical spectrum of migraine, inclusive of chronic, episodic, and probable migraine.

Methods: We recruited 98 participants aged 15–75 years into age/sex matched migraine and control groups. Assessments: edge-light pupil cycle time (PCT) and clinical characterization, including headache severity/frequency and associated symptoms (including craniofacial autonomic symptoms; CAS). For PCT, subjects were comfortably seated at a slit lamp; a horizontally oriented beam of light was positioned below the inferior pupillary margin, creating a cycle of constriction/dilation. 100 cycles were counted for each subject; cycle time reported in milliseconds/cycle (msec/cycle). Kruskal-Wallis was utilized for across group comparisons, and Wilcoxon rank sum test was used for post-hoc pair-wise comparisons. Results were considered significant for p -values ≤ 0.05 , except where Bonferroni was applied. Statistical analyses were performed with R for Windows (Version 3.5.1; R Core

Team, Vienna, Austria) and JMP version 14.2.0 (2019, Windows).

Results: We found significantly increased PCT in probable (PM), episodic (EM), and chronic migraine (CM), compared to controls. Increased PCT correlated with number of craniofacial autonomic symptoms. One or more headache-associated CAS were reported in 29 of 73 (40%) of headache subjects overall; of these, CAS were most commonly reported in CM (48%), followed by EM (40%) and PM (36%). Pupil cycle time significantly correlated with number of CAS in the Migraine-All group (Spearman rho 0.40, $p = 0.04$).

Conclusion: Our findings link pupillary circuit dysfunction in migraine to peripheral trigeminal sensitization. The sensitivity of PCT, especially for all severities of disease, distinguishes it from other physiological phenotypes, which may make it useful as a potential biomarker.

Disclosure of Interest: None Declared.

IHC-PO-108

Triptan Intake Normalizes Altered C-tactile Habituation In Migraineurs

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Objective: Migraine is characterized by sensory hypersensitivity and habituation deficits. Slow brushing over the skin activates c-tactile (CT) nerve fibres which mediate pleasant touch and analgesic effects in healthy subjects. Habituation to repeated CT stimulation is altered in migraineurs, possibly due to neuronal sensitization. As there is evidence for CGRP mediating such sensitization, we aimed to investigate a potential influence of triptan intake on CT habituation.

Methods: We applied 60 CT optimal brush stroking stimuli (3 cm^{-3}) on both the dorsal forearm (body reference area) and the trigeminally innervated cheek of 52 interictal migraineurs and 52 age and gender matched healthy controls. Half of the migraineurs used triptans during migraine attacks (Sumatriptan, Zolmitriptan, 5.58 3.79 days per month) whereas the other half did not use triptans (NSAID, 3.61 2.10 days per month). The participants rated each stimulus on an 11-point visual analogue scale by intensity, pleasantness and painfulness.

Results: Triptan users behaved like controls, showing stable pleasantness ratings in both test areas ($P = 0.43$). Non-triptan users exhibited decreasing pleasantness ratings in the trigeminal area ($P = 0.026$) and stable ratings in the reference area ($P = 0.089$). The frequency of triptan intake had a significant effect on pleasantness perception

in both the reference area ($F(8, 3.1) = 45.5$, $P = 0.001$) and trigeminal area ($F(8, 4) = 26.3$, $P = 0.006$), with frequent triptan intake resulting in stable rating patterns and no or little triptan intake leading to decreasing pleasantness ratings.

Conclusion: Triptan intake has a significant influence on the trigeminal CT habituation in migraineurs and seems to normalize the altered habituation patterns. Knowing that 5-HT receptor activation contributes to the development and maintenance of neuronal sensitization, our findings point to CGRP as a driver of the abnormal information processing. A possible link between CGRP blockage and improved CT function should be subject of future research.

Disclosure of Interest: None Declared.

IHC-PO-109

Shared and distinct patterns of structural network alterations in migraine, insomnia, and their comorbidity

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Objective: Migraine and insomnia are often comorbid; however, the commonalities and differences in neural mechanisms between them are unclear, and the brain structures associated with this comorbidity are unknown. We aimed to identify patterns of neuroanatomical substrate alteration responsible for the comorbidity between migraine and insomnia.

Methods: High-resolution T1-weighted images were acquired from 116 subjects: 40, 22, and 27 subjects with migraine, insomnia, and comorbid migraine and insomnia, respectively, and 27 healthy controls. Direct group comparisons with healthy controls followed by conjunction analysis were used to identify regions of shared gray matter volume (GMV) alterations between the two disorders. To further identify network changes, seed-based structural covariance network (SCN) analysis was applied to the shared GMV change regions. Conjunction analysis also identified the common SCN alteration in disease groups. Additional correlation analyses were performed to identify associations between neuroanatomical comorbid substrates and clinical profiles.

Results: Compared to healthy controls, migraine and insomnia patients showed GMV changes in the cerebellum, lingular, precentral, and postcentral gyri (PCG). Bilateral

PCG were common GMV alteration sites in both groups. Further conjunction showed the SCN of right PCG alterations common to both groups located in the cerebellum. Specifically, the shared regional GMV and global SCN changes were consistently found in patients with comorbid migraine and insomnia, relative to controls. The GMV of the right PCG was also correlated with sleep quality in comorbid migraine and insomnia patients.

Conclusion: Migraine and insomnia have shared and distinct neuroanatomical alteration patterns, with a specific role of right PCG. These findings may correlate with a shared pathophysiology and enable development of neuroimaging-driven biomarkers for these disorders.

Disclosure of Interest: None Declared.

IHC-PO-110

Migraine type-dependent patterns of brain activation after facial and intranasal trigeminal stimulation

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Objective: In migraine, the trigeminal nerve is involved in pathophysiology of the disease. Previous research points towards an abnormal temporal processing of external stimuli and dysfunctional sequential recruitment of neuronal networks involved in pain-processing. We hypothesized that alterations in the sensory trigeminal activation in migraine might be detected by EEG recordings based on a sufficient temporal and spatial resolution. Aim of the study was to investigate differences in the processing of trigeminal stimuli between interictal migraine patients and healthy subjects.

Methods: Differences in trigeminal pain processing were recorded using event-related potential (ERPs) obtained at 128 channels allowing spatial information on the electrical sources located inside the cortices. Each 17 patients with episodic migraine (PM) without aura, with episodic migraine with aura (PMA) and 17 healthy subjects (N) participated in the study. EEG with 128 channels was recorded whilst the first branch of the trigeminal nerve was stimulated using intranasal chemical (CO₂), cutaneous electrical, and cutaneous mechanical (air puff) stimuli.

Results: Spatial properties of EEG sources in healthy controls were initially distributed in the bilateral frontal and prefrontal cortex, primary and secondary somatosensory cortex, motor and premotor cortex and cerebellum. PMA patients presented with activities in more brain areas under CO₂ and electrical stimulation compared with PM and N group. In PMA the activity had a broad extension

from uncus towards amygdala. The puff condition elicited more cortical activity in the PMA group with a strong activity inside the left amygdala, hippocampus and parahippocampal gyrus.

Conclusion: The results of this study suggest that the activity pattern in PMA is similar to the recognized pain matrix, a complex interplay of sensory, affective and cognitive features. The study provides evidence for a primary involvement of amygdala and hippocampus in the modulation of pain in migraine with aura.

Disclosure of Interest: None Declared.

IHC-PO-111

Reduced cerebrovascular reactivity is a determinant of deep white matter hyperintensities in migraine: a BOLD MRI study with the prospective CO₂ targeting method

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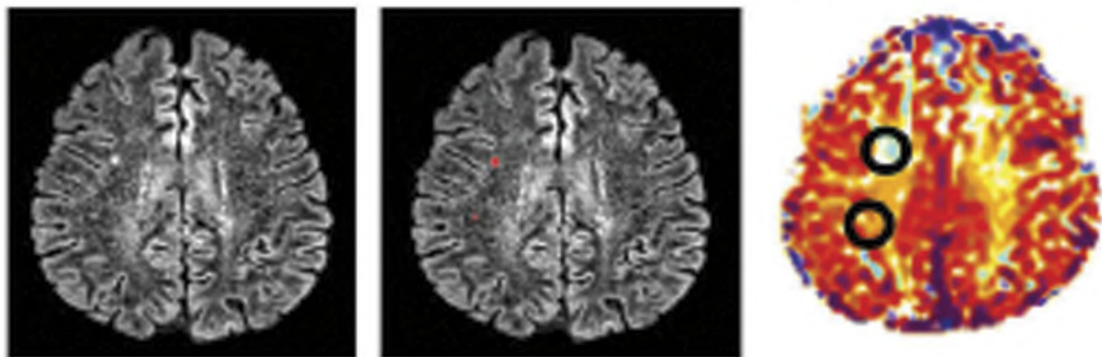
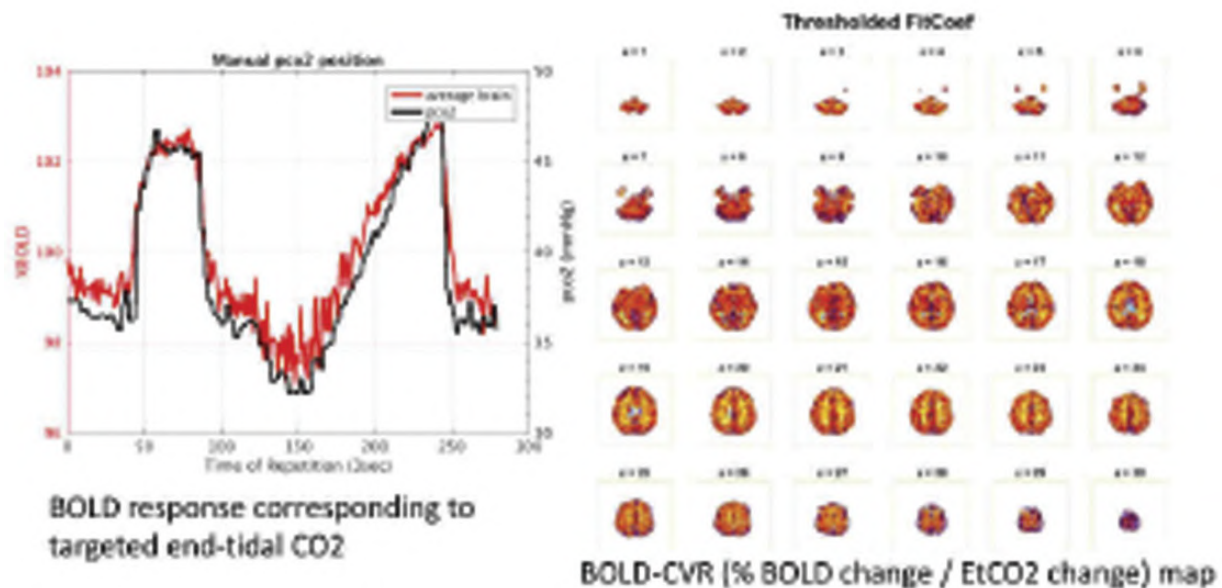
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Objective: To quantitatively measure the cerebrovascular reactivity (CVR) and its effect on the deep white matter hyperintensity (WMH) in patients with migraine.

Methods: Non-elderly patients with episodic migraine without vascular risk factors and age-sex-matched headache-free controls underwent 3-T FLAIR and Blood Oxygen Level-Dependent (BOLD) MR imaging with prospective CO₂ targeting. Deep WMHs were quantified using an automated segmentation method specifically developed for this purpose. The CVR was measured by tracing changes of BOLD signal plotted to subjects' end-tidal CO₂ which was controlled by using a prospective end-tidal CO₂ targeting device. The BOLD CVR of WMH and normal-appearing white matter (NAWM) was compared respectively between patients and controls. The logistic regression was performed to test both the independent and synergistic effect of migraine and CVR on the probability of having WMH in each voxel.

Results: Each group (patient vs control) comprised 37 (25 female and 12 male) participants with a mean age of 34 years (range 19–48). The patient group had a higher number of deep WMHs compared to the control group ($p = 0.039$). Compared to controls, CVR was reduced in



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patients in WMH regions (0.96 ± 1.929 vs. 1.54 ± 2.764 , $p < 0.001$) and to a lesser degree in NAWM regions (2.81 ± 11.096 vs. 3.00 ± 12.201 , $p < 0.001$). Both CVR and migraine were associated with increased probability of WMH in a given voxel (OR = 0.99, 95% CI = 0.99–0.99, $p < 0.001$ for CVR; OR = 5.09, 95% CI = 4.91–5.27, $p < 0.001$ for migraine). Migraine and CVR had a synergistic effect on probability of having WMH (p for interaction < 0.001).

Conclusion: Migraine is associated with increased number of deep WMHs and reduced CVR in both WMHs and NAWM compared to normal controls. CVR and migraine independently and synergistically increased

the probability of having WMH in a given voxel. CVR may be a key determinant of deep WMH in migraine.

Disclosure of Interests: This study was supported by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (Nos. 2017R1A2B2009086 and 2017R1A2B4007254).

IHC-PO-112**Preliminary research on the relationship between cranial autonomic symptoms and central sensitization in migraine patients using the central sensitization inventory**

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Objective: In the previous study we investigated 373 consecutive migraine cases, and Cranial autonomic symptoms (CASs) were reported in 158 cases (42.4%). Compared to migraine cases without CASs, those with CASs had a higher rate of phonophobia, osmophobia, and allodynia, suggesting that central sensitization (CS) may be involved in the mechanism underlying CASs in migraine cases. We therefore investigated the relationship between CASs and CS in migraine patients using the central sensitization inventory (CSI).

Methods: We investigated migraine patients visiting Tominaga Hospital Headache Center from July 2018 to February 2019 using the validated Japanese version of the CSI. CS was evaluated based on the responses to 20 questions in the inventory, with each response rated on a scale of 0 to 5 to give a potential total score of 0–100.

Results: We collected 102 migraine patients (30 with EM and 72 with CM). Medication overuse headache (MOH) was observed in 41 CM patients. The average age was 41.1 years, and the female/male ratio was 78/24. The average CSI score was 34.7. There was no statistically significant difference between CM and EM patients (35.9 vs. 31.8, $p=0.173$), and with MOH and without MOH patients (36.2 vs. 33.7, $p=0.355$). We also investigated the 86 patients with available data on the presence of CASs, and CASs were reported in 39 (45.3%). The average CSI score was 39.9 in the CAS+ patients, which was significantly higher than the score of 29.8 in CAS- patients ($p=0.0005$).

Conclusion: In the present study, the CSI scores were significantly higher in CAS+ patients than in CAS- patients, suggesting that central sensitization may play a role in migraine with CASs. This work was supported by Grants-in the Explanation of a Role of the Central Sensitization in the Refractory Disease Patients with Various Type of Symptoms and an Improvement of the Patients Care to Follow it, Research on Policy Planning and Evaluation for Rate and Intractable Diseases, Health,

Labor and Welfare Sciences Research Grants, the Ministry of Health, Labor and Welfare, Japan.

Disclosure of Interest: None Declared.

IHC-PO-113**The relation between migraine clinical characteristics and white matter hyperintensities in brain magnetic resonance imaging**

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Objective: White matter hyperintensities (WMHs) in brain magnetic resonance imaging (MRI) were often found in migraine patients. The aim of study was to detect the relationship between migraine patients and WMHs in brain MRI, assess their prevalence and its correlation with migraine severity and duration.

Methods: 165 patients with migraine aged from 18 to 50 years were included. All patients were admitted to the headache center of department of neurology at the second hospital of Jilin University between January 2017 and June 2017. Brain MRI, laboratory investigation and 6-month functional outcomes were done for all patients. WMHs in the deep and subcortical white matter were classified as follows: absent (grade 0), only punctate foci (grade 1), early confluent lesions (grade 2) or confluent lesions (grade 3). Migraine severity was assessed by visual analogur scale(VAS) and number of attacks per month.

Results: WMHs were highly more frequent in grade 3severity than grades 1 and 2 in VAS($p < 0.05$). WMHs increased significantly with increase of pain intensity and nausea, disability, tolerability during attack. Treatment efficiency showed statistically significant difference in increase number of WMHs.

Conclusion: WMHs are present in 45.2% of migraine patients. Migraine severity and duration may partly increase the risk of WMHs. Migraine are considered a risk factor for development of WMHs.

Disclosure of Interest: None Declared.

IHC-PO-114

Grey matter volume changes in medication-overuse headache before and after medication withdrawal

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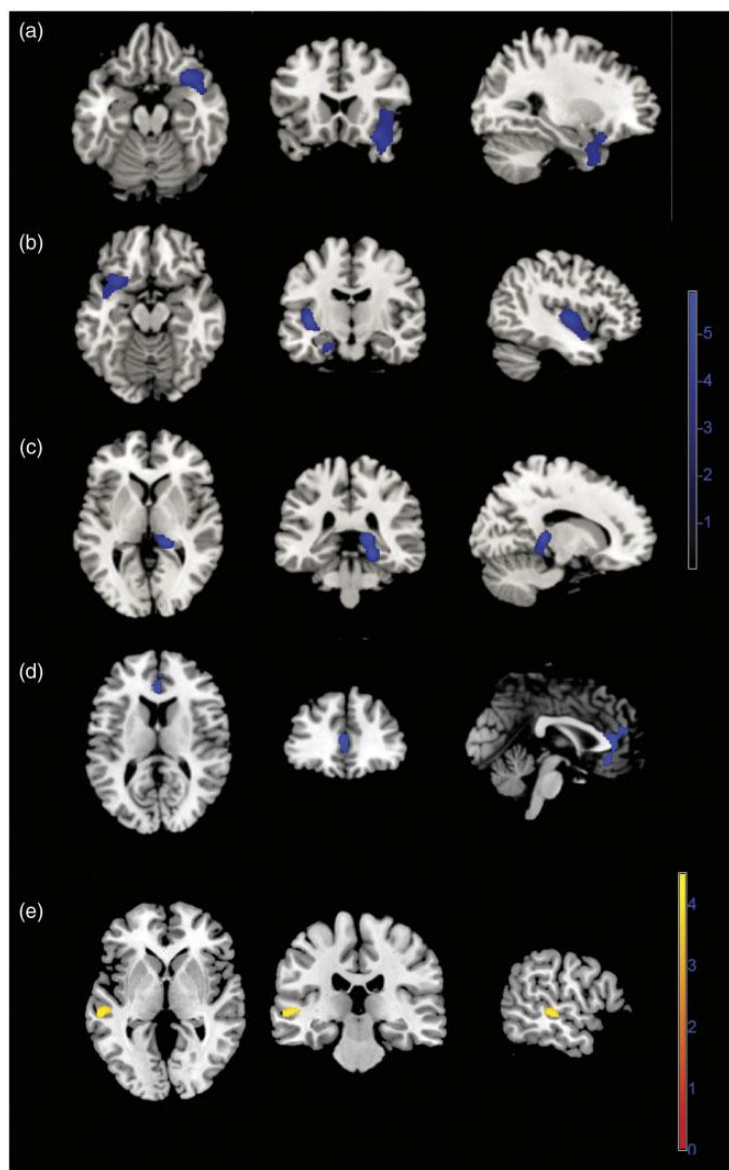
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Objective: The objective of this article is to investigate neurological substrates associated with medication overuse headache (MOH) in patients with chronic tension

type headache (CTTH) before and after medication withdrawal.

Methods: We recruited age- and sex-matched CTTH patients with MOH, and healthy controls (HCs). Magnetic resonance T1-weighted images were processed by voxel-based morphometry in MOH patients before medication withdrawal (n = 23), MOH patients who withdraw the medication successfully after one month of routine treatment (n = 11) and HCs (n = 23). SPM8 was used to analyze voxel-based morphometry. The findings were correlated with clinical variables and treatment responses.

Results: Patients with MOH compared to HCs showed gray matter volume (GMV) decrease in the right inferior temporal cortex, left insula, right parahippocampal cortex/Thalamus and bilateral anterior cingulum as well as GMV



Abstract number: IHC-PO-114

Abstract number: IHC-PO-114 Regions of gray matter volume change in chronic tension type headache with medication overuse headache and healthy controls.

	Region	Hemi	Voxel	Peak voxel MNI coordinates			T value
				X	Y	Z	
A	Temporal_Inf	R	6174	40.5	-1.5	-45	-5.88
B	Insula	L	3964	-28.5	4.5	-30	-5.41
C	ParaHippocampal/Thalamus	R	1267	21	-34.5	-9	-5.72
D	Cingulum_Ant	L/R	536	-1.5	37.5	7.5	-4.16
E	Temporal_Mid	L	187	-58.5	-25.5	-1.5	4.49

increase in the left temporal cortex (As were shown in table and Regions of gray matter volume change in chronic tension type headache with medication overuse headache and healthy controls. A right inferior temporal cortex; B left insula; C right parahippocampal cortex/ Thalamus; D bilateral anterior cingulum; E left temporal cortex). Significantly, we found the decreased and increased GMV of these regions tended to be normal in patients with MOH after medication withdrawal comparing with the MOH patients before withdrawal and HCs, especially in the right inferior temporal cortex.

Conclusion: Our study showed GMV changes in MOH patients before and after medication withdrawal. Abnormalities in this regions in MOH patients may contribute to explaining variance of the analgesics use frequency. These regions may tend to be normal after the medication withdrawal.

Disclosure of Interest: None Declared.

IHC-PO-115

Temporal changes of cerebrovascular reactivity in migraine: a longitudinal observation study

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Objective: Migraine is associated with reduced cerebrovascular reactivity (CVR) especially in the posterior circulation. We aimed to investigate temporal changes of CVR in accordance with the clinical course of migraine.

Methods: We recruited non-elderly (aged 18–50 years) patients with episodic migraine without vascular risk factors. Transcranial Doppler with breath-holding maneuver was used to measure CVR in bilateral middle cerebral arteries, bilateral posterior cerebral arteries, and the basilar artery. Patients were followed up after three months with prospective headache diaries and repeated CVR measurement. We analyzed the correlation between the

change of CVR (Δ CVR) and the change of headache days (Δ headache days).

Results: A total of 77 patients completed the study protocol. The Δ CVR of the basilar artery showed a significant correlation with Δ headache days (Spearman's $\rho = -0.305$, $p = 0.013$), while no correlation between Δ CVR and Δ headache days was found in the MCAs and PCAs. No other factors were associated with Δ CVR of the basilar artery. Multivariable analysis showed the independent effect of Δ headache days on Δ CVR of the basilar artery.

Conclusion: Changes in headache frequency are accompanied with the changes of CVR in the basilar artery: the CVR in the basilar artery increases in association with clinical improvement while worsening headache frequency is accompanied with CVR reduction. The CVR of the basilar artery may change according to the disease severity, suggesting its role as a surrogate marker of disease course. In contrast, CVRs of the middle and posterior cerebral arteries are unaffected by the short-term disease course.

Disclosure of Interests: This study was supported by DongA ST.

IHC-PO-116

Cerebrovascular reactivity as a predictor of triptan efficacy in migraine

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Objective: In migraineurs, decreased cerebrovascular reactivity (CVR) has been reported as one of the pathophysiology. Triptan is used for migraine-specific treatment, although the mechanism of action has never been entirely defined. Recent studies have reported that triptan has effect on the endothelial function. In this study, we investigated the association between CVR and efficacy of triptan treatment in patients with migraine.

Methods: We analyzed patients with migraine using the prospective first-visit headache registry of the Samsung Medical Center headache clinic from January 2015 to May 2018. Patients were followed up after one month after screening. We prescribed triptans for acute treatment and evaluated the efficacy of acute treatment with the migraine assessment of current therapy (Migraine-ACT) questionnaire. Excellent efficacy was defined as Migraine-ACT score of 4. For assessment of CVR, the interictal transcranial Doppler with the breath-holding method was done in all patients. We measured mean breath-holding index (BHI) of the bilateral middle cerebral arteries (MCA-BHI) and posterior cerebral arteries (PCA-BHI), and the basilar artery (BA-BHI). Univariable and multivariable logistic regression analyses were performed to evaluate the BHI and other factors associated with efficacy of triptan treatment.

Results: A total of 115 patients were included in the analysis. Sixty patients (52.2%) had excellent efficacy of triptan. Median MCA-BHI (1.1, IQR = 0.9–1.4, vs. 1.1 IQR = 0.8–1.3), median PCA-BHI (1.1, IQR = 0.8–1.4 vs. 1.1, IQR = 0.8–1.4), median BA-BHI (1.0, IQR = 0.7–1.4 vs. 0.9, IQR = 0.6–1.1) were shown in excellent efficacy group and non-excellent efficacy group, respectively. BA-BHI was independently associated with the efficacy of triptan treatment (multivariable OR = 3.868, 95% CI = 1.13–8.84, $p = 0.039$, adjusted for age, sex, total headache days, caffeine dose per day, allodynia, use of prophylactic medication, use of non-steroidal anti-inflammatory drugs).

Conclusion: In migraine, increased CVR in basilar artery was associated with better efficacy of triptan treatment. The effect of triptan may be dependent on the state of endothelial function. Further confirmatory studies are needed to prove the relationships.

Disclosure of Interests: This study was supported by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (Nos. 2017R1A2B2009086 and 2017R1A2B4007254).

IHC-PO-341

Blood glucose levels increase during spontaneous attacks of migraine with and without aura

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Objective: Alterations in glucose metabolism have been proposed in migraine patients but changes in glucose levels

have never been studied during spontaneous migraine attacks. We investigated plasma glucose changes during spontaneous attacks in migraine patients with and without aura, and correlated blood glucose changes to perceived pain intensity and time since attack onset.

Methods: Blood samples were drawn from 31 patients during and outside of migraine attacks. Differences in plasma glucose levels between attack and baseline states were assessed by paired t-tests. Possible effects of pain intensity, time from onset of migraine or presence of aura symptoms were further assessed by linear regressions between change in glucose levels and the possible dependencies.

Results: A total of 31 patients (13 with aura and 18 without aura) were included in the study (24 F and 6 M). On attack days, the mean time from attack onset to blood sampling was 7.6 hours. Mean pain at the time of investigation was 6 on a 0–10 verbal rating scale. Plasma glucose levels were significantly higher in the ictal phase compared to the interictal phase (mean increase = 0.57 mmol/L, 95% CI = [0.25; 0.89], $p = 0.0010$). The increase was significantly ($p = 0.029$) smaller with time from onset of migraine (–0.080 mmol/L/hour from onset of attack). The attack-related increase in blood glucose was not affected by pain intensity ($p = 0.50$) or from presence of aura symptoms ($p = 0.19$).

Conclusion: We demonstrated higher plasma glucose values during spontaneous attacks of migraine, independent of the presence of aura symptoms and not related to pain intensity, peaking in the early phase of attacks. Additional studies are necessary to confirm our findings and to explore the possible underlying mechanisms.

Disclosure of Interests: Dr Anders Hougaard (AH) has received personal fees and/or honoraria for lecturing from Allergan, Teva and Novartis. AH is a member of advisory board for BalancAir. Dr Faisal Mohammad Amin (FMA) has received personal fees and/or honoraria for lecturing from Teva, Eli Lilly and Novartis. FMA is principal investigator for a Novartis Phase IV trial and member of advisory boards for Eli Lilly and Novartis. Prof. Dr Messoud Ashina (MA) is a consultant or scientific advisor for Allergan, Amgen, Alder, Eli Lilly, Novartis and Teva, principal investigator for Amgen 20120178 (Phase II), 20120295 (Phase II), 20130255 (Open label extension), 20120297 (Phase III), 20150308 (Phase II), ElectroCore GM-11 gamma-Core-R, TEVA TV48125-CNS- 30068 (Phase III), Novartis CAMG334A2301 (Phase III) and Alder PROMISE-2 (Phase III). MA has no ownership interest and does not hold stock in any pharmaceutical company. MA serves as associated editor of Cephalalgia and co-editor of the Journal of Headache and Pain.

IHC-PO-342

White Matter Alterations in Chronic Migraine: A Diffusion Tensor Imaging and Structural Connectivity Study

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Objective: White matter alterations have been observed in patients with migraine. However, no microstructural white matter alterations have been found particularly in Episodic Migraine (EM) with respect to Chronic Migraine (CM) patients. In this study, we investigated whether there are significant differences between EM and CM, and between these groups and healthy controls, using diffusion Magnetic Resonance Imaging (dMRI) data.

Methods: We acquired high-resolution 3D brain T1-weighted and dMRI from 51 Healthy Controls (HC), 55 EM patients and 57 CM patients. Using Tract-Based Spatial Statistics, we compared Fractional Anisotropy (FA), Mean Diffusivity (MD), Radial Diffusivity (RD) and Axial Diffusivity (AD) between the different groups. We also obtained structural connectome matrices for each subject employing both dMRI and T1-weighted acquisitions. Number of streamlines, mean FA and mean AD for each white matter connection were compared between the three groups.

Results: Significant decreased AD ($p < .05$ Family Wise Error corrected and volume $>30 \text{ mm}^3$) were found in CM compared to EM in 38 white matter regions. Significant differences in the number of streamlines were found in 18 connections from the connectome when comparing migraine patients with healthy controls ($p < .05$ False Discovery Rate corrected); significant differences were also found between CM and EM in one of these connections. Furthermore, significant differences in FA and AD were found in three and four connections from the connectome respectively ($p < .05$ False Discovery Rate corrected); significant differences were also found between CM and EM in two of AD connections.

Conclusion: Our findings suggest global white matter structural differences between EM and CM, and structural connectivity alterations in migraine patients with respect to healthy controls, and in CM compared to EM.

Disclosure of Interest: None Declared.

IHC-PO-343

Sensorimotor Integrity is Impaired During Migraine Attacks

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Objective: Migraine is associated with disrupted processing of sensorial information. We hypothesized that sensorimotor integration might also be impaired during a migraine attack. We aimed to evaluate sensorimotor integration by using short latency afferent inhibition paradigm in migraine.

Methods: Twenty-five migraine without aura patients (Ten interictal, five preictal, ten ictal) and sixteen healthy controls were included in the study. Short latency afferent inhibition was elicited by the electrical stimulation of the right median nerve 21 ms prior to the left motor cortical magnetic stimulation. Motor evoked potentials were recorded from right abductor pollicis muscle. Mean motor evoked potential amplitude ratio after single and conditioned stimuli, was calculated as short latency afferent inhibition.

Results: Mean motor evoked potential inhibition ratios after single and conditioned stimuli in migraine without aura patients during the interictal period were comparable to those of healthy controls ($44.5\% \pm 14.75\%$ vs $45.1\% \pm 20.3\%$ [$p = 0.93$]). However short latency afferent inhibition was significantly reduced in migraine without aura patients during preictal ($-14.6\% \pm 42.8\%$ [$p = 0.002$]) and ictal ($-7.4\% \pm 31.1\%$ [$p = 0.0001$]) periods compared to healthy controls.

Conclusion: Pronounced decrease in short latency afferent inhibition during migraine without aura attacks indicating a corticocortical disinhibition between somatosensory and motor cortices, was shown for the first time. Decrease in short latency afferent inhibition during preictal period suggest the presence of increased excitability state with facilitation of motor responses instead of an inhibition several hours prior to headache onset. Considering the association between short latency afferent inhibition, sensorimotor integration, cognitive functions and cholinergic system, reduced short latency afferent inhibition phenomenon could be associated with cortical hyperresponsivity to sensory stimuli and cognitive disturbances accompanying migraine attacks.

Disclosure of Interest: None Declared.

IHC-PO-344**Changes in periventricular white matter microstructure in headache sufferers with idiopathic intracranial hypertension**

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Objective: To evaluate whether increased cerebrospinal fluid (CSF) pressure causes alteration of periventricular white matter (WM) microstructure in patients with idiopathic intracranial hypertension (IIH).

Methods: In a prospective study, patients with refractory chronic headache with and without IIH performed a neuroimaging study including 3T MRI, 3D Phase Contrast MR venography and diffusion tensor imaging (DTI) of the brain. Whole-brain voxel-wise comparisons of DTI abnormalities of WM were performed using tract-based spatial statistics. A correlation analysis between DTI indices and CSF opening pressure, highest peak, and mean pressure was also performed in patients with IIH.

Results: We enrolled 62 consecutive patients with refractory chronic headaches. Thirty-five patients with IIH, and 27 patients without increased intracranial pressure. DTI analysis revealed no fractional anisotropy changes, but decreased mean, axial and radial diffusivity in body (IIHMD = 0.80 ± 0.04 , non-IIHMD = 0.84 ± 0.4 , IIHAD = 1.67 ± 0.07 , non-IIHAD = 1.74 ± 0.05 , IIHRD = 0.38 ± 0.04 , non-IIHRD = 0.42 ± 0.05 [$\text{mm}^2/\text{s} \times 10^{-3}$]) of corpus callosum and in right superior corona radiata (IIHMD = 0.75 ± 0.04 , non-IIHMD = 0.79 ± 0.05 , IIHAD = 1.19 ± 0.07 , non-IIHAD = 1.28 ± 0.09 , IIHRD = 0.59 ± 0.03 , non-IIHRD = 0.53 ± 0.03 [$\text{mm}^2/\text{s} \times 10^{-3}$]) of 35 patients with IIH compared with 27 patients without increased intracranial pressure. DTI indices were negatively correlated with high CSF pressures ($p < 0.05$). After medical treatment, 8 patients showed incremented MD in anterior corona radiata left and right and superior corona radiata right.

Conclusion: There is significant DTI alteration in periventricular WM microstructure of patients with IIH suggesting tissue compaction correlated with high CSF pressure. This periventricular WM change may be partially reversible after medical treatment.

Disclosure of Interest: None Declared.

IHC-PO-345**Central sensitization, pain and depressive symptoms in patients with migraine**

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Objective: To investigate the frequency of central sensitization and its correlation with pain and depressive symptoms in patients with migraine.

Methods: A total of 196 patients with migraine (age, 45.4 ± 13.0 years; 39M/157F) and 77 in-hospital controls without headache disorders (age, 66.9 ± 17.6 years; 33M/44F) were included in this study. Migraine was diagnosed by board certified headache specialists according to the International Classification of Headache Disorders 3rd version (ICHD-3). All participants completed Central Sensitization Inventory (CSI) and Brief Pain Inventory (BPI). Patient Health Questionnaire (PHQ)-9 were used to evaluate depression.

Results: Migraine patients showed significantly higher scores of CSI-A and PHQ-9 scores compared with in-hospital controls, but BPI scores did not differ between the groups. Central sensitization (CSI-A score ≥ 40) was observed in 39 migraine patients (40%) and 3 in-hospital controls (3.9%). Migraine patients with central sensitization showed higher scores of PHQ-9 scores and BPI subscores, such as pain severity score and pain interference scores, compared with migraine patients without central sensitization. The CSI-A score positively correlated with BPI pain severity score, BPI pain interference score and PHQ-9 scores in total participants, migraine patients and in-hospital controls.

Conclusion: Our study confirmed a significant correlation between central sensitization, pain and depressive symptoms in patients with migraine.

Disclosure of Interests: This work was supported by Grants-in the Explanation of a Role of the Central Sensitization in the Refractory Disease Patients with Various Type of Symptoms and an Improvement of the Patients Care to Follow it, Research on Policy Planning and Evaluation for Rare and Intractable Diseases, Health, Labour and Welfare Sciences Research Grants, the Ministry of Health, Labour and Welfare, Japan.

IHC-PO-346**Differences between child- and adult patients with migraine in the effect of tinted glasses on pain intensity**

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Objective: We previously reported that blue, red and white ambient lights exacerbated migraine, while green light ameliorated migraine in adult patients. However, in pre-puberty patients, there was no amelioration from green ambient light. In the present study, we investigated the effect of tinted glasses instead of ambient light in pre-puberty and adult patients with migraine during interictal, prodromal or aura, and ictal phases.

Methods: Fourteen pre-puberty patients (Child group: ages 8–13) with migraine (ICHD-3) and fourteen close relative- adult patients (Adult group: ages 17–50) with migraine were studied. We tested four different types of glasses. Three of which were colored gray, light green and dark green, and one transparent as control. The luminous transmittances of the three colored lenses were approximately 40%, but the blocking rate of light stimulation to S-cone was 59% for gray, 86% for light green and 68% for dark green. We studied degree of discomfort and/or pain intensity before and after wearing tinted glasses during interictal, prodromal or aura, and ictal phases. To evaluate the degree of discomfort and pain intensity, patients were asked to choose from six levels for each color before and after wearing the tinted glasses.

Results: In the adult group, green glasses significantly ameliorated both discomfort and pain intensity during

ictal phase. In the child group, there was no significant ameliorating effect from wearing the glasses. On the other hand, the degree of discomfort during all phases and pain intensity during ictal phase were exacerbated after wearing light green glasses (Figure).

Conclusion: The light green lenses used in this study block blue light at a high rate at a wavelength of 400–450 nm, but has a maximum transmittance of around 500–510 nm. Good et al. reported red glasses were effective for child patients with migraine. Red lenses have a minimum transmittance of around 500–510 nm. In addition, red and green are complementary colors. The results of our study are compatible with the results of the previous study.

Between children and adults, wavelengths of light affecting either migraine or main photoreceptors related with migraine might be different.

Disclosure of Interest: None Declared.

IHC-PO-347**Neuroimaging utilization and findings in headache outpatients: Significance of red and yellow flags**

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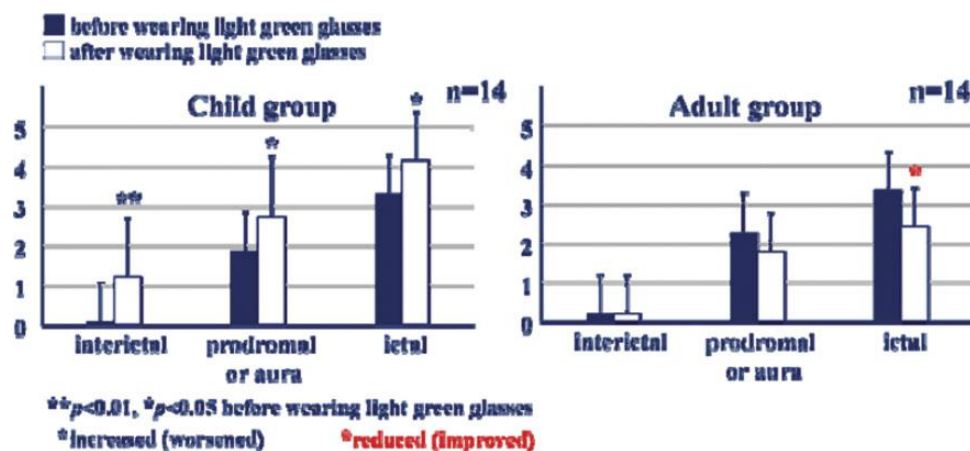
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Objective: Assess the neuroimaging utilization pattern, clinical application of red flags, and concordance with neuroimaging guidelines in a community population of headache patients.

Methods: We conducted a retrospective cross-sectional study of all outpatient community patients at Mayo Clinic



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Rochester who underwent a neuroimaging study for a headache indication in 2015.

Results: We identified 190 outpatients who underwent 304 neuroimaging studies for headache. The median age was 46.5 years (range 18–91 years), 65% were female, and most reported no prior history of headache ($n = 97$, 51%). A minority of patients had prior brain imaging studies ($n = 44$, 23%) and neurological consultations for headache ($n = 29$, 15%). Few studies were ordered after consultation with a neurologist ($n = 14$, 7%). Seventy-seven percent of patients were documented to have a “red flag” justifying the imaging study. Abnormal neuroimaging findings were found in 3.1% of patients with warning flags (5/161); carotid dissection ($n = 3$) and reversible cerebral vasoconstrictive syndrome ($n = 2$). An estimated 35% of patients were imaged against guidelines.

Conclusion: The prevalence of serious causes of headache in a community practice was low despite the presence of a documented red flag symptom. Inadequate understanding or application of red flags may be contributing to recommendations to image patients against current guidelines. Interventions to reduce unnecessary neuroimaging of patients with headache need to be designed and implemented.

Disclosure of Interest: None Declared.

IHC-PO-348

Both headache frequency and time-to-next-headache are dynamically associated with mechanical pain threshold in migraine

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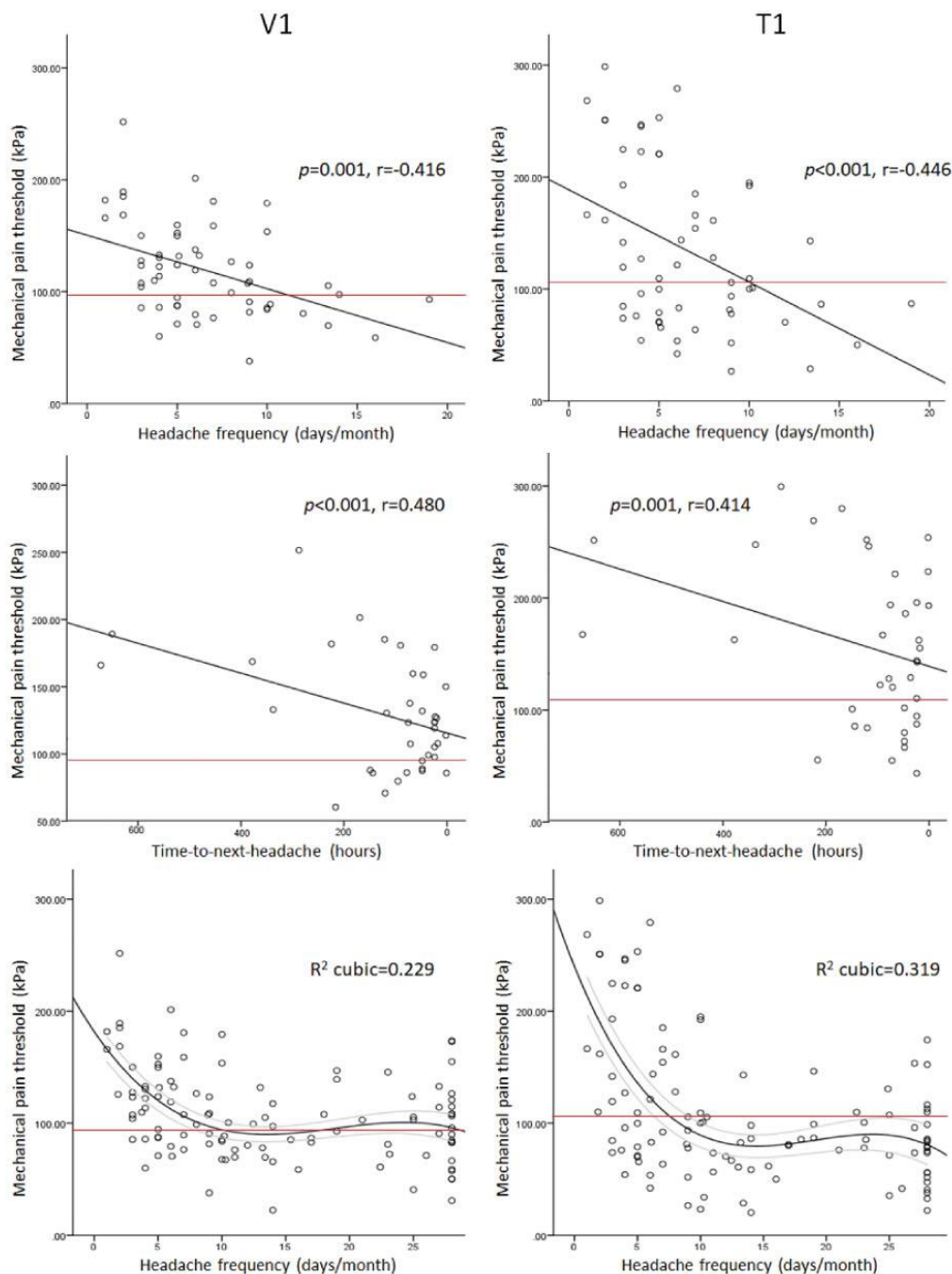
Objective: Clinical correlates of the quantitative sensory testing results are not conclusive in patients with migraine. We hypothesized that both headache frequency (Hfr) and time-to-next-headache might be associated with mechanical pain threshold (MPT).

Methods: Patients with newly diagnosed episodic migraine (EM) or chronic migraine (CM) were recruited from the Headache Clinic of Taipei Veterans General Hospital. Healthy controls (HC) were also recruited for comparison. The clinical profiles were obtained with questionnaires and verified face-to-face by neurologists. MPT was measured by electronic von Frey filament (IITC Life Science Inc., USA.). The supraorbital area (cranial nerve VI dermatome) and the medial side of the forearm (TI dermatome) were tested.

Results: Fifty-seven EM (F/M 44/13, mean age 34.6 yrs), 53 CM (F/M 48/5, mean age 39.5 yrs), and 32 HC (F/M 27/5, mean age 37.8 yrs) completed the study. In CM, there was no significant correlation between MPTs and any clinical profile. However, in EM, both Hfr and time-to-next-headache (table and figure) were correlated with MPTs of the VI and TI dermatomes. Of note, MPTs in EM approached the mean level of HC when Hfr increased or the time-to-next-headache was shorter. Multiple regression analysis showed both factors were independently associated with MPTs in VI and TI and altogether explained 24.5% and 23.4% of the variance. In all migraine patients (EM + CM), MPTs decreased as Hfr increased and plateaued when $Hfr \geq 15$ days/month (figure, variance explained 22.9% and 31.9% respectively).

Conclusion: Our data suggest that both Hfr and time-to-next-headache are independently associated with MPTs in patients with EM. The MPTs show a trend of “normalization” when migraine patients approach ictal stage or become chronified.

Disclosure of Interest: None Declared.



The red lines represent the mean value of mechanical pain threshold in healthy controls. Left panel shows the results of mechanical pain threshold in the 5th cranial nerve V1 dermatome and the right panel, first thoracic (T1) dermatome. The upper panel shows the relationship between the pain threshold and the headache frequency (monthly headache days) in episodic migraine. The middle panel shows the relationship between the pain threshold and the time-to-next-headache (in hours) in episodic migraine. The lower panel shows the relationship between the mechanical pain threshold and headache frequency in episodic and chronic migraine combined.

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Clinical correlates of mechanical pain threshold in patients with episodic migraine.

	Univariate analysis (VI/TI)		Multivariable analysis (VI/TI)	
	r	p	t	p
Headache frequency	-0.42/-0.45	.001/<.001	-2.13/-2.60	.037/.012
Time-to-next-headache	0.48/0.41	<.001/.001	2.74/2.16	.008/.035
Time-from-last-headache	n.s.			
Migraine Disability Assessment	n.s./-0.29	n.s./.029		
Hospital Anxiety and Depression Scale	n.s.			
Age	n.s.			

n.s.: not significant.

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IHC-PO-349

No increase in brain iron content in refractory chronic migraine: a quantitative susceptibility mapping study

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Objective: Iron accumulation in the periaqueductal gray and basal ganglia has been reported in patients with migraine. However, results from previous studies were challenged due to methodological issues. We performed quantitative susceptibility mapping (QSM), a state-of-art MRI technique, to measure iron content in patients with refractory chronic migraine.

Methods: We recruited patients with refractory chronic migraine and age-sex-matched headache-free controls. Using a 3T MR scanner, QSM were obtained from a conventional multi-echo gradient-echo sequence. Caudate nucleus, globus pallidus externa (GPe), globus pallidus interna (GPi), red nucleus, substantia nigra, and periaqueductal gray were manually segmented for each participant. Susceptibility values and R2* values of segmented areas were calculated and compared between groups. Wilcoxon signed-rank test was applied to test the paired group difference.

Results: A total of 10 patients with refractory chronic migraine and 10 age-sex-matched headache-free controls were recruited. Total susceptibility values were not

different between groups in caudate nucleus, GPe, GPi, red nucleus, substantia nigra, and periaqueductal gray. Mean susceptibility values were not different in all segmented regions but GPe, where patients showed decreased values than controls ($p=0.009$). R2* values were also not different between groups.

Conclusion: Using QSM, we found that brain iron content is not increased in patients with refractory chronic migraine. Pathophysiology of chronic migraine may not be associated with iron metabolism or irreversible damage to specific nuclei.

Disclosure of Interests: This study was funded by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (Nos. 2017RIA2B2009086 and 2017RIA2B4007254).

IHC-PO-350

Comparing migraine with- and without aura to healthy controls using RNA-Sequencing

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Objective: Migraine mechanisms are only partly known. Some studies have previously described genes differentially expressed (DE) between blood from migraineurs and controls. The objective of this study was to describe gene expression in subtypes of migraine outside of attack and in healthy controls.

Methods: We extensively phenotyped 17 migraine without aura (MO) and 9 migraine with aura (MA) female patients, and 20 age-matched female controls. Cubital venous blood was RNA-sequenced. Genes DE between migraineurs (MO and MA) and controls, and between MO and MA were identified using a case-control design.

A co-expression network was constructed to investigate the difference between migraineurs and healthy controls at the network level.

Results: We found two DE genes: NMNAT2 and RETN. Both were DE between MA and controls, but they could not be replicated in an independent cohort. Co-expression network analysis resulted in one cluster of highly interconnected genes that was nominally significantly associated with migraine, however, no pathways or gene ontology terms were detected.

Conclusion: We showed no clear distinct difference in gene expression profiles of peripheral blood of migraineurs and controls and were not able to replicate findings from previous studies. A larger sample size may be needed to detect minor differences.

Disclosure of Interest: None Declared.

IHC-PO-351

Electrophysiological Underpinnings of Functional Connectivity in Episodic and Chronic Migraine

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Objective: Preliminary studies have reported electrophysiological differences between episodic and chronic migraine (EM, CM). We aimed to assess differences in brain connectivity to elucidate neural underpinnings in migraine.

Methods: We included 126 subjects: 87 patients (45 EM and 42 CM) and 39 matched control participants. All performed a 10-min resting-state electroencephalographic (EEG) recording using Brain Vision® equipment. Patients were free from migrainous pain on the day of the recording. Once the EEG signals were obtained, functional connectivity between brain regions were estimated using phase-related measures (phase-locking value). Afterwards, graph analysis was performed to summarize the behavior of the brain network into 5 parameters that assessed the segregation, integration, global connectivity, complexity and regularity of the network. For that purpose, clustering coefficient, path length, connectivity strength, Shannon graph complexity and Shannon graph entropy were computed from the functional connectivity brain network. All this procedure was separately carried out for each of the conventional EEG frequency bands. In addition, connectivity parameters were also computed in a particular band of interest (from 23.4 Hz to 29.1 Hz), previously identified in a former study.

Results: No differences were found between EM and CM for the conventional frequency bands in the graph parameters under study. However, the analysis of the band of interest (from 23.4 Hz to 29.1 Hz) showed differences ($p < 0.05$, Mann-Whitney *U*-test) for segregation and global synchronization characteristics. In particular, clustering coefficient as well as the connectivity strength showed significant higher values in CM than in EM.

Conclusion: Our functional connectivity analyses exhibited an increase in segregation and global connectivity in CM as compared with EM. These novel findings could suggest a relationship between migraine chronicity and an increase in hyperexcitability, which would translate into the EEG as a widespread increase in connectivity along with an increase in the overall segregation of the network.

Disclosure of Interest: None Declared.

IHC-PO-352

Lateral inhibitory mechanisms in patients with chronic migraine

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Objective: We had previously detected a reduced percentage of lateral inhibition in the somatosensory cortex of episodic migraineurs during the pain-free period¹. Here, we studied lateral inhibition and habituation/sensitization in the somatosensory cortex of patients evolved from episodic to chronic migraine (CM), and we searched for possible correlations with clinical features.

Methods: We have prospectively enrolled 16 patients with CM and compared them with 17 healthy volunteers (HV). All participants in the study underwent somatosensory evoked potentials (SSEPs) elicited by electrical stimulation of the right median (M) and ulnar (U) nerve at the wrist separately and simultaneously (MU). We measured N20-P25 amplitudes and we calculated the percentage of lateral inhibition by using the formula $100 - (MU / (M + U) * 100)$. We used the responses obtained from the stimulation of the median nerve to calculate the degree of habituation and sensitization.

Results: In patients, the percentage of lateral inhibition was similar to that of HV. Nevertheless, compared to

HV, patients showed a generalized increase in all somatosensory responses and a normal habituation. In patients, the percentage of lateral inhibition correlated positively with the severity of the migraine headache and negatively with the monthly headache days.

Conclusion: At the group level, our data clearly points against the existence of atypical lateral inhibitory mechanisms in CM patients. This normal neurophysiological response, together with the sensitization responses and normal habituation, form a pattern similar to that observed in episodic migraine during an attack. We think that during the process of transformation from episodic to chronic migraine the mechanisms of lateral inhibition physiologically try to counterbalance the increase in the frequency of attacks and their severity, but without success.

Disclosure of Interest: None Declared.

IHC-PO-353

Neuromodulation by electroacupuncture for migraine: An analysis using resting state functional magnetic resonance imaging

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Objective: Acupuncture is used for medication-resistant migraine patients, but the mechanism underlying its effects is unclear. Neuromodulation surgery, such as peripheral nerve field stimulation (PNfS), is also used to treat migraine. However, some complications of PNfS have been reported, and its mechanism also has yet to be clarified. We previously reported on the successful reproduction of the effects of C2 PNfS using electro-acupuncture (EAP-C2-PNfS). In this study, we investigated the mechanism underlying the effects of acupuncture using resting state functional magnetic resonance imaging (rsfMRI).

Methods: A board-accredited headache physician diagnosed headache using the International Classification of Headache Disorders 3rd edition. Eleven patients were diagnosed with migraine (1 man, 10 women; mean age 43.8 ± 15.9 years old) and underwent 3.0-T MRI, including rsfMRI, before and after EAP-C2-PNfS. The acupuncture

needles were subcutaneously inserted into the bilateral occipital scalp to a depth of roughly 15 to 20 mm, and biphasic electrical pulse waves were applied for 15 minutes; this technique was performed once a week for three months. For the imaging analysis, we conducted a region-of-interest (ROI)-to-ROI analysis using the CONN toolbox. We evaluated the numerical rating scale (NRS), Headache Impact Test (HIT-6) and self-rated depression scale (SDS). We also assessed the functional connectivity (FC) in the pain matrix regions (anterior/posterior cingulate cortex [ACC/PCC], insula, postcentral gyrus, thalamus, hypothalamus, amygdala, and brainstem).

Results: The NRS and HIT-6 significantly improved after three months of treatment, while the SDS was not significantly changed. The FC between the PCC and brainstem decreased after the therapy.

Conclusion: Patients who had chronic migraine with a high frequency of attacks showed a higher FC in the pain matrix than those with a low frequency of attacks. In addition, the patients with fibromyalgia showed clinical improvement and a reduced FC by acupuncture. Decreasing the FC through EAP-C2-PNfS may help normalize a sensitized pain matrix.

Disclosure of Interest: None Declared.

IHC-PO-354

Structural brain network characteristics in migraine patients

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Objective: Migraine is a multifactorial neurovascular disorder affecting about 12% of the general population. Migraine is classified into an episodic (EM, headaches occurring <15 days/month) and a chronic form (CM ≥ 15 days/month). Network analysis within the graph-theoretical framework (based on connectivity patterns) provides an approach to observe large-scale structural integrity. We analyse structural MRI images to observe various network measures and their alteration using a whole brain approach.

Methods: 19 healthy controls (HC) (31.7 ± 9.2 years, 10 females (f)), 17 EM patients (32.7 ± 9.9 , 13 f.) and 12 CM patients (38.2 ± 16.2 , 8 f.) were included, according to the

ICHD-3 diagnostic criteria. Participants completed headache diaries, MIDAS and HADS questionnaires. Whole brain T1-weighted images were obtained using 3T MRI. Cortical thickness (CT) was computed using FreeSurfer 5.3.0 and network topology was analysed using graph theory analysis based on connectivity patterns derived from the CT correlation matrix.

Results: CT was found to be significantly ($p < 0.001$, uncorrected) increased in EM in lateral occipital cortex (V3A), supramarginal gyrus, right insula and precuneus in comparison to HC. Similarly, CT was significantly increased in insula and posterior cingulate cortex and decreased in parietal and occipital cortex for CM in comparison to HC. CT was significantly decreased in insula and increased in supramarginal and postcentral gyrus for EM in comparison to CM patients. Higher transitivity, modularity, assortativity, mean node and edge betweenness were observed in migraineurs compared to HC. CM demonstrated higher modularity but lower clustering coefficient and transitivity than EM.

Conclusion: The more transitive and modular network in migraine patients compared to HC is indicative of a more segregated network, suggesting that the relative strength of within-network connections to between-network connections is disturbed in migraineurs. Higher modularity but lower clustering coefficient observed in CM indicative of being more segregated than EM. Higher modularity in CM indicates a disturbed network reorganization reflected as sparse connections across networks in comparison to EM.

Disclosure of Interest: None Declared.

IHC-PO-355

Frontal cortical changes in chronic migraine patients. An exploratory study

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Objective: To identify cortical thickness (CTh) differences in chronic migraine patients.

Methods: Exploratory case control study. Episodic (EM), chronic migraine (CM) and healthy controls (HC) were included. We collected demographic and clinical data.

MR images were acquired in a 3.0T magnet (Trio, Siemens). 3D-T1 weighted images were segmented with FreeSurfer (version 6.2). Mean CTh were obtained for each brain cortical region (ipsilateral to pain side or bilateral) and were compared between groups using linear models adjusted for age and depression. Results were corrected for multiple comparisons (Bonferroni). Independent variables associated with diagnosis were computed using logistic regression analysis.

Results: We included 25 women (10 HC, 8 EM and 7 CM), mean age: 38.1 ± 14.0 years. We did not find significant clinical differences between groups except for depression ($p < 0.05$). We found significantly higher CTh in CM patients compared to HC in 3 frontal areas: caudal middle frontal (HC-2.44mm[mI] ± 0.05 vs. MC-2.57 mm ± 0.05 , $p = 0.02$), rostral middle frontal (HC-2.23 mm ± 0.10 vs. MC-2.36 mm ± 0.07 , $p = 0.04$) and superior frontal areas (HC-2.61 mm ± 0.10 vs. MC-2.74 mm ± 0.09 , $p = 0.03$). Parahippocampal area was thinner in CM (HC-2.97 mm ± 0.21 vs. MC-2.71 mm ± 0.24 , $p = 0.02$). CTh values for EM patients were intermediate between HC and CM, but significant differences were only found for the rostral middle frontal ($p = 0.03$), superior frontal ($p = 0.05$) and fusiform ($p < 0.01$). Caudal middle frontal and rostral middle frontal CTh predicted CM diagnosis in the logistic regression analysis. Caudal middle frontal measurements positively correlate with headache frequency but we did not find any other clinical correlations.

Conclusion: CM patients showed differences on prefrontal cortical structures. These alterations reflect structural changes that may correlate with pain frequency or/and cognitive and emotional processes related to migraine.

Disclosure of Interest: None Declared.

IHC-PO-356

The modulation effect of Qinggan Jieyu Herbal Formula Granule in insula of Salience Network for migraine patients with liver depression of the heat syndrome

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Objective: The objectives of this study were to evaluate the change of the rs-fc in migraineurs with liver depression of the heat syndrome before and after treatment and the relationship between the clinical outcomes and functional connectivity changes.

Methods: This is a randomized, double-blind, placebo-controlled study. 30 MwoA patients will be recruited compared with 30 healthy controls. Diagnosis of MwoA was based on the International Classification of Headache

Disorders, 3rd Edition. Inclusion criteria were as follows: (1) To be diagnosed as MWoA and considered as liver depression of the heat syndrome, (2) Aged between 18–65 years and right-handed, (3) had at least six months of migraine duration, (4) had not taken any prophylactic medicine during the last three months, (5) Written informed consent was provided. Participants will be excluded if they met any of the following criteria: (1) were alcohol or drug abusers, (2) were pregnant or during lactation, (3) suffered from psychiatric, neurologic, cardiovascular, respiratory or renal illnesses, (4) suffered from other chronic pain conditions, (5) had MRI contraindications, and (6) unable to complete headache diary, (7) were allergic to Chinese medicine. Another 30 age- and gender matched right-handed healthy controls will be recruited. Eligible migraineurs will be randomly allocated to treatment group or control group. MRI scans will be applied twice for migraine patients before and after four weeks of treatment and will be only applied at baseline for the healthy controls. The primary outcome measure is the functional connectivity changes of the salience network. The secondary outcomes include frequency of migraine attacks, the intensity of migraine, migraine days, the changes of liver depression of the heat syndrome, Migraine-Specific Quality of Life, Self-Rating Depression Scale, and Self-Rating Anxiety.

Results: Not applicable for this part.

Conclusion: In this study, we will investigate the functional connectivity changes between migraine patients and healthy controls, and the modulation effects of an effective Chinese Qinggan Jieyu herbal formula granule. The results of this trial will reveal the central mechanism of Qinggan Jieyu Herbal Formula Granule in migraine treatment.

Disclosure of Interest: None Declared.

IHC-PO-357

Clinical course of anomalies of cerebral vessels in patients without cephalic syndrome

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Objective: To study and assess the features of the course of the anomaly of cerebral vessels in patients without cephalic syndrome.

Methods: The study involved 50 patients treated in 2nd Clinics of Tashkent Medical Academy between 2015–2017 years. Anomalies of cerebral vessels without cephalic syndrome were examined. Clinical-neurologic, neurological imaging (MSCT with angiography, DS ACS) was performed.

Results: The study showed that 50 (100%) patients with anomalies of cerebral vessels without cephalic syndrome

were examined. Among them, women are 15 (30%), men are 35 (70%). The main complaints of these patients were systemic dizziness in 43 (86%) cases, nausea and vomiting in 9 (18%), and hearing loss was also observed in two patients. It should be noted that 2 (4%) healthy individuals were identified during the recruitment of the control group, without complaints and deviations in the neurological status. In which, in one case, the deformation of the vertebral artery in another of its hypoplasia is disturbed. Thus, these two anomalies of the vertebral arteries were diagnostic findings. In general, in 43 (86%) cases, the combination of deformation of vertebral arteries with its hypoplasia was revealed in 3 patients (6%), only vertebral arteries (VA) deformity, in one cases, one-sided in combination with asymmetry of blood flow in the internal carotid artery (ICA). In the remaining two cases, the tortuosity of both VA and ICA was observed. At one patient with the diagnosis chronic leptomeningitis of fossae cranii posteriori (FCP), hypoplasia of VA is revealed. It should be noted that in 3 (6%) patients with deformities only ICA, and one-sided, in the absence of headaches, dizziness was noted, which requires subsequent dynamic monitoring and recruitment of patients. Patients with VA anomalies also had different degrees of ICA deformity in 9 (18%) cases in combination with its hypoplasia, without hemodynamically significant disorders of cerebral circulation.

Conclusion: Thus, in the group of patients without cephalic syndrome, but with anomalies of cerebral vessels, hemodynamically significant changes in VA were observed, while pathological tortuosities and underdeveloped ICA, although present, were hemodynamically insignificant in relation to cerebral blood circulation.

Disclosure of Interest: None Declared.

Migraine Acute Therapy

IHC-PO-117

Safety and Tolerability of Ubrogepant Following Intermittent, High-Frequency Dosing

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Objective: To evaluate the safety and tolerability of ubrogepant, focusing on hepatic safety, when administered intermittently with high frequency dosing, to healthy participants.

Methods: Phase 1, multicenter, double-blind, parallel-group trial. Participants randomized 1:1 to placebo or ubrogepant 100 mg. Those on ubrogepant took 100 mg on 2 consecutive days followed by 2 consecutive days of placebo, alternating for 8 weeks. Adults (age 18–50 years) with no significant medical history and normal hepatic function were included. Primary outcome measures were safety and tolerability.

Results: A total of 518 participants were randomized; 516 in the safety population (n = 260 placebo; n = 256 ubrogepant). Participants' mean age was 32 years, 55% female, 68% white, 25% black/African-American, average BMI = 25; population differed from the typical migraine population. Treatment-emergent adverse events (AEs): 45% participants on placebo, 44% ubrogepant; most common was headache (10% placebo; 11% ubrogepant). Treatment-related AEs: 19% placebo, 22% ubrogepant. Serious AEs: 0.4% placebo, 0.8% ubrogepant, none considered treatment-related. Seven cases of ALT/AST $\geq 3 \times$ ULN (5 placebo, 2 ubrogepant) were reported and adjudicated by a panel of independent liver experts blinded to treatment. All but 3 cases were judged unlikely related based on plausible alternative etiologies/confounding factors. Two cases (1 placebo, 1 ubrogepant) were judged possibly related. One case (ubrogepant) was judged probably related. ALT increases $\geq 3 \times$ ULN were not confirmed with repeat testing and resolved with continued dosing. All cases were asymptomatic and no cases with concurrent bilirubin elevation.

Conclusion: Ubrogepant was well tolerated following intermittent, high frequency dosing in healthy participants with no identified safety concerns. Treatment with ubrogepant was not associated with persistent increased ALT/AST compared to placebo, supporting liver safety.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

Author Disclosures:

Peter J. Goadsby reports personal fees from Allergan, and related grants and personal fees from Amgen and Eli-Lilly and Company, and personal fees from Alder Biopharmaceuticals, Autonomic Technologies Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Novartis, Scion, Teva Pharmaceuticals, and Trigemina Inc., and personal fees from MedicoLegal work, Massachusetts Medical Society, Up-to-Date, Oxford University Press, and Wolters Kluwer; and a patent Magnetic stimulation for headache assigned to eNeura without fee.

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employer, Dartmouth-Hitchcock Medical Center, American Headache Society (AHS), receives research grants from Adler, Allergan, Amgen, ATI, Dr. Reddy's, Scion, Teva, and Zosano. He receives a salary as Editor-in-Chief of Headache Currents from AHS and royalties for books published by Springer.

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IHC-PO-118

Efficacy Is Maintained With Long-term Intermittent Use of Ubrogepant for the Acute Treatment of Migraine

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Objective: To analyze the efficacy of intermittent use of the oral CGRP receptor antagonist, ubrogepant, for acute treatment of migraine over 1 year.

Methods: Phase 3, multicenter, randomized, 52-week extension trial of adults with migraine randomized 1:1:1 to usual care, ubrogepant 50 mg, or ubrogepant 100 mg. Participants treated ≤ 8 migraine attacks (of any pain level) every 4 weeks for 1 year. Efficacy of ubrogepant treatment was assessed via pain freedom and pain relief at 2 hours, and use of rescue medication and optional second dose. We calculated the proportion of treated attacks achieving each efficacy endpoint for each participant, then averaged across equally weighted participants.

Results: Of 1254 participants randomized, 808 made up the mITT population. Participants averaged 42 years, mean BMI was 30 kg/m², 90% were female, and 84% were white. A total of 21,454 migraine attacks were treated (31,968

ubrogepant doses). Pain freedom at 2 hours was achieved in an average of 23% of attacks treated with ubrogepant 50 mg and 25% of attacks treated with ubrogepant 100 mg. Pain relief at 2 hours was achieved in 65% of attacks treated with ubrogepant 50 mg and 68% treated with 100 mg. Efficacy was maintained over the 1-year period. An optional second dose of ubrogepant was taken for an average of 36% of attacks treated with ubrogepant 50 mg and 34% of attacks treated with ubrogepant 100 mg. Rescue medication was used for an average of 13% of attacks treated with ubrogepant 50 mg and 12% of attacks treated with 100 mg. Treatment-related adverse events were reported by 42/404 (10%) in the ubrogepant 50 mg group and 43/409 (10%) in the ubrogepant 100 mg group.

Conclusion: In this extension trial, efficacy comparable to the placebo-controlled, blinded phase 3 trials was achieved and maintained for 1 year. Pain freedom was achieved in $\sim 1/4$ and pain relief in $\sim 2/3$ of treated attacks. Ubrogepant 50 mg or 100 mg alone (1 or 2 doses) appeared sufficient for most participants, as shown by the low use of rescue medication. No safety concerns were identified.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

Author Disclosures:

Richard B. Lipton, MD serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS; serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache, 8th Edition (Oxford University Press, 2009), and Informa. He holds stock options in eNeura Therapeutics and Biohaven.

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IHC-PO-119

Orally Administered Atogepant Was Efficacious, Safe, and Tolerable for the Prevention of Migraine: Results From a Phase 2b/3 Study

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Objective: To evaluate the efficacy, safety, and tolerability of atogepant versus placebo in a phase 2b/3 trial for prevention of episodic migraine.

Methods: Multicenter, randomized, double-blind, placebo-controlled, parallel-group trial (NCT02848326). Adults with a history of migraine, with or without aura, and 4–14 migraine days in the 28-day baseline period were randomized 2:1:2:1:2:1 to placebo, atogepant 10 mg QD, 30 mg QD, 30 mg BID, 60 mg QD, or 60 mg BID, respectively, and treated for 12 weeks. Primary efficacy endpoint was change from baseline in mean monthly migraine days. Safety and tolerability were evaluated.

Results: Of 834 subjects randomized, 825 composed the safety population and 795 composed the efficacy population. Mean age was 40.1 years; the majority was white (76.1%), female (86.5%), and had never taken preventive treatment for migraine (71.9%). Mean baseline migraine days were 7.67 (SD = 2.49). Mean change in migraine days across the 12-week treatment period (*P* values versus placebo): placebo (−2.85), atogepant 10 mg QD (−4.00, *P* = 0.0236), 30 mg QD (−3.76, *P* = 0.0390), 30 mg BID (−4.23, *P* = 0.0034), 60 mg QD (−3.55, *P* = 0.0390), 60 mg BID (−4.14, *P* = 0.0031). Treatment-emergent AEs were reported by 480 subjects (58.2%); for 170 (20.6%), the AEs were considered treatment-related. Seven subjects (0.8%) reported serious AEs,

none considered treatment-related. There were 10 cases of treatment-emergent ALT/AST elevations >3x the upper limit of normal, balanced across groups.

Conclusion: All 5 atogepant treatment arms showed statistically significant, clinically relevant differences from placebo in reductions from baseline in mean migraine days. Atogepant was well tolerated, with no treatment-related serious AEs.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

Author Disclosures:

Peter J. Goadsby, MD, PhD, reports personal fees from Allergan, and related grants and personal fees from Amgen and Eli-Lilly and Company, and personal fees from Alder Biopharmaceuticals, Autonomic Technologies Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Novartis, Scion, Teva Pharmaceuticals, and Trigemina Inc., and personal fees from MedicoLegal work, Massachusetts Medical Society, Up-to-Date, Oxford University Press, and Wolters Kluwer; and a patent Magnetic stimulation for headache assigned to eNeura without fee.

David W. Dodick reports: Personal fees: Amgen, Autonomic technologies, Axsome, Aural Analytics, Allergan, Alder, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Neuroliief, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, Oppenheimer. CME fees or Royalty payments Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal meeting management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer; Stock options: Aural analytics, Healint, Theranica, Second Opinon/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Consulting without fee: Aural Analytics, Healint, Second Opinion/Mobile Health, Epien; Board of Directors: Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1-1466:vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis without fee. Professional society fees or reimbursement for travel: American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society. Other: Use agreement through employer: MyndshftJessica Ailani, MD is a speaker for Alder, Amgen, Avanir, Allergan, Eli Lilly and Company, Electrocore, Promius, and Teva. She has served as consultant to or advisory board member of Alder, Amgen, Allergan, Eli Lilly and Company, Electrocore, Impel, Promius, Teva, Miller Communications, and Alpha Sites Consulting. She is also a section editor for Current Pain and Headache.

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IHC-PO-120

Responder Rates to Atogepant in Patients With Episodic Migraine: A Post Hoc Analysis of Results From a Phase 2b/3, Randomized, Double-Blind, Placebo-Controlled Trial

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Objective: To determine the proportion of patients with at least a 25%, 50%, 75%, and 100% reduction in migraine days from baseline following daily dosing of atogepant, a novel oral calcitonin gene-related peptide (CGRP) receptor antagonist in development for the prevention of migraine.

Methods: Multicenter, randomized, double-blind, placebo-controlled, parallel-group trial (NCT02848326). Adults with a history of migraine were randomized 2:1:2:1:2:1 to placebo, atogepant 10 mg QD, 30 mg QD, 30 mg BID, 60 mg QD, or 60 mg BID, respectively, for 12 weeks. The proportion of patients with at least a 25%, 50%, 75%, or 100% response (ie, reduction from baseline in monthly migraine days) was calculated every 4 weeks and over the 12-week treatment period.

Results: Of 834 patients randomized, 795 (95.3%) were included in the efficacy analyses. Mean change from baseline in migraine days across the 12-week treatment period (primary endpoint) was statistically significant for all 5 atogepant treatment arms compared with placebo ($P < 0.05$ for all comparisons; adjusted P values). In an exploratory analysis, proportions of patients with at least a 25% or 75%, or a complete 100%, reduction in mean monthly migraine days across the 12-week treatment period were statistically significantly higher in all atogepant dose groups than placebo ($P < 0.05$; unadjusted P values). Differences from placebo in the 50% responder group

across the 12-week treatment period were statistically significant for the atogepant 30 mg QD, 30 mg BID, and 60 mg BID groups ($P < 0.05$; based on unadjusted P values). The analysis by 4-week intervals revealed significant differences from placebo at weeks 1–4 for all responder groups (25%, 50%, 75%, and 100%) and atogepant dose groups ($P < 0.05$, all doses; based on unadjusted P values).

Conclusion: Across the 12 week treatment period, the mean percentage of patients who achieved at least 25%, 50%, or 75%, or a complete 100%, reduction from baseline in monthly migraine days across all doses of atogepant was 77%, 57%, 34%, and 10%, respectively.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

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David W. Dodick reports: Personal fees: Amgen, Autonomic technologies, Axsome, Aural Analytics, Allergan, Alder, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Neuroliet, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, Oppenheimer. CME fees or Royalty payments Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal meeting management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer; Stock options: Aural analytics, Healint, Theranica, Second Opinon/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Consulting without fee: Aural Analytics, Healint, Second Opinion/Mobile Health, Epien; Board of Directors: Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1–1466.vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis without fee. Professional society fees or reimbursement for travel: American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society. Other: Use agreement through employer: Myndshft.

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and personal fees from MedicoLegal work, Massachusetts Medical Society, Up-to-Date, Oxford University Press, and Wolters Kluwer; and a patent Magnetic stimulation for headache assigned to eNeura without fee.

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IHC-PO-121

Unmet Treatment Needs of People With Migraine: Results of the CaMEO Study

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Objective: To evaluate the unmet acute treatment needs of people with migraine from the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study.

Methods: Eligible respondents who met migraine ICHD-3 criteria completed the CaMEO Web-based survey and Comorbidities/Endophenotypes survey module. Six unmet treatment need domains were defined and evaluated: (1) lack of current acute treatment optimization (≥ 2 negative responses to the Migraine Treatment Optimization Questionnaire [mTOQ-5] with dichotomous scoring); (2) moderate or severe headache-related disability (Migraine Disability Assessment Scale [MIDAS] score ≥ 11); (3) opioid or barbiturate use ≥ 4 days/month or acute medication overuse (MO; by ICHD-3 definitions); (4) emergency department (ED) or urgent care use for headache within preceding 6 months; (5) self-reported history of cardiovascular (CV) events (indicating possible contraindication [CI] to triptan use); and (6) history of gastrointestinal (GI) condition (indicating possible relative CI to NSAID use).

Results: Data were provided by 12,810 respondents (11,699 episodic migraine [EM]; 1,111 chronic migraine [CM]); 7,936 (62.0%) had ≥ 1 unmet treatment need

Abstract number: IHC-PO-121

n (%)	EM (n = 11,699)	CM (n = 1,111)	Total (N = 12,810)
Moderate or severe headache-related disability	4,021 (34.4)	894 (80.5)*	4,915 (38.4)
Acute treatment not optimized	3,514 (33.1)	627 (58.6)*	4,141 (35.4)
MO or barbiturate/opioid use \geq 4 days/month	1,659 (14.2)	730 (65.7)*	2,389 (18.6)
MO	1,443 (12.3)	710 (63.9)*	2,153 (16.8)
Barbiturate/opioid use \geq 4 days/month	536 (4.6)	199 (17.9)*	735 (5.7)
CV CI	668 (5.7)	123 (11.1)*	791 (6.2)
ED/urgent care for headache	487 (4.2)	124 (11.2)*	611 (4.8)
GI relative CI	1,598 (13.7)	247 (22.2)*	1,845 (14.4)

* $P < 0.001$ for comparison between EM and CM; Chi-square test.

(58.8% of those with EM [6,881/11,699] and 95.0% [1,055/1,111] of those with CM). The **Table** summarizes the percentage of respondents reporting unmet needs. CM had significantly ($P < 0.001$) higher rates of each unmet need than EM.

Conclusion: Unmet needs are apparent for the acute treatment of migraine and greater for CM than EM, underscoring the need for better treatment options.

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Todd J. Schwedt, MD, serves on the Board of Directors for the American Headache Society and the International Headache Society and on the editorial boards for Headache, Cephalalgia, and Pain Medicine. He has received research support from the U.S. Department of Defense, the Patient Centered Outcomes Research Institute, National Institutes of Health, American Migraine Foundation, and the Henry Jackson Foundation. Within the past 12 months, he has served as a consultant or advisory board member for Alder, Allergan, Amgen, Dr. Reddy's, Eli Lilly, Ipsen Bioscience, Novartis, and Teva. He holds stock options in Aural Analytics, Nocira, and Second Opinion.

Kristina M. Fanning, PhD is an employee of Vedanta Research, which has received research funding from Allergan, Amgen, Dr. Reddy's Laboratories, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Novartis, via grants to the National Headache Foundation. Vedanta has received funding directly from Allergan for work on the CaMEO Study.

Michael L Reed, PhD is Managing Director of Vedanta Research, which has received research funding from Allergan, Amgen, Dr. Reddy's Laboratories, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Novartis, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study.

Aubrey Manack Adams, PhD is a full-time employee of Allergan plc and owns stock in the company.

Richard B. Lipton, MD serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS; serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache, 8th Edition (Oxford University Press, 2009), and Informa. He holds stock options in eNeura Therapeutics and Biohaven.

IHC-PO-122**Assessment to Identify Predictors of 2-hour Pain Freedom Among Patients Enrolled in Two Phase 3 Studies of Lasmiditan for Acute Treatment of Migraine**

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Objective: To identify the patient phenotype or the migraine attack characteristics predictive of achieving 2-hour pain freedom following oral lasmiditan for the acute treatment of migraine.

Methods: Integrated analyses were completed from 2 similarly designed Phase 3, double-blind, studies SAMURAI (NCT02439320) and SPARTAN (NCT02605174). Key inclusion criteria: 3 to 8 migraine attacks/month and Migraine Disability Assessment Score (MIDAS) of at least 11 (moderate disability). Patients (N = 3700) were randomized equally to receive lasmiditan (200 mg, 100 mg, 50 mg [SPARTAN only]) or placebo within 4 hours of onset of a migraine attack of at least moderate severity. Logistic regression models were used to identify statistically significant predictors associated with response. P-values were determined from tests of subgroup-by-treatment interaction with terms for study, subgroup (patient phenotype or migraine attack characteristic), treatment, and interaction.

Results: Both studies met the primary endpoint of 2-hour pain freedom for all lasmiditan doses. No patient phenotype was identified that predicted 2-hour pain freedom response to lasmiditan relative to placebo across dose groups, including gender, race (Caucasian vs non-Caucasian), ethnicity (Hispanic vs non-Hispanic), baseline body mass index, number of cardiovascular risk factors, concomitant topiramate or propranolol use, triptan use within prior 3 months, history of aura, migraine duration history, average migraine attacks/month in the 3 months prior to enrollment, and baseline MIDAS. No migraine attack characteristic predicted response including headache pain severity at time of treatment, time to treatment from migraine onset, presence of nausea, and migraine attack-related disability.

Conclusion: Lasmiditan's efficacy (2-hour pain freedom) is not influenced by patient phenotype or migraine characteristic parameters.

Disclosure of Interests: Drs Vargas and Magis are consultants for Eli Lilly and Company. Drs. Doty, Ruff, Vasudev, Krege, Hake are employees and minor stockholders of Eli Lilly and Company.

IHC-PO-123

Real-world Factors Associated with Acute Medication Overuse in Patients with Migraine: Results From the Medical Expenditure Panel Survey (MEPS)

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Objective: Overuse of acute medications to treat migraine attacks often results in higher healthcare costs and greater risk of disease progression. This study aimed to identify factors associated with acute medication overuse (AMO) for patients with migraine.

Methods: Data from the Medical Expenditure Panel Survey-Household Component (2008–2012), a nationally representative survey of noninstitutionalized civilians in the US, were analyzed. Adults ≥ 18 yrs diagnosed with migraine (ICD code: 346.XX) and treated with a prescription medication for migraine were included. AMO was defined as ≥ 5 months (mo) of use of: opioids 8+ days/mo; barbiturates 5+ days/mo; triptans 8+ days/mo or any combination of ergotamine, triptans, analgesics, and/or opioids for 10+ days/mo. All analyses utilized sampling weights of the complex survey design. Logistic regression models with outcome of AMO (yes/no) were constructed controlling for patients demographics, comorbidities, use of migraine preventive medication, and health status to identify statistically significant factors.

Results: The total weighted sample of the treated migraine cohort was 6,418,794 (1,745 unweighted) including 79.8% females with a mean \pm SE age of 39 ± 0.4 yrs; 24.1% met the criteria for AMO vs 75.9% without AMO. Significant factors associated with AMO included increasing age (yrs) (OR [95% CI] = 1.09 [1.01, 1.17], $p = 0.0332$), female gender (1.89 [1.28, 2.79], $p = 0.0015$), insured (2.15 [1.33, 3.47], $p = 0.0019$), lower Short Form-12 Physical Component Score (PCS) (0.98 [0.96, 0.99], $p = 0.0033$), asthma (1.60 [1.02, 2.51], $p = 0.0424$), and use of preventive treatment for migraine (1.86 [1.36, 2.54], $p = 0.0001$).

Conclusion: Findings suggest that below average PCS was a significant factor associated with AMO in patients with migraine. Cumulative or individual comorbidities were not significant factors, with the exception of asthma. When treating patients with migraine, health status and treatment should not be ignored for reduction of AMO.

Disclosure of Interests: Dr. Joshi is a consultant for Eli Lilly and Company.

Wenyu Ye, Janet Ford, David Nelson, and Sheena Aurora are employees of Eli Lilly and Company.

IHC-PO-124

AXS-07 (MoSEIC Meloxicam/Rizatriptan): Novel oral therapeutic in clinical development for the acute treatment of migraine

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Objective: Migraine is the leading cause of neurological disability. Migraine sufferers remain dissatisfied with existing acute treatments citing incomplete pain relief, suboptimal onset of action, and migraine recurrence.

AXS-07 is a novel, oral, investigational medicine, consisting of MoSEIC™ meloxicam and rizatriptan, in Phase 3 for the acute treatment of migraine. Meloxicam is a potent, COX-2 preferential NSAID which is limited by slow absorption. AXS-07 utilizes proprietary MoSEIC™ (Molecular Solubility Enhanced Inclusion Complex) delivery technology to substantially improve solubility and absorption, and maintain durability of action of meloxicam after oral administration. Rizatriptan is a 5-HT_{1B/D} agonist with known efficacy in migraine.

Methods: In a Phase I trial, healthy volunteers were randomized to receive a single dose of AXS-07 or rizatriptan (Maxalt™). Resulting concentrations of meloxicam and rizatriptan were measured and pharmacokinetic parameters were calculated.

AXS-07 is being evaluated in a Phase 3 trial. Patients with a history of inadequate response to treatment, will be randomized to AXS-07, rizatriptan, meloxicam, or placebo. The co-primary endpoints of the trial are the proportion of patients who are pain free two hours after dosing, and the proportion of patients who no longer suffer from their most bothersome symptom two hours after dosing.

Results: The completed Phase I trial of AXS-07, revealed a rapid absorption of meloxicam with plasma concentrations reaching therapeutic levels in less than 30 minutes (compared to a reported T_{max} of 5 to 6 hours for standard meloxicam), and with a half-life of approximately 20 hours. This rapid absorption and extended half-life support the development of AXS-07 for the acute treatment of migraine.

An update on the status of the MOMENTUM Phase 3 clinical trial will be provided.

Conclusion: AXS-07 is a novel, oral, investigational medicine consisting of MoSEIC™ meloxicam and rizatriptan in clinical development for the acute treatment of migraine. The distinct mechanism of action and potential rapid absorption of MoSEIC™ meloxicam, combined with the known efficacy of rizatriptan, hold potential for rapid, superior and consistent relief of migraine pain, with lower symptom recurrence, as compared to currently available therapies.

Disclosure of Interest: None Declared.

IHC-PO-125

Rimegepant 75 mg is Effective for the Acute Treatment of Migraine Regardless of Attack Frequency: Results From 3 Phase 3 Trials

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Objective: Rimegepant, a small molecule calcitonin gene-related peptide receptor antagonist, has demonstrated efficacy in the acute treatment of migraine. The objective of this analysis was to evaluate the influence of migraine attack frequency on the efficacy of rimegepant.

Methods: Three double-blind, randomized, placebo-controlled, multicenter trials of identical design (Studies 301, 302, 303) were conducted in adults ≥ 18 years of age with ≥ 1 -year history of ICHD 3-beta migraine. Subjects were randomized to rimegepant 75 mg tablet (301&302), 75 mg orally dissolving tablet (ODT) (303), or placebo and instructed to treat a single migraine attack of moderate to severe pain intensity. The coprimary endpoints were 2-hour pain freedom and freedom from the most bothersome symptom (MBS). Efficacy was assessed in subjects with self-reported ≥ 4 and < 4 attacks per month over the preceding 3 months.

Results: In total, 3507 subjects participated (rimegepant $n = 1749$, placebo $n = 1758$); 2426 (69.2%) self-reported ≥ 4 attacks/month (rimegepant $n = 1217$, placebo $n = 1209$). Respective pooled 2-hour pain-free rates (95% CIs) for rimegepant and placebo among those with ≥ 4 attacks/month were 20.6% (18.3, 22.9) and 12.6% (10.8, 14.5); for MBS-free, they were 35.8% (33.1, 38.5) and 26.9% (24.4, 29.3). In subjects with < 4 monthly attacks, respective pooled 2-hour pain-free rates (95% CIs) for rimegepant and placebo were 18.8% (15.4, 22.1) and 11.3% (8.6, 13.9); for MBS-free, they were 37.6% (33.5, 41.7) and 26.1% (22.4, 29.7). Results from the individual studies were consistent with the pooled results. Rimegepant was well-tolerated, and no individual AEs were reported by $> 2\%$ of subjects.

Conclusion: Rimegepant was effective for the acute treatment of migraine regardless of attack frequency even among those with ≥ 4 attacks per month in 3 Phase 3 clinical trials; tolerability was good and similar to placebo.

Disclosure of Interests: Dawn C. Buse, PhD, has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Lilly, Promius, and Teva. She is on the editorial board of Current Pain and Headache Reports.

Andrew Blumenfeld, MD, serves as a consultant for Alder, Allergan, Amgen, Biohaven, electroCore, Lilly, Novartis, Promius, Supernus, and Teva.

Richard B. Lipton, MD, serves on the editorial board of *Neurology* and *Cephalalgia* and as senior advisor to Headache but is not paid for his roles on *Neurology* or *Headache*. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's *Headache* (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

Alexandra Thiry, PhD, Beth A. Morris, BA, Vladimir Coric, MD, and Robert Croop, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

IHC-PO-126

Rimegepant is Effective for the Acute Treatment of Migraine in Subjects Taking Concurrent Preventive Medication: Results From 3 Phase 3 Trials

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Objective: Rimegepant is a small molecule calcitonin gene-related peptide receptor antagonist with demonstrated efficacy in the acute treatment of migraine. Acute treatment is still required by the majority of patients using preventive migraine medication since preventive therapy rarely eliminates all attacks. This analysis was conducted to compare the efficacy of rimegepant with placebo in subjects taking preventive medication.

Methods: Three double-blind, randomized, placebo-controlled, multicenter trials of identical design (Studies 301, 302, 303) were conducted in adults ≥ 18 years of age with ≥ 1 -year history of ICHD 3-beta migraine. Subjects were randomized to rimegepant 75 mg tablet (301&302), 75 mg ODT (303), or placebo and instructed to treat a single migraine attack of moderate to severe pain intensity.

Subjects receiving preventive migraine medication were eligible if they were on a stable dose regimen for ≥ 3 months prescreening. The coprimary endpoints were pain freedom and freedom from the most bothersome symptom (MBS) at 2 hours.

Results: Of 3507 subjects evaluated for efficacy (rimegepant $n = 1749$, placebo $n = 1758$), 547 (15.6%) were using preventive medication (rimegepant $n = 272$, placebo $n = 275$). Pooled 2-hour pain-free rates (95% CIs) for rimegepant and placebo were 20.6% (15.8, 25.4) vs 10.2% (6.6, 13.8); for MBS-free, they were 37.1% (31.4, 42.9) for rimegepant and 20.4% (15.6, 25.1) for placebo. Results from the individual studies were consistent with the pooled results. Rimegepant was well-tolerated, and no individual AEs were reported in $>2\%$ of subjects.

Conclusion: Among subjects taking concurrent preventive medications in 3 Phase 3 clinical trials, rimegepant was effective for the acute treatment of migraine; tolerability was similar to placebo.

Disclosure of Interests: David W. Dodick reports the following conflicts: Personal fees: Amgen, Autonomic technologies, Axsome, Aural Analytics, Allergan, Alder, Biohaven, Charleston Laboratories, Dr. Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Neuroief, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, Oppenheimer. CME fees or Royalty payments Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal meeting management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer; Stock options: Aural analytics, Healint, Theranica, Second Opinon/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Consulting without fee: Aural Analytics, Healint, Second Opinion/Mobile Health, Epien; Board of Directors: Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1-1466:vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis without fee. Professional society fees or reimbursement for travel: American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society. Other: Use agreement through employer: Myndshft.

Lawrence C. Newman, MD, serves on the advisory board for Biohaven Pharmaceuticals.

Richard B. Lipton, MD, serves on the editorial board of *Neurology* and *Cephalalgia* and as senior advisor to Headache but is not paid for his roles on *Neurology* or *Headache*. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache

Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

Alexandra Thiry, PhD, Beth Morris, BA, Vladimir Coric, MD, and Robert Croop, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

IHC-PO-127

Long-Term, Open-Label Safety Study of Rimegepant 75 mg for the Treatment of Migraine (Study 201): Interim Analysis of Safety and Exploratory Efficacy

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Objective: Rimegepant is a small molecule CGRP receptor antagonist with demonstrated efficacy and safety in the acute treatment of migraine. Long-term safety and potential benefits of repeated dosing on monthly migraine days have not previously been assessed. The objective of this study was to evaluate the long-term safety of rimegepant 75 mg. The objective of this analysis is to evaluate a subgroup with scheduled, high-frequency dosing (every other day, QOD) supplemented by as-needed (PRN) dosing for 12 weeks.

Methods: This was a multicenter, long-term, open-label safety study (Study 201) of rimegepant 75 mg oral tablets in adults aged ≥ 18 years with ≥ 1 -year history of migraine with 2–14 migraine attacks of moderate to severe intensity per month. Subjects used rimegepant 75 mg up to once daily PRN to treat attacks of any pain intensity for up to 52 weeks. A subgroup with 4–14 moderate to severe monthly attacks was assigned to rimegepant 75 mg QOD for 12 weeks supplemented by PRN dosing (QOD + PRN) on nonscheduled dosing days.

Results: Subjects in the 12-week QOD + PRN cohort ($n=283$) were exposed to 11,239 rimegepant 75 mg

tablets. Results indicate that rimegepant was well tolerated, and rimegepant-treated subjects did not experience ALT or AST levels $\geq 3\times$ ULN during the treatment period ($n=279$). An exploratory analysis demonstrated that 43% of subjects experienced at least a 50% reduction from baseline in the frequency of monthly attacks of moderate to severe pain intensity.

Conclusion: This open-label safety study shows that long-term dosing of rimegepant 75 mg up to once daily appears to be safe and well tolerated in adults with migraine, with no signs of hepatotoxicity. The data also suggest that rimegepant, dosed at 75 mg QOD + PRN, may reduce migraine frequency. A Phase 3 trial is ongoing to evaluate rimegepant as a preventive treatment for migraine.

Disclosure of Interests: Richard B. Lipton serves on the editorial board of Neurology and Cephalalgia and as senior advisor to Headache but is not paid for his roles on Neurology or Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

Gary Berman, MD, has received fees for speaker's bureau from Amgen and for consulting from Alder.

David Kudrow, MD, has received fees for advisory board from Alder, Biohaven, Eli Lilly, Amgen, and Xoc and for speaker's bureau from Xoc, Teva, Amgen, Novartis, and Eli Lilly. He has also received research support from Amgen, Novartis, Eli Lilly, Teva, Alder, Biohaven, Biogen, and Roche-Genentech.

Kate Mullin, MD, serves as a consultant, advisory board member, or has received honoraria from Amgen, Biohaven, electroCore, and Eli Lilly.

Vladimir Coric, MD, Alexandra C. Thiry, PhD, Meghan Lovegren, BS, and Robert Croop, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

IHC-PO-128

Greater Headache-Related Burden and Disability Among Those With Medication Overuse: Results From the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study

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Objective: Medication overuse (MO) is associated with an increased risk of migraine progression and headache (HA)-related disability. The primary objective of this analysis was to characterize MO prevalence in the Chronic Migraine Epidemiology and Outcomes (CaMEO) study. Sociodemographics, HA characteristics, healthcare resource utilization, and HA-related burden was also compared between MO and non-MO respondents.

Methods: This analysis focused on CaMEO survey respondents who met modified *International Classification of Headache Disorders, 3rd edition* (ICHD-3) migraine criteria. MO was identified from ICHD-3 criteria for single medication class and multiple medication class overuse. HA characteristics, anxiety, depression, disability, interictal burden, and emergency department (ED) and urgent care (UC) facility utilization for migraine were assessed.

Results: Of 16,789 CaMEO respondents with migraine, 2,975 (17.7%) met MO criteria. The single medication classes in which respondents met MO criteria were non-opioid analgesics (10.5% [1,767/16,789]), combination analgesics (5.6% [938/16,789]), opioids (2.5% [422/16,789]), triptans (1.2% [205/16,789]), and ergotamines (0.1% [19/16,789]). Sociodemographic features of MO and non-MO respondents were comparable. The MO group had a higher number of mean (SD) monthly HA days than non-MO respondents (11.2 [8.2] vs 3.7 [4.4]; $P < 0.001$). Also more common among MO than non-MO respondents were moderate to severe depression (53.8% vs 27.7%, respectively; $P < 0.001$), moderate to severe anxiety (48.6% vs 25.9%; $P < 0.001$), moderate to severe HA-related disability (73.1% vs 31.6%; $P < 0.001$), ED and UC for HA use within 6 months (12.8% vs 3.3%; $P < 0.001$), and severe interictal burden (48.6% vs 18.7%; $P < 0.001$).

Conclusion: Respondents with MO had more HA-related disability, interictal burden, anxiety, depression, and ED and UC use for migraine than those without MO. Utilizing comprehensive treatment plans, along with

improved acute and preventive treatment options, may help reduce MO prevalence and associated burden.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

Author Disclosures:

Todd J. Schwedt, MD, serves on the Board of Directors for the American Headache Society and the International Headache Society and on the editorial boards for Headache, Cephalalgia, and Pain Medicine. He has received research support from the U.S. Department of Defense, the Patient Centered Outcomes Research Institute, National Institutes of Health, American Migraine Foundation, the Henry Jackson Foundation, and Amgen. Within the past 12 months, he has served as a consultant or advisory board member for Alder, Allergan, Amgen, Cipla, Dr. Reddy's, Eli Lilly, Ipsen Bioscience, Novartis, and Teva. He holds stock options in Aural Analytics, Nocira, and Second Opinion.

Dawn C. Buse, PhD, has received grant support and honoraria from Allergan, Avanir, Amgen, Biohaven, Eli Lilly and Company, and Promius and for work on the editorial board of Current Pain and Headache Reports.

Charles Argoff, MD reports no conflicts of interest.

Michael L. Reed, PhD, is Managing Director of Vedanta Research, which has received research funding from Allergan, Amgen, Dr. Reddy's Laboratories, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Novartis, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study.

Kristina M. Fanning, PhD, is an employee of Vedanta Research, which has received research funding from Allergan, Amgen, Dr. Reddy's Laboratories, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Novartis, via grants to the National Headache Foundation. Vedanta has received funding directly from Allergan for work on the CaMEO Study.

Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company.

Richard B. Lipton, MD, serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS; serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr. Reddy's, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache, 8th Edition (Oxford University Press, 2009), and Informa. He holds stock options in eNeura Therapeutics and Biohaven.

IHC-PO-129**Two hour CGRP infusion causes gastrointestinal hyperactivity**Katrine Falkenberg^{1,*} and Jes Olesen¹¹Danish Headache Center, Glostrup, Denmark

Objective: CGRP infusion for 20 minutes is known to cause migraine in migraine patients, but only a mild headache in healthy volunteers. The 20 minutes infusion is, in addition to the headache, only known to cause vascular side effects such as palpitations, flushing, hypotension and warm sensation. Since healthy volunteers are easier to recruit than migraine patients, the present study aimed to test whether a 2 hour CGRP infusion could induce more headache in healthy volunteers than the usual 20 minutes infusion. If so it could be used as a human migraine model. In this paper, we present the side effects of the long infusion, which were thoroughly noted during and after the infusion.

Methods: Twenty-nine healthy volunteers, 14 males and 15 females, were recruited to receive a 2 hour continuous intravenous infusion of CGRP 1.5 µg/min. During the infusion, a questionnaire was administered every 10 minutes asking about headache, premonitory symptoms and side effects. ECG and heart rate were continuously monitored. Blood pressure was measured every 10 minutes. After the infusion, the participants filled out a questionnaire at home every 30 minutes until 12 h after the infusion start.

Results: Ninety-three percent of the participants experienced stomach problems during the infusion; 62% experienced rumbling, 38% had stomach pain, 38% had an urge to defecate (5 subjects had diarrhea during the infusion) and 41% experienced nausea. Due to hypotension 48% had their legs elevated and saline infusion was given to 31%. Heart rate increased significantly over time ($p < 0.0001$). Fatigue, concentration issues, and yawning were the most frequently experienced CNS symptoms. All participants experienced flushing and a warm sensation and 82% experienced palpitations.

Conclusion: We conclude that a 2 hour infusion of CGRP causes more side effects than the usual 20 minutes infusion, especially from the gastrointestinal system. Due to our findings, it seems relevant to pay more attention to constipation as a possible side effect when using CGRP antagonists.

Disclosure of Interest: None Declared.

IHC-PO-130**The novel subtype-selective GABAA receptor modulator NSI 1394 is effective in a spontaneous rat model of migraine**Jes Olesen^{1,*}, Gordon Munro¹ and Steffen Petersen¹¹Righospitalet – Glostrup, Glostrup, Denmark

Objective: To assess the efficacy of various mechanistically distinct drugs that target specific facets of nociceptive transmission within peripheral and/or central pain circuits.

Methods: Spontaneous trigeminal allodynia (STA) rats are a unique inbred strain that are hypersensitive in the head but not in the hind paws. Allodynia was tested using the Von Frey method. All drugs were tested blindly.

Results: The serotonin (5-HT)_{1B/1D/1F} receptor agonist sumatriptan (1 mg/kg, s.c.) and the non-steroidal anti-inflammatory drug ibuprofen (100 mg/kg, i.p.) increased the periorbital threshold to mechanical stimulation in STA rats ($P < 0.001$ vs vehicle). Periorbital thresholds were also increased by the partial m-opioid receptor agonist buprenorphine (0.1 mg/kg, s.c.), ($P < 0.001$ vs vehicle). However, hind paw thresholds were also affected by buprenorphine indicating a lack of selectivity for trigeminal pain circuits. The mechanistically distinct anticonvulsant drugs gabapentin (100 mg/kg, p.o.) and sodium valproate (600 mg/kg, p.o.), and the novel subtype-selective GABA_A receptor modulator NSI 1394 (10–30 mg/kg, p.o.), all of which attenuate nociceptive transmission via central sites of action selectively increased periorbital thresholds in STA rats ($P < 0.001$ vs vehicle). However, the 5-HT and noradrenaline reuptake inhibitor duloxetine (30 mg/kg, p.o.) was completely ineffective suggesting that descending noxious inhibitory control inputs remain intact in this model.

Conclusion: Both central and peripheral mechanisms may play a role in migraine. Subtype specific GABA A agonists may represent a novel target for migraine drug development.

Disclosure of Interest: None Declared.

IHC-PO-131**Rimegepant Has No Clinically Relevant Effect on ECG parameters at Therapeutic and Supratherapeutic Doses: A Thorough QT Study Versus Placebo and Moxifloxacin in Healthy Subjects**Michael Hanna^{1,*}, Vladimir Coric¹, Joseph Stringfellow¹, Andrea Ivans¹ and Robert Croop¹¹Biohaven Pharmaceuticals, New Haven, United States

Objective: The objective of this study was to evaluate the effect of therapeutic and supratherapeutic concentrations

of rimegepant, a small molecule calcitonin gene-related peptide receptor antagonist with efficacy in migraine, on the QTcF interval in healthy fasted adults.

Methods: This was a single-center, Phase I, partially double-blind, randomized, placebo-controlled, 12-sequence, 4-period crossover study. Fasted adults aged ≥ 18 years were randomized to one of 12 sequences consisting of: a 4-tablet dose of rimegepant 75 mg (1 x 75 mg + 3 placebo); rimegepant 300 mg (4 x 75 mg); placebo (4 x); or 1 tablet of moxifloxacin hydrochloride 400 mg as a positive drug control to establish assay sensitivity. From baseline through 24 hours postdose in each treatment period, PK, safety, and ECG parameters were assessed.

Results: Subjects were randomized to rimegepant 75 mg ($n = 37$), rimegepant 300 mg ($n = 38$), moxifloxacin, and placebo ($n = 36$ each). A single rimegepant dose of 75 mg (therapeutic) or 300 mg (supratherapeutic) had no clinically relevant effect on ECG parameters, including the RR, PR, QRS and QT/QTcF intervals. Compared with the 75 mg dose, the 300 mg dose showed an increased rate (C_{max}) and extent of absorption (AUC_{0-t}) (approximately 5.7 to 7.1-fold, respectively). There were no SAEs or AEs leading to discontinuation reported in this study. There were no reports of alanine aminotransferase, alkaline phosphatase, or aspartate aminotransferase values $>3\times$ ULN and no subjects had total bilirubin levels $>2\times$ ULN.

Conclusion: In healthy adults, therapeutic (75 mg) and supratherapeutic (300 mg) doses of rimegepant were safe and well tolerated, as demonstrated by the absence of clinically relevant effects on ECG parameters and the safety of exposures significantly above those of the therapeutic dose.

Disclosure of Interests: Michael Hanna, MD, Vladimir Coric, MD, Joseph Stringfellow, MS, Andrea Ivans, MHS, and Robert Croop, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

IHC-PO-132

Successful Gepant-Monoclonal Antibody Combination: Rimegepant 75 mg for Acute Treatment of Attacks During Preventive Therapy With Erenumab

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Objective: Calcitonin gene-related peptide (CGRP) has been confirmed as a therapeutic target in migraine, with

small molecule CGRP receptor blockers (gepants) for acute and preventive treatment and monoclonal antibodies (mAbs) to the CGRP receptor or ligand for preventive only. The effects of their combined use are currently unknown. This is the first clinical report that anti-CGRP therapies can be used concomitantly to control refractory migraine.

Methods: Case reports of 2 patients participating in a long-term safety study of rimegepant 75 mg oral tablets for acute treatment. After CGRP mAbs were approved by FDA, their concomitant use for prevention was allowed per protocol.

Results: Patients were women aged 44 and 36 years with ≥ 2 decades of suboptimal response to multiple migraine medications. Patient 1 used rimegepant for 6 months before starting erenumab 70 mg monthly. Despite a response to erenumab, she experienced substantial relief treating acute attacks with rimegepant in 7 of 7 attacks. She eliminated regular, frequent use of ibuprofen and a caffeinated analgesic. Patient 2 used rimegepant for 60 days prior to starting erenumab 140 mg monthly. While on erenumab, 9 of 9 attacks treated with rimegepant responded. She stopped near daily use of injectable ketorolac and diphenhydramine. While using rimegepant alone or together with erenumab for breakthrough attacks, participants reported no adverse events.

Conclusion: These 2 patients provide preliminary evidence that rimegepant 75 mg may be effective for acute treatment when combined with erenumab in treatment-refractory patients. Rimegepant may access and block receptors that remain available despite erenumab treatment. Additional benefit from rimegepant may be due to its smaller molecular size than erenumab (0.53 vs ~ 150 kDa), ability to access sites not blocked by antibodies, decreased susceptibility to displacement by CGRP, and improved receptor kinetics.

Disclosure of Interests: Kathleen Mullin, MD, serves as a consultant, advisory board member, or has received honoraria from Amgen, Biohaven, electroCore, and Eli Lilly. David Kudrow, MD, has received fees for advisory board from Alder, Biohaven, Eli Lilly, Amgen, and Xoc and for speaker's bureau from Xoc, Teva, Amgen, Novartis, and Eli Lilly. He has also received research support from Amgen, Novartis, Eli Lilly, Teva, Alder, Biohaven, Biogen, and Roche-Genentech.

Robert Croop, MD, Meghan Lovegren, BS, Charles M. Conway, PhD, and Vladimir Coric, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals. Richard B. Lipton, MD, serves on the editorial board of Neurology and Cephalalgia and as senior advisor to Headache but is not paid for his roles on Neurology or Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan,

Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

IHC-PO-133

Rimegepant 75 mg Demonstrates Safety and Tolerability Similar to Placebo: Results from 3 Phase 3 Trials in Adults With Migraine

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Objective: Most (52%) triptan users experience adverse events, which can cause delays or avoidance of treatment, and 3.5 million adults with migraine must avoid or use triptans with caution due to cardiovascular concerns. Rimegepant is a small molecule calcitonin gene-related peptide receptor antagonist that has demonstrated efficacy in the acute treatment of migraine. This analysis was conducted to compare the safety and tolerability of rimegepant 75 mg with placebo.

Methods: Three double-blind, randomized, placebo-controlled, multicenter trials of identical design (Studies 301, 302, 303) were conducted in adults ≥ 18 years of age ≥ 1 -year history of ICHD 3-beta migraine. Subjects were randomized to rimegepant 75 mg tablet (301&302), 75 mg ODT (303), or placebo and instructed to treat a single migraine attack of moderate or severe pain intensity. Safety assessments included adverse events (AEs), ECGs, vital signs, and routine laboratory tests, including liver

	Rimegepant N = 1771 N (%)	Placebo N = 1782 N (%)
≥ 1 on-treatment AE ¹	192 (10.8)	154 (8.6)
Nausea	26 (1.5)	14 (.8)
UTI	14 (.8)	6 (.3)

(continued)

Continued.

	Rimegepant N = 1771 N (%)	Placebo N = 1782 N (%)
SAEs ²	1 (.1)	2 (.1)
AST or ALT >ULN	48 (2.7)	52 (2.9)
>3 \times ULN	2 (.1)	2 (.1)
>5 \times ULN	1 (.06) ^a	0
>10 \times ULN	0	0

^aAlso included in >3 \times category.

function tests, such as aspartate and alanine transaminase (AST and ALT).

Results: Altogether, 3553 subjects were analyzed for safety (rimegepant n = 1771, placebo n = 1782). Pooled results from Studies 301, 302, and 303 indicate that rimegepant was well tolerated. The most common AEs were nausea and urinary tract infection ($\leq 1.5\%$). No serious treatment-related AEs were reported. No liver safety concerns were identified, and no subjects had bilirubin >2 \times ULN. The table provides on-treatment AEs and on-study LFTs.

Conclusion: Across 3 Phase 3 randomized controlled clinical trials in the acute treatment of migraine, the tolerability of rimegepant was similar to placebo, with no liver safety issues.

Disclosure of Interests: Susan Hutchinson, MD, has served as a consultant/advisory board member for Alder, Allergan, Amgen, Avanir, Biohaven, electroCore, Lilly, Novartis, Promius, Supernus, Teva and on the speaker's bureau for Allergan, Amgen, Avanir, electroCore, Lilly, Novartis, Promius, Supernus, and Teva.

Richard B. Lipton, MD, serves on the editorial board of Neurology and Cephalalgia and as senior advisor to Headache but is not paid for his roles on Neurology or Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

Alexandra Thiry, PhD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Beth Morris, BA, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Vladimir Coric, MD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

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IHC-PO-134

A Single Dose of Rimegepant Demonstrates Sustained Efficacy and Low Rescue Medication Use in the Acute Treatment of Migraine: Results From 3 Phase 3 Trials

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Objective: Recurrence of migraine pain and associated symptoms often causes dissatisfaction with acute treatment. Rimegepant is a small molecule calcitonin gene-related peptide receptor antagonist with efficacy in migraine; its half-life may provide sustained benefits in acute treatment. The objective of this analysis was to assess the clinical benefits of rimegepant versus placebo through 24 and 48 h postdose.

Methods: Three double-blind, randomized, placebo-controlled, multicenter trials (Studies 301, 302, 303) were conducted in adults with migraine. Subjects randomized to rimegepant 75 mg tablet (301&302), 75 mg ODT (303), or placebo treated a single moderate-severe migraine attack. Endpoints were pain freedom, pain relief, freedom from functional disability, freedom from

the most bothersome symptom (MBS), and use of rescue medication.

Results: In total, 3507 subjects were evaluated (rimegepant n = 1749, placebo n = 1758). In pooled results, rimegepant was superior to placebo on sustained pain freedom and pain relief through 24 and 48 h postdose.

In Study 303, rimegepant was significantly superior to placebo for sustained freedom from functional disability and the MBS 2–24 and 2–48 h postdose ($p \leq .0018$ for each). Rimegepant was well-tolerated; no individual AEs were reported in >2% of subjects.

Conclusion: Rimegepant 75 mg significantly outperformed placebo on a range of endpoints through 48 h postdose. Few rimegepant-treated subjects used rescue medication; tolerability was similar to placebo.

Disclosure of Interests: Jelena M. Pavlovic serves on the advisory board for Biohaven Pharmaceuticals.

David W. Dodick reports the following conflicts: Personal fees: Amgen, Autonomic technologies, Axsome, Aural Analytics, Allergan, Alder, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Neuroief, Novartis, Ipsen, Impel, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco, Foresite Capital, Oppenheimer. CME fees or Royalty payments Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal meeting management, Haymarket, Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer; Stock options: Aural analytics, Healint, Theranica, Second Opinon/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies. Consulting without fee: Aural Analytics, Healint, Second Opinion/Mobile Health, Epien; Board of Directors: Epien, Matterhorn/Ontologics, King-Devick Technologies. Patent :17189376.1-1466.vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis without fee. Professional society fees or reimbursement for travel: American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society. Other: Use agreement through employer: Myndshft.

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Richard B. Lipton, MD, serves on the editorial board of Neurology and Cephalalgia and as senior advisor to Headache but is not paid for his roles on Neurology or Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as

	% (95%CI)	
	Rimegepant N = 1749	Placebo N = 1758
Pooled results		
Sustained pain-free		
2–24 h	14.1 (12.5, 15.8)	6.8 (5.7, 8.0)
2–48 h	11.8 (10.3, 13.3)	6.2 (5.0, 7.3)
Sustained pain relief		
2–24 h	43.5 (41.2, 45.8)	27.4 (25.3, 29.5)
2–48 h	37.8 (35.5, 40.0)	24.0 (22.0, 26.0)
Rescue medication within 24 h	18.2 (16.4, 20.0)	32.4 (30.2, 34.5)

consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

Alexandra Thiry, PhD, Beth A. Morris, BS, Vladimir Coric, MD, and Robert Croop, MD are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

IHC-PO-135

Rimegepant 75 mg Provides Pain Relief and Return to Normal Function with a Single Dose: Results from 3 Phase 3 Trials in Adults With Migraine

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Objective: Patients with migraine consider pain relief and restoration of function among the most important attributes of acute treatment. Rimegepant is a small molecule calcitonin gene-related peptide receptor antagonist with demonstrated efficacy in the acute treatment of migraine. The objective of this analysis was to compare the efficacy of rimegepant with placebo as measured by rates of pain relief and freedom from functional disability.

Methods: Three double-blind, randomized, placebo-controlled, multicenter trials of identical design (Studies 301, 302, 303) were conducted in adults ≥ 18 years of age with ≥ 1 -year history of ICHD 3-beta migraine. Subjects were randomized to rimegepant 75 mg tablet (301&302), 75 mg ODT (303), or placebo and instructed to treat 1 migraine attack of moderate to severe pain intensity. The coprimary endpoints were 2-hour freedom from pain and the most bothersome symptom; secondary endpoints included pain relief and functional disability freedom.

Results: Among 3507 subjects evaluated for efficacy (rimegepant $n = 1749$, placebo $n = 1758$), pooled 2-hour pain relief rates (95% CIs) for rimegepant and placebo were 57.9% (55.6, 60.2) and 43.9% (41.6, 46.2), respectively; for functional disability freedom, 2-hour rates were 34.9% (32.7, 37.2) and 23.8% (21.8, 25.8). Results from the individual studies were consistent with the pooled results. At 60 minutes postdose in Study 303, rimegepant ODT was significantly more effective than placebo for pain relief

(36.8% vs 31.2%, $p = 0.014$) and functional disability freedom (22.3% vs 15.8%, $p = 0.0025$). Rimegepant was well-tolerated; no individual AEs were reported in $>2\%$ of subjects.

Conclusion: Rimegepant provided effective pain relief and return to normal function in 3 clinical trials, and the ODT form demonstrates more rapid onset of action with statistically significant benefit in pain relief and functional disability freedom at 60 minutes; tolerability was similar to placebo.

Disclosure of Interests: Richard B. Lipton, MD, serves on the editorial board of Neurology and Cephalalgia and as senior advisor to Headache but is not paid for his roles on Neurology or Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

Stewart Tepper, MD, serves as an advisory board member for Biohaven Pharmaceuticals.

Deborah Friedman, MD, has served as a speaker, advisory board member, and received grant support for Allergan, Merck, Supernus, Eli Lilly, Autonomic Technologies, electroCore, Zosano, Alder, Amgen, Teva, Biohaven, Promius, Axon Optics. She also serves on the editorial board of Neurology Reviews.

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IHC-PO-136**Safety of Rimegepant 75 mg in Adults With Migraine: No Effects of Age, Sex, or Race in 3 Phase 3 Trials**

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Objective: Safety and tolerability issues with migraine treatments — adverse events causing delay or avoidance of treatment, cardiovascular contraindications with triptans — can be complicated by patient sex, age, and race. Rimegepant is a small molecule calcitonin gene-related peptide receptor antagonist that has demonstrated efficacy in the acute treatment of migraine. This analysis was conducted to assess any effects of subject sex, age, and race on the safety and tolerability of rimegepant 75 mg vs placebo.

Methods: Three double-blind, randomized, placebo-controlled, multicenter trials of identical design (Studies 301, 302, 303) were conducted in adults ≥ 18 years of age with ≥ 1 -year history of ICHD 3-beta migraine. Subjects were randomized to rimegepant 75 mg tablet (301&302), 75 mg ODT (303), or placebo and instructed to treat a single migraine attack of moderate or severe pain intensity. They were grouped by sex, age (<40 , ≥ 40 , <65 , ≥ 65), and race for analyses of safety, including adverse events (AEs) and liver function tests.

Results: The sex, age, and race subgroup populations drawn from the 3553 subjects in the safety population (rimegepant $n = 1771$, placebo $n = 1782$) were demographically balanced, with 86% female (rimegepant $n = 1529$, placebo $n = 1534$); 88 subjects ≥ 65 years of age (rimegepant $n = 36$, placebo $n = 52$); and 851 non-Caucasians (696 black or African-American; rimegepant $n = 365$, placebo $n = 331$). Rimegepant was well tolerated, with no notable differences in safety based on sex, age, and race. The most common AEs in all subgroups were nausea and urinary tract infection. No serious treatment-related AEs were reported. No liver safety concerns were identified.

Conclusion: The tolerability of rimegepant was similar to placebo, with no liver safety issues and no notable differences by sex, age, or race.

Disclosure of Interests: Susan Hutchinson, MD, has served as a consultant/advisory board member for Alder, Allergan, Amgen, Avanir, Biohaven, electroCore, Lilly, Novartis, Promius, Supernus, and Teva and on the speaker's bureau for Allergan, Amgen, Avanir, electroCore, Lilly, Novartis, Promius, Supernus, and Teva.

Jack Schim, MD, is on the advisory board for Biohaven Pharmaceuticals.

Richard B. Lipton, MD, serves on the editorial board of *Neurology* and *Cephalalgia* and as senior advisor to Headache but is not paid for his roles on *Neurology* or *Headache*. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's *Headache* (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

Alexandra Thiry, PhD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Beth Morris, BA, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Vladimir Coric, MD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

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IHC-PO-358**Safety of Ubrogapant in Participants With Moderate to High Cardiovascular Risk**

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Objective: To evaluate the safety of ubrogapant, a novel, oral CRGP receptor antagonist, based on participants' cardiovascular (CV) risk factors, using data from the ACHIEVE I and ACHIEVE II phase 3 trials of acute treatment for migraine.

Methods: ACHIEVE I (NCT02828020) and ACHIEVE II (NCT02867709) were multicenter, double-blind, single-attack, phase 3 trials that included adults with a history of migraine. Participants were randomized 1:1:1 to placebo or ubrogapant (50 mg or 100 mg, ACHIEVE I; 25 mg or 50 mg, ACHIEVE II). Data from ubrogapant 50 mg and placebo treatment groups were pooled for this analysis.

Participants were categorized as having moderate to high, low, or no CV risk factors at baseline.

Results: A total of 3358 participants were randomized in the ACHIEVE I and II trials (N = 2901 safety population). The average age was 41 years; the majority was female and white. Of the safety population, 11% of participants were categorized as having a moderate to high CV risk (n = 311), 32% a low CV risk (n = 920), and 58% no CV risk factors (n = 1670). The proportion of participants in the ubrogepant treatment groups reporting a treatment-emergent adverse event (TEAE) was comparable across risk categories and did not differ greatly from placebo. No serious AEs were reported within 48 hours of initial dose. Six participants reported serious AEs within 30 days of dosing (5 in ACHIEVE I and 1 in ACHIEVE II); all were categorized under no CV risk factors. The investigator considered one of the 6 serious AEs (seizure) related to investigational product, but the relation was confounded by alprazolam use and possible withdrawal. The most commonly reported TEAE at 48 hours post initial dose was nausea (reported by <5% of participants in any CV risk category).

Conclusion: There was no evidence of increased AEs with higher CV risk. Overall, ubrogepant is safe and well tolerated, with no identified safety concerns.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

Author Disclosures:

Susan Hutchinson, MD has served on advisory boards for Alder, Allergan, Amgen, Avanir, Biohaven, ElectroCore, Eli Lilly, Supernus, and Teva. She is on the speakers bureau for Allergan, Amgen, Avanir, ElectroCore, Eli Lilly, Promius, Supernus, and Teva.

Stephen D. Silberstein, MD as a consultant and/or advisory panel member, receives honoraria from Alder Biopharmaceuticals, Allergan, Amgen, Avanir Pharmaceuticals, eNeura, ElectroCore Medical, Labrys Biologics, Medscape, Medtronic, Neuralie, NINDS, Pfizer, and Teva. Dr. Silberstein's employer receives research support from Allergan, Amgen, Cumberland Pharmaceuticals, ElectroCore Medical, Labrys Biologics, Eli Lilly, Merz Pharmaceuticals, and Troy Healthcare.

Andrew M. Blumenfeld, MD has served on advisory boards and/or has consulted for Allergan, Pernix, Teva, Avanir, Depomed, and Supernus, and has received funding for travel, speaking, and/or royalty payments from Allergan.

Richard B. Lipton, MD serves on the editorial boards of *Neurology* and *Cephalgia* and as senior advisor to *Headache*. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS; serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr.

Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's *Headache*, 8th Edition (Oxford University Press, 2009), and Informa. He holds stock options in eNeura Therapeutics and Biohaven.

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IHC-PO-359

Comparison of intranasal ketamine, dihydroergotamine, and valproic acid for abortive migraine treatment in a pediatric emergency department

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Objective: Pediatric migraineurs in emergency departments (ED) are often treated with nonsteroidal anti-inflammatory drugs, dopamine receptor antagonists, or dihydroergotamine (DHE). Intravenous (IV) DHE has become a standard abortive migraine treatment; but DHE is contraindicated in some instances, and a less efficacious alternative such as IV valproic acid (VPA) is utilized (i.e. triptan within 24 hours, uncontrolled hypertension). Intranasal ketamine (INK) has emerged as a potential alternative. In a recent quality assurance review at our institution, 25/36 pediatric migraineurs (65.4%) responded to INK 0.1–0.2 mg/kg/dose (mean pain reduction: –7.2). The aim of this study compare efficacy and safety of INK, DHE, and VPA in pediatric ED patients to better elucidate INK's place in therapy.

Methods: A retrospective review of 59 pediatric migraineurs (7–18 years old) receiving INK, DHE, or VPA in the Cook Children's ED was performed. Pain scores were obtained utilizing a 0–10 numeric pain scale. Response was defined as pain score decrease by ≥50% and/or final pain score ≤3. Patient reported or clinically observed AEs, vital sign changes, admissions, and ≤72 hour readmissions were recorded.

Results: Response was seen in 19/26 (73.1%) INK patients, 10/19 (52.6%) DHE patients, and 9/14 (64.3%) VPA patients and was not statistically significant (INK/DHE, p = 0.174; INK/VPA, p = 0.574). Mean percent pain reduction from ED presentation to treatment end was –56.9% with INK, –55.6% with DHE, and –67.5% with

VPA and were not significantly different. INK had significantly fewer inpatient admissions than DHE (9 vs 14; $p=0.009$); this was not significant compared to VPA. AEs and ≤ 72 hour readmissions were minimal and not significantly different between groups.

Conclusion: In this small cohort, INK had a similar response rate and percent pain reduction compared to DHE and VPA without the need for IV access or pre-medication. These results support consideration of INK for abortive migraine treatment, particularly when DHE or VPA may be contraindicated. Larger trials are warranted to substantiate INK's integration into pediatric migraine treatment.

Disclosure of Interest: None Declared.

IHC-PO-360

Consistency of response of remote electrical neuromodulation for the acute treatment of migraine

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Objective: Efficacy analyses of new migraine acute treatments are typically performed on single attacks. However, given the chronic recurrent nature of migraine, the effect of repeated treatment has great clinical relevance. It has been recently demonstrated that remote electrical neuromodulation (REN), a non-invasive, drug-free acute migraine treatment, provides superior clinically meaningful pain relief with a favorable safety profile. The objective of the current study was to determine the consistency of response of REN.

Methods: We performed prespecified and post-hoc analyses on data of participants aged 18–75 years old with episodic migraine from a randomized, double-blind, parallel-group, sham-controlled study. This study included a 6-week double-blind treatment phase in which multiple attacks were treated with an active or sham device. Several methods, including group average response and within-patient measures, were used to assess the consistency of pain relief at 2 hours post-treatment.

Results: Of the 252 patients randomized, 99 in the active group and 103 in the sham group were available for analysis. 362 attacks (328 with pain level at 2 hours) and 371 attacks (352 with pain level at 2 hours) were treated with the active and sham devices, respectively. The average number of attacks per subject was 3.5. In the active group, 74 participants treated at least three attacks. Across all attacks, pain relief at 2 hours was achieved in more attacks in the active group than the sham group (51.3% vs. 38.1%; $p=0.031$). In a within-patient

consistency analysis, pain relief in at least 50% of treatments was achieved by 63.1% of the participants in the active group vs. 43.3% in the sham group ($p=0.004$). Moreover, in the active group, 82.4% (61/74) and 55.4% (41/74) of the participants achieved pain relief at 2 hours in at least 1 of 3 attacks and in at least 2 of 3 attacks, respectively.

Conclusion: The results demonstrate that most participants who used REN achieved pain relief at 2 hours in most of their treated attacks. These results indicate that REN is consistently effective across multiple attacks. The consistency of REN is comparable with pharmacological treatments such as triptans, suggesting that REN may offer an alternative for acute treatment of migraine.

Disclosure of Interests: This study was funded by Theranica. ML has been a consultant for Alder BioPharmaceuticals Inc; Allergan plc; Amgen Inc; Lilly; Supernus Pharmaceuticals, Inc; Teva Pharmaceuticals; Theranica; Xoc, Biohaven and Upsher-Smith Laboratories, LLC. TL, DH, AI and RJ are employees of Theranica.

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Triptan Use and Associated Patient Reported Outcomes in Migraine Patients

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Objective: To describe and compare triptan use, treatment satisfaction and health related quality of life (HRQoL) in patients with migraine.

Methods: Data were drawn from the 2017 Adelphi Migraine Disease Specific Programme, a cross sectional survey of physicians and their patients with migraine in USA, France, Germany, Italy, Spain, UK. Primary care physicians, neurologists and headache specialists completed patient record forms capturing patients' acute treatment history. Patients completed a questionnaire which included treatment satisfaction, Migraine Disability Assessment Scale (MIDAS), EuroQoL (EQ-5D-5L) and Migraine Specific Quality of Life Questionnaire v.2.1 (MSQ). Patients were divided into current and non-current triptan users, with subgroups based on past triptan use defined within each. Analysis was conducted descriptively.

Results: Data were analyzed for 6,035 patients: 62% ($n=3735$) currently on a triptan and 38% ($n=2,300$) not on a triptan. 73% of patients in the USA were currently on a triptan vs. 58% in the EU5. Of non-current triptan users, 94% had never tried a triptan. Patients who had discontinued a triptan were the least satisfied with their

Abstract number: IHC-PO-361**Table 1.** HRQoL by Triptan Use

	Current		Not Current		p-value*
	Present triptan users (n = 3,233)	Triptan switchers (n = 502)	Never used a triptan (n = 2,161)	Triptan discontinuers (n = 139)	
MIDAS mean (sd)	10.3 (15.7)	15.4 (21.5)	8.5 (12.5)	18.7 (34.6)	<.001
EQ-5D-5L mean (sd)	0.88 (0.15)	0.83 (0.18)	0.87 (0.15)	0.79 (0.22)	<.001
MSQ Total Score mean (sd)	72 (19)	68 (21)	75 (18)	70 (24)	<.001

*Comparison among 4 groups by ANOVA.

Higher MIDAS score indicates greater disability; lower MSQ score indicates lower HRQoL; lower EQ-5D-5L score indicates lower HRQoL. Triptan groups from PRF; results from PSC with lower base numbers.

current acute treatment, with 14% noting dissatisfaction, compared to 4% of current triptan users. Patients who had switched triptans or discontinued their triptan, reported greater disability via MIDAS, and lower HRQoL via EQ-5D-5L and MSQ (Table 1).

Conclusion: Triptan use differs considerably between the USA and EU5. Patients who switched triptans or discontinued their triptan reported a greater burden of migraine on their HRQoL, indicating a need for efficacious alternatives for those not adequately managed on triptans.

Disclosure of Interest: None Declared.

IHC-PO-362

Comparison of the pharmacokinetics of STS101, an intranasal dry powder formulation of dihydroergotamine, with other intranasal, injectable, and orally inhaled DHE formulations

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Objective: To perform a literature review to compare pharmacokinetic (PK) parameters for several formulations of dihydroergotamine mesylate (DHE) including intravenous (IV), intramuscular (IM), intranasal liquid sprays, orally inhaled, and intranasal dry powder.

Methods: A literature search was performed to compare PK results of several formulations of DHE including the approved products Migranal[®] (liquid nasal spray) and D.H.E.45[®] (administered IV and IM), and the development-stage products INP104 (liquid nasal spray), MAP0004 (orally inhaled), and STS101.

Results: IV DHE C_{max} is approximately 54,189 pg/mL while IM DHE C_{max} is between 2890–4440 pg/mL. STS101 had a C_{max} (2175 pg/mL) higher than intranasal sprays Migranal and INP104 and comparable to the orally inhaled MAP0004 (961, 1281, and approximately 2500–2720 pg/ml, respectively). The STS101 AUC_{0–2hr} (2979 h*pg/mL) was 2-fold or more larger than for

Migranal, INP104, and MAP0004 (1316, 1595, and 1447 h*pg/mL, respectively). The STS101 AUC_{0–inf} (12030 h*pg/mL) was 2-fold or more larger than for Migranal, INP104, and MAP0004 (6498, 6153, and 4472 h*pg/mL, respectively) and approached IM DHE (approximately 13650 h*pg/ml). The coefficient of variation (%CV) for C_{max} and AUC_{0–inf} were lower with STS101 (41% and 39%) versus Migranal (76% and 55%) and INP104 (51% and 42%) and approached MAP0004 (40% and 34%). Plasma concentrations and AUC values for Migranal were similar across multiple historical studies and in the STS101 study, but were significantly lower in the INP104 study. INP104 plasma concentrations and AUC values were similar to those reported for Migranal in historical studies and in the STS101 study.

Conclusion: As compared with DHE liquid nasal spray products (Migranal and INP104), STS101 demonstrated superior PK (C_{max} and AUC at various time points) and less PK variability. As compared with orally inhaled DHE (MAP0004), STS101 achieved similar C_{max} and higher AUC at all time points after ~30 minutes as well as similar PK variability. STS101 showed high sustained plasma concentrations and AUC_{0–inf} approaching IM DHE. A Phase 3 efficacy study with STS101 is planned to evaluate the product as an acute treatment for migraine.

Disclosure of Interests: The authors are employees of Satsuma Pharmaceuticals, Inc.

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STS101 (Dry Powder Intranasal Dihydroergotamine) Drug-Device Combination Achieves Consistent and Robust Drug Delivery Performance for Migraine Patients

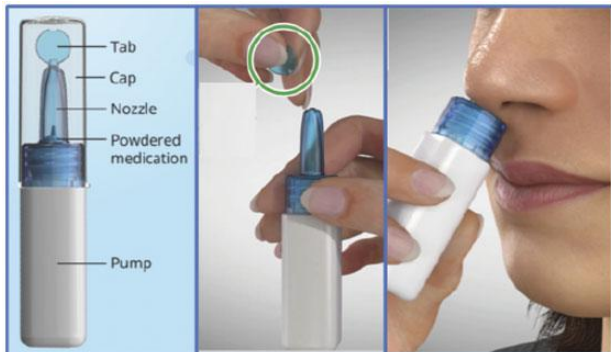
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Objective: To design and create STS101, an intranasal drug-device combination product, which ensures

consistent delivery of dihydroergotamine (DHE) for migraine patients.

Methods: Design specifications for STS101 were defined to produce consistent nasal delivery of DHE. STS101 drug-device combination product was manufactured and tested for delivered dose and aerodynamic particle size distribution using Next Generation Impactor. Additionally, the consistency of delivery with respect to variations in STS101 device actuation parameters were assessed. The STS101 device is shown in the image below.



Results: Design of STS101 resulted in a dry-powder DHE mesylate formulation utilizing a proprietary mucoadhesive carrier, which is contained in a novel, prefilled, single-use, disposable device. In-vitro delivery characterization demonstrated an average delivered dose of 96% with a relative standard deviation of 3.5%. The aerodynamic particle size analysis showed 1.3% of delivered dose DHE particles with aerodynamic particle size below 5 μm . STS101 showed greater than 95% of the target amount was delivered even when lowering the actuation velocity to 50% of the optimal value.

Conclusion: STS101 is a novel intranasal drug-device combination product of DHE that can consistently deliver the complete clinical dose and that has optimal aerodynamic particle size for nasal deposition with negligible respirable fine particle fraction that may deposit in the lungs. STS101 also has robust and consistent delivery even with suboptimal actuation. STS101 has the delivery characteristics to satisfy the unmet need for a reliable non-parenteral form of DHE.

Disclosure of Interest: None Declared.

IHC-PO-364

Results of a Phase I, Open-label, Single-dose, Parallel-group Study of Rimegepant 75 mg in Subjects with Hepatic Impairment

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Objective: Hepatic impairment can have clinically significant effects on the pharmacokinetics (PK) of migraine medications. Rimegepant is a small molecule calcitonin gene-related peptide receptor antagonist with efficacy in migraine. The objective of this study was to determine the effect of hepatic impairment on the PK of a single dose of rimegepant 75 mg.

Methods: This was a 2-center, Phase I, open-label, single-dose, 4-group PK study. Subjects included adult nonsmokers aged ≥ 18 and ≤ 80 years, with BMI ≥ 18.5 and ≤ 40.0 kg/m²; weight ≥ 50.0 kg (males) and ≥ 45.0 kg (females); and a score of 0 on the Sheehan Suicidality Tracking Scale (S-STs). They were grouped by degree of hepatic impairment based on Child-Pugh score: normal (controls); mild (5–6 points); moderate (7–9 points); and severe (10–15 points). Healthy subjects were matched with hepatic impairment subjects by gender, age, and BMI. The primary PK endpoints were AUC_{0-t}, AUC_{0-inf}, and C_{max}. Subjects received a single 75 mg tablet of rimegepant under fasting conditions.

Results: In total, 36 subjects were enrolled, treated, completed the study, and analyzed for safety and PK. The PK results in subjects with mild or moderate hepatic impairment were similar to controls. In subjects with severe hepatic impairment, log-transformed ratios (severe impairment/controls) were 202.25 (90% CI: 154.30, 265.10; $p < .001$) for AUC_{0-t}; 202.21 (90% CI: 154.20, 265.17; $p < .001$) for AUC_{0-inf}, and 189.14 (90% CI: 132.11, 270.80; $p = .009$) for C_{max}. Three (8.3%) subjects reported at least 1 TEAE: 2 with normal hepatic function and 1 with severe hepatic impairment. No event was reported in more than 1 subject, and all events were reported as mild in intensity.

Conclusion: There were no notable differences in rimegepant exposure between mild or moderate hepatic impairment groups and matched controls. Subjects with severe hepatic impairment had approximately 2-fold increases in AUC and C_{max} compared to the matched controls. Rimegepant was well tolerated in healthy adults and in subjects with hepatic impairment.

Disclosure of Interests: Robert Croop, MD, Joseph Stringfellow, MS, Andrea Ivans, MHS, and Vladimir Coric, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

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Cardiovascular Safety of Rimegepant 75 mg in 3 Randomized Clinical Trials and Systematic Evaluations from In Vitro, Ex Vivo and In Vivo Nonclinical Assays

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Objective: In America, 2.6 million migraine sufferers have had a cardiovascular (CV) event, condition or procedure that contraindicates triptan treatment (Buse et al., 2017). Rimegepant, a small molecule calcitonin gene-related peptide (CGRP) receptor antagonist, has demonstrated efficacy in three Phase 3 trials for the acute treatment of migraine with a single oral 75 mg dose. This study characterized the CV safety profile of rimegepant in nonclinical assays and compared results to clinical exposures and experience regarding CV adverse events (AEs).

Methods: Rimegepant's CV safety profile was evaluated using in vitro, ex vivo, and in vivo assays. Nonclinical data were compared to clinical exposures from 75 mg oral rimegepant and to pooled data for on-treatment CV AEs from three Phase 3 trials (Studies 301, 302, 303).

Results: In vitro, rimegepant up to 30 μ M was a weak inhibitor in the human ether-a-go-go related gene (hERG) assay and had no effects on rabbit Purkinje fiber action potentials. This concentration is $>20\times$ the human C_{max} for repeat-dose oral 75 mg rimegepant (1.46 μ M, Phase I Day 14). Ex vivo, rimegepant showed no vasoconstriction of human coronary or cerebral arteries up to 3–10 μ M. In vivo, cynomolgus monkeys receiving 60 mg/kg rimegepant showed exposures (15.5 μ M, 8 hr) $>10\times$ the repeat-dose human C_{max} with no effects on hemodynamic/electrocardiographic parameters, and one month daily dosing showed no changes in CV parameters at $AUC_{[0-24h]}$ of 63,150 ng·h/mL, $\sim 17\times$ the human repeat-dose AUC (3,729 ng·h/mL). Pooled clinical data for on-treatment CV AEs from three Phase 3 trials administering 1,771 rimegepant 75 mg oral doses vs. 1,782 placebo doses showed zero CV AEs.

Conclusion: Nonclinically, rimegepant showed an absence of undesirable CV safety signals at multiples of 10–20 \times (C_{max}) and 17 \times (AUC) the oral 75 mg repeat-dose human exposure. Data from three Phase 3 pivotal trials with oral 75 mg rimegepant ($n = 1,771$) showed zero cases of on-treatment CV AEs. These data highlight an emerging new treatment option for patients with CV contraindications to triptans, oral 75 mg rimegepant.

Disclosure of Interests: Charles M. Conway, PhD, Robert Croop, MD, Gene M. Dubowchik, PhD, and Vladimir Coric, MD are employed by and hold stock/stock options in Biohaven Pharmaceuticals. Richard B. Lipton, MD, serves on the editorial board of Neurology and Cephalalgia and as senior advisor to Headache but is not paid for his roles on Neurology or Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS

and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

IHC-PO-366

Phase I Safety, Tolerability and Pharmacokinetics of Single and Multiple Dose Rimegepant as Compared to the Predicted Clinically Efficacious Dose Range

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Objective: The hand-off from pharmaceutical discovery to clinical development is often challenging, particularly with regard to identifying the target safe and efficacious human dose. The objective of this study was to evaluate the safety, tolerability and pharmacokinetics (PK) of rimegepant in healthy subjects, including identification of a maximum tolerated dose (MTD), as compared to the predicted clinically therapeutic dose range.

Methods: Allometric scaling from discovery assays predicted the therapeutic dose range for acute treatment of migraine to be a single oral dose of 70 to 140 mg rimegepant. The dose range was projected by considering efficacy in the marmoset facial blood flow assay, volume of distribution, plasma clearance and oral bioavailability. On that basis, a Phase I study was designed to evaluate the safety, tolerability and PK of single (SAD) or multiple (MAD) dose rimegepant with the aim of identifying an MTD and selecting doses for Phase 2/3. For SAD, 8 healthy subjects received a single dose (25, 75, 150, 300, 600, 900 or 1,500 mg) of rimegepant or placebo. For MAD, 8 healthy subjects received daily doses (75, 150, 300, 450 or 600 mg) of rimegepant or placebo.

Results: Single doses of rimegepant were well tolerated up to 1,500 mg and likewise multiple doses up to 600 mg for 14 days without serious adverse events (AEs). A maximum tolerated dose was not reached despite achieving exposures that were $>50\times$ higher (C_{max} 20,499 ng/mL and AUC 198,750 ng·h/mL) than those observed near the low predicted therapeutic dose 75 mg (C_{max} 784 ng/mL and AUC 3,729 ng·h/mL).

Conclusion: Rimegepant appeared to be safe and well tolerated over the doses tested in this healthy population, including exposures $>50\times$ beyond the lowest predicted

efficacious dose. In the absence of an MTD, doses below and above the target therapeutic doses (70–140 mg) were selected (25, 75, 150, 300 and 600 mg) for advancement into Phase 2/3 dose ranging clinical trial for the acute treatment of migraine (Study 201).

Disclosure of Interests: Charles M. Conway, PhD, Gene M. Dubowchik, Robert Croop, MD, and Vladimir Coric, MD, are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

IHC-PO-367

Rimegepant 75 mg Is More Effective for Migraine Than Nonsteroidal Anti-inflammatory Drugs: Post Hoc Analysis of Data From 2 Phase 3 Trials

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Objective: Nonsteroidal anti-inflammatory drugs (NSAIDs) and caffeinated analgesics available over-the-counter (OTC) are frequently used for migraine attacks, but can be inadequate for treating migraine and associated symptoms and have potential cardiovascular and gastrointestinal safety issues. Rimegepant is a small molecule calcitonin gene-related peptide receptor antagonist that has demonstrated efficacy and safety in migraine. The objective of this analysis was to compare the efficacy of rimegepant to NSAIDs for the acute treatment of migraine.

Methods: This post hoc analysis used data from 2 double-blind, randomized, placebo-controlled trials (Studies 301 and 302) to compare subjects who took a single dose of rimegepant 75 mg with subjects initially randomized to placebo who used a caffeinated analgesic, ibuprofen, or any NSAID as rescue medication. Kaplan-Meier curves were used to compare the efficacy endpoints of time to first report of pain freedom and time to first report of pain relief. Time to event was calculated from either the dose of rimegepant or the first dose of rescue medication.

Results: Initially, subjects were randomized to rimegepant 75 mg ($n = 1080$) or placebo (1076). Of the subjects initially randomized to placebo, those subjects whose first rescue medication was a caffeinated analgesic ($n = 78$), ibuprofen ($n = 91$), or any NSAID ($n = 241$) were retained for analysis. Over the first 4 hours post-dose, rimegepant was significantly more effective in terms of time to first report of pain freedom than the caffeinated analgesic ($p = 0.0013$), ibuprofen ($p = 0.0037$), and all NSAIDs ($p < 0.0001$). For time to first report of pain relief, rimegepant was also

significantly better than the caffeinated analgesic ($p = 0.0067$), ibuprofen ($p = 0.0223$), and all NSAIDs ($p = 0.0002$).

Conclusion: This post hoc analysis shows rimegepant 75 mg significantly outperformed NSAIDs, including caffeinated analgesics and ibuprofen, as measured by time to first report of pain freedom and time to first report of pain relief.

Disclosure of Interests: Andrew Blumenfeld, MD, serves as a consultant for Alder, Allergan, Amgen, Biohaven, electroCore, Lilly, Novartis, Promius, Supernus, and Teva.

Dawn C. Buse, PhD, has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Lilly, Promius, and Teva. She is on the editorial board of Current Pain and Headache Reports.

Ira M. Turner, MD, has received research support or served as a consultant or member of the advisory board or speakers' bureau for Alder, Allergan, Amgen, ATI, Biohaven, Depomed, ElectroCore, Impax, Lilly, Novartis, Promius, Revance, Supernus, and Teva.

David A. Stock, PhD, Beth Morris, BA, Vladimir Coric, MD, and Robert Croop, MD are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

IHC-PO-368

Paracetamol vs Ibuprofen for the Acute Treatment of Migraine Headache in Children: A Randomized Controlled Trial

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Objective: To compare the number of children achieving Pain-freedom at 2 hours after either oral Paracetamol or oral Ibuprofen for acute treatment of migraine headache.

Methods: We included 50 children (aged 6 to 12 years) with Migraine without aura as per International Classification for Headache Disorders (ICHD-3) criteria, after IEC clearance and informed written consent. Patients were randomized by block randomization to the two study groups, with one group ($n = 25$) receiving oral paracetamol and the other group ($n = 25$) oral ibuprofen, at home, during an episode of acute migraine headache. The study drugs were dispensed in a blinded fashion, and the outcome assessor and the statistician were unaware of the group allocation.

Pain-freedom (score of zero in an 11-point Visual analogue pain scale) and Pain-relief (≥ 2 point reduction from baseline in 11-point VAS) two hours after the study drug were the main outcome measures. All analyses were Intention-to-treat.

Results: Forty three children (22 paracetamol group, 21 ibuprofen group) completed the study. The two groups were similar at baseline with respect to age, sex, headache severity and disability.

Overall 15 (34.9%) children achieved Pain-freedom and 40 (93%) children achieved pain-relief two hours after the study drug intake. Both pain-freedom (32% vs 28%, $P=0.77$) and pain-relief (80% vs 80%, $P=0.86$) were not different between the Paracetamol and Ibuprofen groups, respectively.

Relief was seen in all associated symptoms viz., photophobia (37, 92.5%), phonophobia (37, 92.5%), nausea (26, 92.8%), and vomiting (16, 94.1%); the response was similar in the two groups. Ten (23.2%) children had a mild side-effect due to the study drug; there was no statistically significant difference between the groups (13.6% vs 33.3%; $P=0.11$).

Conclusion: Our results indicate that both Paracetamol and Ibuprofen may be considered equi-efficacious as first line drugs in the treatment of an acute migraine attack in children.

Disclosure of Interest: None Declared.

IHC-PO-369

Gastrointestinal Comorbidities Representing a Relative Contraindication to NSAID Use: Results From the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study

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Objective: To assess the frequency of gastrointestinal comorbidities (GICs) that cause relative contraindications to NSAID use in persons with migraine and to evaluate patterns of acute medication use by those with and without these GICs.

Methods: In the Chronic Migraine Epidemiology and Outcomes (CaMEO) study, we characterized respondents meeting modified *International Classification of Headache Disorders, 3rd edition* criteria for migraine with respect to 3 self-reported (SR) GICs to NSAIDs: gastroesophageal reflux disease (GERD), peptic ulcer disease, and ulcerative colitis or Crohn's disease (inflammatory bowel disease [IBD]). Acute medication use for migraine among respondents with and without ≥ 1 GIC was also evaluated.

Results: There were 12,810 respondents with migraine eligible for this analysis. At least one GIC to NSAIDs was reported by 1845 (14.4%) respondents, including treated

Abstract number: IHC-PO-369

Table 1. Acute Medication Use by Presence of GI Comorbidities (GICs)

Medication, n (%)	No GIC (n = 10,965)	GIC (n = 1845)
NSAID (any)	6626 (60.4)	1153 (62.5)
NSAID (Rx)	1047 (9.5)	321 (17.4)*
Barbiturate	268 (2.4)	106 (5.7)*
Ergotamine	51 (0.5)	23 (1.2)*
Opioid	1031 (9.4)	398 (21.6)*
Triptan	1149 (10.5)	298 (16.2)*
Barbiturate, opioid, or NSAID (Rx)	1953 (17.8)	642 (34.8)*

* $P < 0.0001$.

GERD (11.0%), SR diagnosed ulcer (4.0%), and SR diagnosed IBD (1.3%). Acute medication use by those with and without GICs is summarized in the **Table**.

Conclusion: A substantial proportion of respondents with migraine (14.4%) reported ≥ 1 GIC to NSAIDs; as not all GICs were captured and as we relied on self-report, this likely represents a lower bound estimate. NSAIDs were the most widely used acute treatment for migraine. Triptan use was 1.5 times greater in those with GICs, likely reflecting appropriate prescribing. Barbiturate use and opioid use were each 2.3 times more common in persons with GICs; as these are not recommended treatment options, this may reflect the lack of availability of better options. The use of NSAIDs in participants with GICs may also reflect the lack of availability of better options.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

Author Disclosures:

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Stephanie J. Nahas, MD, MEd, FAHS, FAAN, has served as consultant, advisory board member, or speaker for Allergan, Amgen, Biohaven, electroCore, Eli Lilly, Supernus, and Teva. She has received author/editor honoraria from Demos Medical, MedLink Neurology, and UpToDate.

Kristina M. Fanning, PhD, is an employee of Vedanta Research, which has received research funding from Allergan, Amgen, Dr. Reddy's Laboratories, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Novartis, via grants to the National Headache Foundation. Vedanta has received funding directly from Allergan for work on the CaMEO Study.

Michael L. Reed, PhD, is Managing Director of Vedanta Research, which has received research funding from Allergan, Amgen, Dr. Reddy's Laboratories, Eli Lilly, GlaxoSmithKline, Merck & Co., Inc., and Novartis, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study.

Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company.

Richard B. Lipton, MD, serves on the editorial boards of *Neurology* and *Cephalalgia* and as senior advisor to Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS; serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from *Wolff's Headache, 8th Edition* (Oxford University Press, 2009), and Informa. He holds stock options in eNeura Therapeutics and Biohaven.

IHC-PO-370

Oxygen delivered by a high flow concentrator for the treatment of medication-overuse headache: a prospective open labeled pilot feasibility study

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Objective: Treatment of medication-overuse headache (MOH) relies on detoxification, during which patients face rebound headache without alternative to painkiller. As oxygen has been proven effective for cluster and other headache subtypes, we sought to evaluate use of normobaric oxygen delivered by a high flow concentrator (HFC) in patients suffering MOH.

Methods: Twenty patients with MOH were included in this prospective monocentric open labeled feasibility study (Clinicaltrials NCT02302027). All patients received standard care with detoxification in addition to HFC delivering normobaric oxygen at 9l/min, used to their discretion to treat rebound headache. Primary endpoint was acceptance of HFC and secondary endpoints evaluated its efficacy.

Results: Four patients were lost of follow-up after inclusion, one was excluded.

HFC was accepted by 14/15 (93.3%). At M6 of follow-up, 15/15 (100%) reverted to episodic headache.

Conclusion: Normobaric oxygen delivered by HFC appears to be safe, feasible and probably efficient to help patient with MOH who undergo withdrawal therapy. A larger double-blind, sham-controlled prospective study is needed.

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Dominique Valade received received travel, accommodation and meeting expenses from Adep assistance and a punctual payment for consultancy from Air Liquide.

Marie Vigan and Cedric Laouenan declare no financial conflict of interest.

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IHC-PO-371

Acute Treatment Administered Early May Improve Episodic Migraine Outcomes

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Objective: Most data supporting acute treatment given early when migraine is mild are for triptans, which generally require a prescription but are available over the counter (OTC) in some markets. OTC analgesics offer immediate access, but data regarding their use early are limited. Expanded access to triptans and further research with OTC treatments could improve the rationale for early use.

Methods: Literature review using Embase, Medline, and Cochrane Library (database inception through February 2019) to identify clinical studies, cost-effectiveness analyses, or systematic reviews evaluating early use of acute treatments in adults with episodic migraine.

Results: We identified 52 relevant papers on acute treatment administered early for episodic migraine; 50 with triptans. The triptan studies consistently reported a benefit with treatment of early migraine (generally ≤ 1 h from pain onset while pain was mild) vs treatment when

migraine was moderate/severe. A study with acetylsalicylic acid + paracetamol + caffeine also suggested an increased benefit with early migraine treatment. These results suggest that earlier treatment may blunt or stop migraine progression. Early vs late use of acute treatments was compared in 24 studies, with varying definitions of early administration: ≤ 1 h from pain onset, while the pain was mild (17 studies); ≤ 2 h from pain onset, while the pain was mild (1 study); by mild vs moderate/severe pain (3 studies); not defined (3 studies). Better efficacy outcomes (pain-free rates at 2 h and sustained pain-free rates at 24 h) were reported with earlier use in 20 of 21 studies. Three health economic studies of early vs late use showed that early use reduced treatment costs and productivity loss. One study reported up to 57% reduction in the average cost per pain-free treatment success for migraines treated while pain was mild vs moderate/severe. Another study reported a 92% probability of early treatment providing overall cost savings from a societal perspective.

Conclusion: Clinical efficacy benefits and improvement in quality of life/productivity were observed with early use of acute treatments for episodic migraine.

Disclosure of Interests: All authors are employees of GlaxoSmithKline Consumer Healthcare Companies.

IHC-PO-372

Traditional chinese medicine YangXueQingNao granular treatment for acute migraine

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Objective: YangXueQingNao granular, a traditional chinese medicine, is used for headache no matter what style. The primary aim of this study was to evaluate the efficacy of YangXueQingNao granular for acute migraine patients.

Methods: This was a retrospective study and we reviewed 328 patients captured data of consecutive adult

patients with acute migraine in the headache center of department of neurology at the second hospital of Jilin University between January 2017 and December 2017. All patients were given one granular every time and took three times one day for two weeks. The pain severity was limited for mild and moderate. Visual analogur scale was assessed the pain severity (VAS < 7). The efficiency of YangXueQingNao granular was evaluated with decrease of headache hours and pain severity. All patients were explored laboratory measurements, brain magnetic resonance imaging (MRI). The data entered and analyzed on SPSS 16 software.

Results: The pain severity of YangXueQingNao granular preventive acute migraine was assessed by VAS. The VAS were decreased during the first week of therapy, a benefit that was maintained through the second week ($p < 0.05$). The pain duration was limited in the second week ($p < 0.05$).

Conclusion: Oral traditional chinese medicine (YangXueQingNao granular) was effective for pain severity and pain duration in acute migraine treatment. We sought to provide a new therapy of traditional chinese medicine for the clinical management.

Disclosure of Interest: None Declared.

IHC-PO-373

Non-Invasive, Automated Variable Pressure Insufflation (AVPI) of the Ear for Acute Migraine Treatment – Clinical Pilot Study

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Abstract number: IHC-PO-373

HEADACHE PAIN RESPONSE		Pre-Tx	0 Hrs Post-Tx	2 Hrs Post-Tx	24 Hrs Post-Tx
SCORES	Active	7.2 ± 1.3	1.4 ± 2.2	1.1 ± 1.8	0.8 ± 1.6
	Sham	6.9 ± 1.4	5.1 ± 2.8	4.5 ± 2.7	2.6 ± 2.2
	<i>p-value</i>	0.40	<.005	<.005	<.005
FREEDOM (PFR) (%) ¹	Active		60.0	66.7	50.0
	Sham		6.9	10.3	0.0
≥50% RELIEF (HRR) (%) ¹	Active		90.0	93.3	90.0
	Sham		31.0	44.8	37.9

¹24 Hr post-Tx = sustained from 2 Hr.

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Objective: Evaluate the clinical safety & effectiveness of a novel AVPI device for acute migraine treatment (Tx).

Methods: 59 episodic migraine patients were enrolled under informed consent in this IRB-approved, prospective, single-blind, randomized study comparing Active AVPI Tx (n = 30) vs Sham control Tx (n = 29) for moderate-severe migraines. Active used an investigational AVPI device [Nocira[®], LLC; sponsor] for unilateral ear pressure modulation. Sham used a modified AVPI device to deliver sounds without pressure. Tx was conducted by an investigator for 20 min. Patient demographics & headache characteristics were recorded pre-Tx. Patient-reported scores (0–10) for headache pain (P), & other associated nausea & photo/phonophobia symptoms (AS), were recorded pre-Tx & 0, 2, 24 hrs post-Tx. Primary endpoint: P freedom (F) rate (PFR) at 2 hrs. Secondary endpoint: 24 hr sustained PFR. Patient satisfaction & adverse events (AEs) were recorded post-Tx. Score distributions, & $\geq 50\%$ response rates (RR) in P (HRR) & AS scores, were evaluated & compared between groups & longitudinally.

Results: Active/Sham groups had similar% women (80,72), & non-significantly different (NS) for (overall): age (42.4 ± 11.8), hrs from P onset to Tx (16.5 ± 32.7), & pre-Tx P scores (Table). Both groups had significant P score reduction from pre-Tx to each post-Tx point ($p < .005$). However, at all post-Tx points, Active had (vs. Sham, $p < .005$): lower P scores, higher PFR & HRR, & greater P score reduction from pre-Tx (Table). Active/Sham AS scores were NS (but Active had >1 point higher photophobia, $p = .02$) pre-Tx; but were lower for Active ($p < .005$) at all post-Tx points (but 24 hr nausea = NS). Active had $>2x$ higher F & RR for all AS at all post-Tx times. 93% of Active patients reported a comfortable Tx. No significant AEs were reported.

Conclusion: AVPI Tx of moderate-severe migraines, during advanced headache stage typically considered Tx-resistant, was safe, well-tolerated, comfortable, & highly effective for rapid relief of P & AS in this study.

Disclosure of Interests: The following co-authors have no interest to report: Douville A, Carrick F, Oggero E. The following co-authors have the following interests in Nocira LLC (study sponsor): (A) Stock Ownership – George D, Buckler G, Peacock J, Walker M, Pagnacco G; (B) Salaried management – George D, Peacock J; (C) Hourly consulting fees – Walker M, Benz R.

IHC-PO-374

Rimegepant 75 mg Demonstrates Superiority to Placebo on Nausea Freedom: Results from a Post Hoc Pooled Analysis of 3 Phase 3 Trials in the Acute Treatment of Migraine

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Objective: Rimegepant is a small molecule CGRP receptor antagonist with demonstrated efficacy in the acute treatment of migraine. Because nausea is less common than photophobia and phonophobia, power for detecting differences in nausea freedom in individual rimegepant clinical trials was relatively low. The objective of the present study was to determine the effect of rimegepant 75 mg on nausea freedom at 2 hours postdose by pooling data across 3 clinical trials for the acute treatment of migraine.

Methods: Three double-blind, randomized, placebo-controlled, multicenter, Phase 3 clinical trials in adults with migraine were conducted: 2 evaluated rimegepant 75 mg oral tablet (Studies 301&302), and 1 evaluated rimegepant 75 mg ODT (Study 303). Subjects randomized 1:1 to rimegepant or placebo treated 1 migraine attack of moderate or severe pain intensity. The coprimary endpoints were 2-hour freedom from pain and the most bothersome symptom (MBS). Secondary endpoints included freedom from nausea at 2 hours postdose. Data for 2-hour nausea freedom were pooled across all 3 trials and analyzed.

Results: Altogether, 3507 subjects were evaluated for efficacy (rimegepant 75 mg n = 1749, placebo n = 1758). In each trial, rimegepant 75 mg was superior to placebo on 2-hour freedom from pain and the MBS, as well as on 2-hour freedom from photophobia and phonophobia. In the pooled analysis, rimegepant 75 mg was superior to placebo on nausea freedom at 2 hours postdose (48.9% vs 43.5%, $p = .0128$).

Conclusion: Pooled data show that rimegepant 75 mg is more effective than placebo for migraine-associated nausea. Populations in the individual trials were likely too small to detect the therapeutic gain. These results demonstrate the positive effects of rimegepant on migraine-associated nausea and further define the efficacy profile of rimegepant in the acute treatment of migraine.

Disclosure of Interests: Peter McAllister, MD, has received research support from Amgen, Alder, Lilly,

Biohaven, Allergan, Electrocore, Novartis, and Teva. He has received fees for consulting/speakers bureau from Amgen, Lilly, Teva, Biohaven, Xoc, and Allergan.

Gary Berman, MD, has received fees for speaker's bureau from Amgen and for consulting from Alder.

David Kudrow, MD, has received fees for advisory board from Alder, Biohaven, Eli Lilly, Amgen, and Xoc and for speaker's bureau from Xoc, Teva, Amgen, Novartis, and Eli Lilly. He has also received research support from Amgen, Novartis, Eli Lilly, Teva, Alder, Biohaven, Biogen, and Roche-Genentech.

Timothy Smith, MD, has received fees for speaker's bureau from Amgen, Novartis, Lilly, and Promius and for advisory boards or consultancies from Biohaven, Amgen, Lilly, Alder, Promius, and Zosano. He has received research support from Amgen, Alder, Lilly, Teva, Allergan, Biohaven, Dr. Reddy's, Zosano, Electrocore, Scion Neurostim, Novartis, Novo Nordisk, Ionis, and Impel.

Robert Croop, MD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Vladimir Coric, MD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

David A. Stock, PhD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Richard B. Lipton, MD, serves on the editorial board of *Neurology* and *Cephalalgia* and as senior advisor to Headache but is not paid for his roles on *Neurology* or *Headache*. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He receives research grants from Allergan, Amgen, Dr. Reddy's Laboratories, and Novartis. He has reviewed for the NIA and NINDS and serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven Pharmaceuticals, Boston Scientific, CoLucid, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's *Headache* (8th Edition, Oxford Press University, 2009) and Informa. He holds stock options in eNeura Therapeutics and Biohaven Pharmaceuticals.

IHC-PO-375

Intravenous chlorpromazine in chronic headache

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Objective: To analyze the efficacy of intravenous chlorpromazine (IVC) for the treatment of patients with chronic headache (CH).

The term CH is used when the headache frequency is ≥ 15 days/month for longer than three months. It affects 1–4% of the general population. It is frequently associated with medication overuse headache (MOH) and psychiatric morbidity. To date, there is scarce evidence about the best treatment strategy for these patients.

Methods: A retrospective review of medical records of patients with CH followed in our institution who required at least one hospitalization for IVC administration was done. Demographic and clinical characteristics, dose of chlorpromazine, frequency of emergency consultations, and preventive treatment, were analyzed in each case.

A multivariate Poisson regression model of random coefficients was used to estimate the effect of the intervention in terms of hospital visits.

Results: We reviewed 35 medical records of patients with CH, 30 female and 5 male, with a median age of 42 years (range: 19 to 72 years). 94% of those patients also had MOH, with a median of 12 months of medication overuse (range: 3 months to 22 years). The most overused drugs were non steroidal anti inflammatory drugs (74% of patients).

Chlorpromazine was administered during an average of 3.4 days (range: 1 to 5 days). No serious adverse effects were reported. During hospitalization, 71% of patients switched or initiated preventive treatment.

Incidence rate ratio of emergency consultations after IV chlorpromazine was 0.28 (95% CI 0.12–0.69, $p = 0.009$), demonstrating a decrease of 72% in emergency visits. Furthermore, there was a 76% reduction of pain intensity at discharge measured in a scale of 1 to 10 ($p < 0.0001$) and 59% of patients did not qualify as CH three months after inpatient treatment.

Conclusion: To the best of our knowledge, this is the first case series that evaluated the use of IVC for inpatient treatment of CH. According to our results, IVC could be an effective and safe strategy for CH and MOH patients alongside additional measures of treatment of CH, leading to a drastical reduction in the need of future emergency consultations.

Our observations should be confirmed by prospective multicentric randomized clinical trials.

Disclosure of Interest: None Declared.

IHC-PO-376

Follow-up of patients with migraine receiving injection of sumatriptan at Emergency Room

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Objective: Subcutaneous injection of sumatriptan has been recommended for the acute treatment of migraine in the past twenty years in Japan. We studied the motivation and the state of headache of patients with migraine who visited the Emergency Room (ER) of our hospital. In this study, we made a follow-up analysis of patients with migraine who received sumatriptan subcutaneous injection for the first time at our emergency room.

Methods: Ota Memorial Hospital is a core municipal hospital accepting emergency patients all day from a medical area with the population of 400,000. In this retrospective study, patients with headache who visited ER and were injected sumatriptan were extracted from the electronic medical record system during the year of 2014 to 2018. The age of onset of migraine, diagnosis of migraine, treatment with triptan, family history of migraine, aura, introduction of self-injection and visits to ER were examined.

Results: In the past 5 years, 121 patients with migraine received injection of sumatriptan. Patients were 31 men and 90 women, with the average age of 35.9 years. Seventeen patients came by ambulance. Twenty-five patients had been diagnosed as migraine and 20 were treated with triptan before their visit to ER. In the ER situation it was often difficult to confirm detailed family history or presence of aura, but there were 27 people with family history. There were 21 patients with aura, 36 people without aura. The age of onset of headache was during elementary school in 13 patients, middle and high school years in 17, above the age of 20 years in 16 patients. Forty-two patients were instructed to visit our headache clinic (who did not visit) and 18 were instructed to consult a family doctor. Nine patients started self-injection of sumatriptan at headache clinic.

Conclusion: Many patients with migraine visit ER because of severe headache. Our study showed many of them had not been diagnosed as migraine or given triptan. Public awareness that migraine is a disease to be treated is still low. It is necessary to strengthen continuing education of general practitioners for the diagnosis and treatment of migraine. In addition, it is important to continue research on migraine prevention and development of therapeutic strategies.

Disclosure of Interest: None Declared.

IHC-PO-377

STOP 301: Open-label Safety and Tolerability of Chronic Intermittent Usage for 24/52 Weeks of INP104 [Nasal Dihydroergotamine Mesylate (DHE) Administered by Precision Olfactory Delivery (PODTM) Device] in Migraine Headache

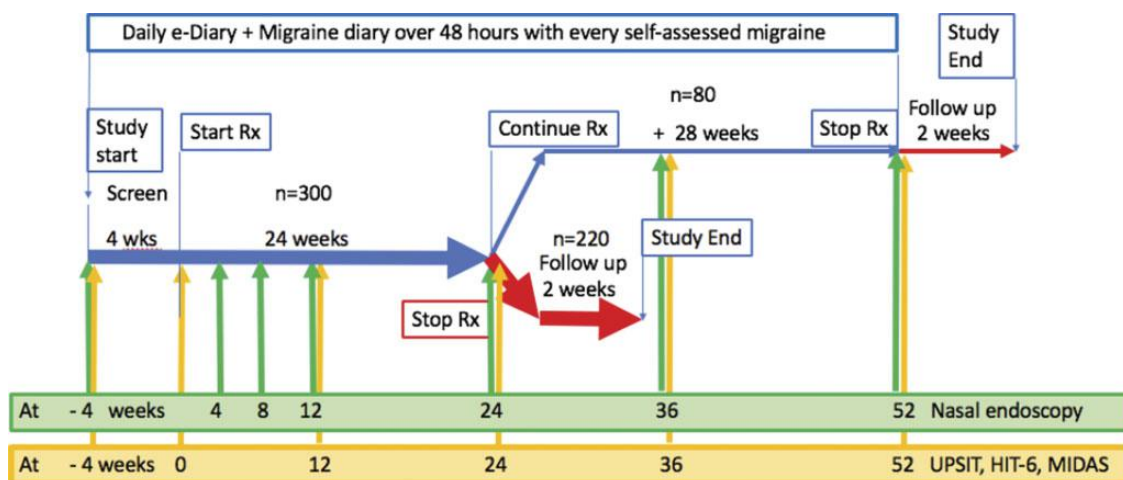
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Objective: 1) Establish safety and tolerability of repeated INP104 exposure 2) Explore efficacy of INP104 in migrainers (compared to baseline) 3) Explore INP104 effects on Quality of Life and Healthcare Utilisation during the 24/52 weeks.

Methods: ~300 patients will enter the 24-week study, with ~80 enrolling into a further 28-week treatment period. Main inclusion criteria: 18 to 65 years; migraine with or without aura, ³2 attacks/month for previous 6 months; >80% e-diary compliance; contracepting. Main exclusion criteria: trigeminal autonomic cephalalgias;



Abstract number: IHC-PO-377

migraine aura without headache, hemiplegic migraine or migraine with brainstem aura; chronic migraines, medication overuse headache or other chronic headache syndromes; status migrainosus; coronary artery disease (CAD) or significant risk of CAD; abnormal, clinically significant laboratory tests at screening; recent acute illness or uncontrolled infection; recurrent sinusitis or epistaxis; significant pre-existing nasal disease or upper space mucosal abnormality; excessive triptan or ergot use; significant use of barbiturates or opiates in 2 months prior or during screening.

All subjects will have extensive migraine history, healthcare utilization and quality of life assessments conducted during screening and treatment response recorded in an e-diary. Olfactory mucosal integrity and function will be collected by endoscopy of the upper (and lower) nasal spaces and by University of Pennsylvania Smell Identification Test (UPSIT) at intervals.

Results: As a result of the strategic considerations and to achieve the objectives of the study, the study design was formulated (see image).

Conclusion: STOP 301 is designed to assess safety, tolerability and explore efficacy of repeat administration of DHE drug to the upper nasal space.

Disclosure of Interest: None Declared.

IHC-PO-378

Migraine; The greatest disability of all in Australia

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Objective: Migraine is the leading cause of adult disability in Australia beating stroke and dementia as second and third leading causes of adult disability (1). The nature of invisible disability, lack of a biomarker, strong nonmedical lay model of headache and stress, headache and hormones, headache and poor work place (misdiagnosis of migraine as stress related, hormone related etc.) lead this disabling disorder to be the most neglected, most underdiagnosed medical disorder worldwide(2).

Methods: The fascinating entity of late life migraine accompaniments (LLMA) is one of the critically important stroke mimics in neurological emergencies(3–7). Difficulty in differentiation of migraine from vascular insults such as stroke, transient ischemic attacks and amyloid angiopathy make this an important public health problem. Migraine is more than just a headache. The Deloitte Access Economics reports on “Migraine in Australia Whitepaper reveals burden of migraine on 4.9 million Australians and

\$35.7 billion cost to the economy annually(8). Australian people with migraine and their families pay it themselves over \$2.2 billion of health system costs every year (8). Australians suffering regular migraines often resort to hospital care with up to one third of these patients presenting to emergency departments at least once every three months(9). Hospital admissions and emergency department visits together make up a very high proportion of health system expenditure at \$6.8 billion every year(8). Nearly 90% of Australian people with migraine are of working age with significant impact on productivity as a result of up to eight months of migraine days per year. In 2018, the total economic cost of migraine in Australia is estimated as \$35.7 billion (\$14.3 billion of health system costs, \$16.3 billion of productivity costs and \$5.1 billion of other financial costs such as reduced carer productivity, loss of wellbeing, loss of efficiency)(8). Despite this huge tax hole in the budget, the amount of research funding for migraine remains low.

Results: N/A.

Conclusion: The National Health and Medical Research Council (NHMRC) is Australia’s leading expert body promoting the development and maintenance of public and individual health standards. The NHMRC has allocated less than 0.09% of its total funding towards research in migraine during the last ten years (Table 1). It is critically important to address this gross injustice now. We make the strongest argument to raise funding for targeted migraine research as there are many unanswered questions about migraine, and little effective treatment for a disorder that causes personal, and societal havoc for millions(10).

Disclosure of Interest: None Declared.

Migraine Preventive Therapy

IHC-PO-137

Early onset of response to fremanezumab in migraine patients with moderate to severe depression and documented inadequate response to 2–4 classes of migraine preventive treatments: subgroup analysis of the randomised, placebo-controlled FOCUS study

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Objective: Fremanezumab is a fully-humanised monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide (CGRP). The FOCUS study of fremanezumab was the first and largest study of a migraine preventive treatment in adults with both chronic and episodic migraine (CM and EM) and documented inadequate response to 2–4 classes of migraine preventive medications. A post hoc subgroup analysis evaluated early efficacy in patients (pts) with moderate to severe depression (Patient Health Questionnaire [PHQ-9] score ≥ 10).

Methods: Pts were randomised (1:1:1) to quarterly (qtlly) fremanezumab (Month [Mo] 1: 675 mg; Mo 2 and 3: placebo), monthly (mthly) fremanezumab (Mo 1: CM, 675 mg; EM, 225 mg; Mo 2 and 3: 225 mg), or matched mthly placebo (PBO) for 12 weeks (wks). Changes from baseline (BL) in weekly (wkly) migraine and headache days were evaluated during Wks 1–3.

Results: Of 838 randomised pts, 154 had moderate to severe depression at BL. Reductions from BL in wkly migraine days were significantly greater with fremanezumab (LSM[SE] change: qtlly, $-0.9[0.29]$; mthly, $-0.6[0.30]$) vs PBO ($0.3[0.33]$) by Wk 1 and at each wkly time point through Wk 3 (all $P < 0.05$). Reductions from BL in wkly headache days of at least moderate severity were significantly greater with fremanezumab (qtlly, $-1.1[0.32]$; mthly, $-0.9[0.33]$) vs PBO ($0.0[0.36]$) by Wk 1 and at each wkly time point through Wk 3 (all $P < 0.05$).

Conclusion: Fremanezumab demonstrated early onset of efficacy in pts who would traditionally be considered difficult to manage in that they had failed on 2–4 migraine preventive medications and also had moderate to severe depression. Significantly greater reductions from BL in wkly migraine and headache days were achieved as early as Wk 1 with fremanezumab vs PBO.

Disclosure of Interests: A. Blumenfeld has nothing to disclose. R. Yang, J. M. Cohen, and V. Ramirez-Campos are employees of Teva Pharmaceuticals. P. Pozo Rosich has received honoraria as a consultant and speaker for: Allergan, Almirall, Chiesi, Eli Lilly, Novartis and Teva. P. Pozo-Rosich's research group has received research grants from Allergan and has received funding for clinical trials from Alder, Electrocore, Eli Lilly, Novartis and Teva. P. Pozo-Rosich does not own stocks from any pharmaceutical company.

IHC-PO-138

Efficacy with fremanezumab in migraine patients with comorbid moderate to severe depression and documented inadequate response to 2–4 classes of migraine preventive treatments: subgroup analysis of the randomised, placebo-controlled FOCUS study

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Objective: The FOCUS study of fremanezumab, a fully-humanised monoclonal antibody (IgG2 Δ a) that selectively targets the calcitonin gene-related peptide (CGRP), was the first and largest study of a migraine preventive treatment in adults with both chronic and episodic migraine (CM and EM) and documented inadequate response to 2–4 classes of migraine preventive medications. A post hoc subgroup analysis evaluated efficacy in patients (pts) with comorbid moderate to severe depression (Patient Health Questionnaire-9 score ≥ 10).

Methods: Pts were randomised (1:1:1) to quarterly (qtlly) fremanezumab (Month [Mo] 1: 675 mg; Mo 2 and 3: placebo [PBO]), monthly (mthly) fremanezumab (Mo 1: CM, 675 mg; EM, 225 mg; Mo 2 and 3: 225 mg), or matched mthly PBO for 12 weeks (wks). Changes from baseline (BL) in mthly average migraine and headache days of at least moderate severity were evaluated in pts with moderate to severe depression. Pts with significant psychiatric issues (eg, major depression) that, in the investigator's opinion, would compromise the pt's ability to participate in the study were excluded.

Results: Of 838 randomised pts, 154 had moderate to severe depression and were included in these analyses. Reductions from BL in mthly average migraine days were significantly greater with fremanezumab vs PBO at 4 wks (LSM[SE] change: qtlly, $-3.5[0.91]$; mthly, $-3.5[0.95]$ vs $0.9[1.03]$; $P < 0.001$) and 12 wks (qtlly, $-3.2[0.93]$; mthly, $-3.9[0.97]$ vs $0.2[1.05]$; $P < 0.01$). Reductions from BL in mthly average headache days were significantly greater with fremanezumab vs PBO at 4 wks (qtlly, $-4.5[1.01]$; mthly, $-4.5[1.07]$ vs $-0.1[1.16]$; $P \leq 0.001$) and 12 wks (qtlly, $-4.3[1.01]$; mthly, $-4.7[1.06]$ vs $-0.8[1.15]$; $P < 0.01$).

Conclusion: Fremanezumab demonstrated efficacy, based on reductions in mthly migraine and headache days, vs PBO in pts with migraine, moderate to severe depression,

and inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: R. B. Lipton is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. Dr. Lipton receives research support from the NIH: 2PO1 AG003949 (mPI), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), IRF1 AG057531 (Site PI), RF1 AG054548 (Investigator), IRO1 AG048642 (Investigator), R56 AG057548 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor), IK01AG054700 (Mentor). Dr. Lipton also receives support from the Migraine Research Foundation and the National Headache Foundation. Dr. Lipton serves on the editorial board of *Neurology*, senior advisor to Headache, and associate editor to *Cephalalgia*. Dr. Lipton has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. Dr. Lipton receives royalties from Wolff's *Headache* 7th and 8th Edition, Oxford Press University, 2009, Wiley and Informa. J. M. Cohen, V. Ramirez-Campos, R. Yang, X. Ning, and M. Galic are employees of Teva Pharmaceuticals. D. C. Buse has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Lilly, Promieus and Teva. D. C. Buse is on the editorial board of *Current Pain and Headache Reports*.

Disclosure of Interest: None Declared.

IHC-PO-139

Temporal Response Patterns to Erenumab in Patients with Chronic Migraine

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Objective: To evaluate the timing of response to continued erenumab treatment in patients with chronic migraine (CM).

Methods: This was a post-hoc analysis of data from a pivotal study of erenumab in patients with CM (NCT02066415). A $\geq 50\%$ reduction from baseline in monthly migraine days (MMD) was used to define a response. Time-to-event analyses was conducted for patients who achieved a response to erenumab in any study month. An initial responder is defined as a patient who achieved a $\geq 50\%$ reduction in MMD at Month 1. For those who were not initial responders, we analysed the likelihood of responding to erenumab in subsequent months. Patients who were not initial responders were

Patients who were	Erenumab 70 mg	Erenumab 140 mg
not initial responder		
Modest reduction in MMD at Month 1	31 (45/143)	25 (34/134)
No/limited reduction in MMD at Month 1	69 (98/143)	75 (100/134)
Response during Months 2 and/or 3	44 (63/143)	36 (48/134)

Data presented as % (n/N1). n = Responders; N1 = Number of subjects who did not achieve at least 50% reduction in MMD at Month 1. MMD, monthly migraine days.

classified as having modest ($\geq 30\%$ to $< 50\%$) or no/limited ($< 30\%$) reductions in MMD.

Assessment of response with continued erenumab treatment.

Results: The initial responders were 24% (45/188) and 28% (53/187) of patients in erenumab 70 and 140 mg groups; 57% and 54%, achieved a response at least once during the 3-month study, with a median time to first response of 2 (1, 2) and 1 (1, 2) months, respectively. The proportion of patients who achieved a response increased over time with continued treatment (Table). Among patients who initially achieved a modest reduction in MMD, 64% (29/45) in the erenumab 70 mg group and 79% (27/34) in the erenumab 140 mg group achieved a response during the Months 2 and/or 3 of treatment.

Conclusion: Patients with CM who do not have an initial response to erenumab may experience improvement during subsequent months of continued treatment. Clinical benefit from preventive medications may take time to achieve, and an adequate duration of preventive treatment should be considered before assessing therapeutic outcome. The results of our analysis support recent guidance from the American Headache Society that recommends 3 months of assessment following initiation of migraine preventive treatment.

Disclosure of Interests: This study was supported by Amgen Inc., Thousand Oaks, CA, USA. Erenumab is co-developed by Amgen and Novartis. Stewart J. Tepper –

consulting fees: Acorda, Alder, Alexsa, Allergan, AlphaSights, Amgen, ATI, Axsome Therapeutics, Cefaly, Charleston Labs, DeepBench, electroCore, eNeura, ExpertConnect, GLG, Guidepoint Global, GSK, Impel, M3 Global Research, Magellan Rx Management, Medicxi, Navigant Consulting, Neurolied, Nordic BioTech, Novartis, Reckner Healthcare, Relevale, Satsuma, Scion NeuroStim, Slingshot Insights, Sorrento, Sudler and Hennessey, Teva, Theranica, Trinity Partners, XOC and Zosano; advisory board: Acorda, Alder, Allergan, Amgen, ATI, Biohaven, Charleston Labs, Dr. Reddy's, GSK, Impel, Novartis, Pfizer, Satsuma, Supernus, XOC and Zosano; research grants: Alder, Allergan, Amgen, ATI, Dr. Reddy's, electroCore, eNeura, Neurolied, Novartis, Scion NeuroStim, Teva and Zosano; board of directors: American Headache Society; royalties: Springer; stock options: ATI; employee: Dartmouth-Hitchcock Medical Center, Headache Currents and American Headache Society. Sylvia Lucas – consulting fees: Eli Lilly; advisory board: Amgen and Teva. Messoud Ashina – consulting/speakers' fees: Allergan, Amgen, Alder, Novartis, Eli Lilly and Teva; advisory board: Allergan, Amgen, Eli Lilly, Novartis and Teva; and research support: Allergan, Amgen, Alder and electroCore. Todd J. Schwedt – consulting fees: Alder, Allergan, Amgen, Avanir, Cipla, Dr. Reddy's, Eli Lilly, Ipsen Bioscience, Nocira, Novartis, Second Opinion and Teva; stocks, stock options: Aural Analytics, Second Opinion and Nocira; board member – American Headache Society and American Academy of Pain Medicine. Jessica Ailani – consulting/speakers' fees: Alder, Allergan, Amgen, Avanir, electroCore, Eli Lilly, Impel, Promius, and Teva; Section Editor: Current Pain and Headache Reports. Jan Klatt – employee and stocks: Novartis. James V. Scanlon, Denise E. Chou, Sharon Richards and Gabriel Paiva da Silva Lima – employees and stocks: Amgen.

IHC-PO-140

Sustained Response to Erenumab over Time in Patients with Chronic Migraine

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Objective: To evaluate whether initial responses to erenumab in patients with chronic migraine (CM) are maintained and improved with continued treatment.

Methods: This was a post-hoc analysis of data from a pivotal study of erenumab in patients with CM (NCT02066415). An analysis of response was conducted in the subset of patients who achieved a $\geq 50\%$ reduction in monthly migraine days (MMD) from baseline during the first month of treatment (initial responders). Sustained responses among initial responders were assessed at Months 2 and 3. During continued treatment, initial responders were classified as having an excellent ($\geq 75\%$ reduction in MMD) or good (50% to $< 75\%$ reduction in MMD) response. Patients were also assessed for modest (≥ 30 to $< 50\%$) reductions in MMD.

Results: The initial responders were 24% (45/188) and 28% (53/187) of patients in erenumab 70 and 140 mg groups, and 57% (108/188) and 54% (101/187) responded at least once through Month 3, respectively. Among the subset of initial responders who received erenumab 70 mg or 140 mg, 49% (22/45) and 70% (37/53), respectively, maintained a good or excellent response at Months 2 and 3; 84% (38/45) and 91% (48/53) achieved a good or excellent response at Months 2 or 3. Furthermore, 18% (8/45) and 32% (17/53) achieved an excellent response throughout all 3 months, and 56% (25/45) and 59% (31/53) achieved an excellent response at Months 2 or 3. Of the patients who were not initial responders and had modest reduction in MMD at Month 1, 64% (29/45) and 79% (27/34) achieved a good or excellent response at Months 2 or 3 with continued erenumab 70 and 140 mg treatment, respectively.

Conclusion: The majority of erenumab-treated patients with CM who achieved initial modest, good, or excellent reductions in MMD at Month 1 experienced sustained or improved clinical benefit with continued erenumab treatment.

Disclosure of Interests: This study was supported by Amgen Inc., Thousand Oaks, CA, USA. Erenumab is co-developed by Amgen and Novartis. Stewart J. Tepper – consulting fees: Acorda, Alder, Alexsa, Allergan, AlphaSights, Amgen, ATI, Axsome Therapeutics, Cefaly, Charleston Labs, DeepBench, electroCore, eNeura, ExpertConnect, GLG, Guidepoint Global, GSK, Impel, M3 Global Research, Magellan Rx Management, Medicxi, Navigant Consulting, Neurolied, Nordic BioTech, Novartis, Reckner Healthcare, Relevale, Satsuma, Scion NeuroStim, Slingshot Insights, Sorrento, Sudler and Hennessey, Teva, Theranica, Trinity Partners, XOC and Zosano; advisory board: Acorda, Alder, Allergan, Amgen, ATI, Biohaven, Charleston Labs, Dr. Reddy's, GSK, Impel, Novartis, Pfizer, Satsuma, Supernus, XOC and Zosano; research grants: Alder, Allergan, Amgen, ATI, Dr. Reddy's, electroCore, eNeura, Neurolied, Novartis, Scion NeuroStim, Teva and Zosano; board of directors:

American Headache Society; royalties: Springer; stock options: ATI; employee: Dartmouth-Hitchcock Medical Center, Headache Currents and American Headache Society. Sylvia Lucas – consulting fees: Eli Lilly; advisory board: Amgen and Teva. Messoud Ashina – consulting/speakers' fees: Allergan, Amgen, Alder, Novartis, Eli Lilly and Teva; advisory board: Allergan, Amgen, Eli Lilly, Novartis and Teva; and research support: Allergan, Amgen, Alder and electroCore. Todd J. Schwedt – consulting fees: Alder, Allergan, Amgen, Avanir, Cipla, Dr. Reddy's, Eli Lilly, Ipsen Bioscience, Nocira, Novartis, Second Opinion and Teva; stocks, stock options: Aural Analytics, Second Opinion and Nocira; board member – American Headache Society and American Academy of Pain Medicine. Jessica Ailani – consulting/speakers' fees: Alder, Allergan, Amgen, Avanir, electroCore, Eli Lilly, Impel, Promius, and Teva; Section Editor: Current Pain and Headache Reports. Jan Klatt – employee and stocks: Novartis. James V. Scanlon, Denise E. Chou, Sharon Richards and Gabriel Paiva da Silva Lima – employees and stocks: Amgen.

IHC-PO-141

Erenumab (AMG 334), an antagonist of the Canonical Calcitonin Gene-Related Peptide Receptor, does not impair vasodilatory or contractile responses to other agents in human isolated cerebral arteries

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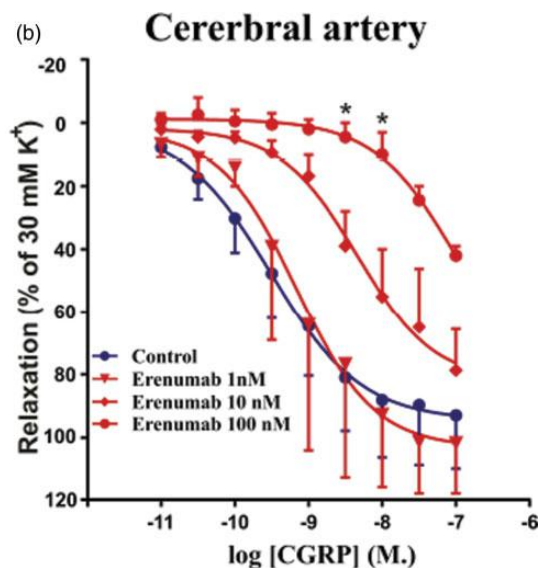
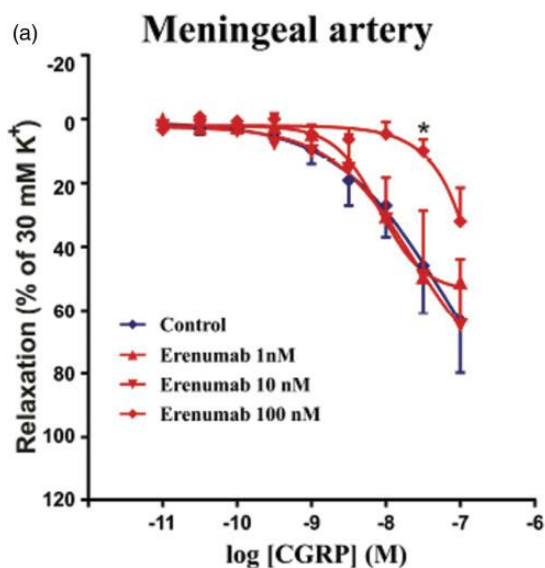
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Objective: The present study compares the functional responses to α CGRP and the antagonistic effects of erenumab in human meningeal and cerebral arteries. We also study the effect of erenumab on different vasoconstrictors and vasodilators.

Methods: Ring segments of human isolated meningeal and cerebral arteries were mounted in a myograph. Functional responses were studied by inducing pre-contraction with 30 mM KCl, followed by administration of CGRP in increasing concentrations (0.1 nM–0.1 mM) in the absence/presence of different erenumab concentrations. Additionally, contractile responses to sumatriptan and dihydroergotamine (DHE), and relaxant responses to substance-P and nicardipine were examined.

Results: In the meningeal artery, α CGRP induced concentration-dependent relaxation of 30 mM K⁺ in the control ($E_{MAX} = 37 \pm 16$, $\log EC_{50} = -7.2 \pm 1.9$), and in presence of 1 nM ($E_{MAX} = 49 \pm 27$, $\log EC_{50} = -8.1 \pm 0.4$), 10 nM ($E_{MAX} = 35 \pm 21$, $\log EC_{50} = -7.6 \pm 1.0$) and 100 nM. There was significant inhibition at 100 nM of erenumab. In the cerebral arteries we observe a more potent dilatation to α CGRP, which gave more evident shifts in the response to α CGRP. The control had an E_{MAX} of 7 ± 17 and a $\log EC_{50}$ of -9.5 ± 0.5 , which was attenuated by 1 nM ($E_{MAX} = -2 \pm 17\%$, $\log EC_{50} = -9.2 \pm 1.9$), 10 nM



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($E_{MAX} = 21 \pm 13$, $\log EC_{50} = -8.3 \pm 0.3$) and significantly attenuated by 100 nM erenumab ($E_{MAX} = 58 \pm 3$, $\log EC_{50} = -7.0 \pm 1.2$). Nicardipine, Substance P, DHE and sumatriptan were tested in pre-contracted or relaxed vessel segments and elicited concentration-dependent responses. The presence or absence of erenumab or its IgG control did not alter these concentration-response relationships. Pre-treatment with erenumab antagonized CGRP-induced relaxation in a competitive manner. Erenumab did not show any contractile or relaxant effects per se.

Conclusion: Erenumab, while not associated with vasoactive properties per se, specifically inhibits CGRP-induced relaxation of cranial vessels without impacting vasorelaxant or contractile responses of endogenous or pharmacological vasoactive compounds.

IHC-PO-142

Long-term impact of fremanezumab on response rate, acute headache medication use, and disability in chronic migraine patients with acute medication overuse at baseline: results of a 1-year study

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Objective: Fremanezumab, a fully humanized monoclonal antibody that selectively targets calcitonin gene-related peptide, is approved in the US and the EU for the preventive treatment of migraine in adults. Herein we evaluated the long-term impact of fremanezumab in chronic migraine (CM) patients (pts) with acute medication overuse (AMO) at baseline (BL).

Methods: In this 12-month, randomized, double-blind, parallel-group study, CM pts received fremanezumab quarterly (675 mg every 3 months) or monthly (225 mg monthly; starting dose of 675 mg). CM patients with BL AMO (acute headache medication use [≥ 15 days], migraine-specific acute medication use [≥ 10 days], or combination medication use [≥ 10 days]) were analyzed *post hoc*. The proportions of pts with $\geq 50\%$ reduction in the monthly number of migraine days and headache days of at least moderate severity, respectively, and the change from baseline in the monthly number of days with use of any acute headache medications and in headache-related disability (assessed by six-item Headache Impact Test [HIT-6]) were measured at Months 6 and 12.

Results: At baseline, 599 CM patients (quarterly: $n = 292$, monthly: $n = 307$) had AMO. The proportion of pts with a

$\geq 50\%$ reduction in monthly migraine days was 37% with quarterly and 48% with monthly dosing at Month 6; response was sustained at Month 12 (quarterly: 51%; monthly: 52%). The proportion of patients with a $\geq 50\%$ reduction in the monthly number of headache days of at least moderate severity was 42% with quarterly and 53% with monthly dosing at Month 6; response was sustained at Month 12 (quarterly: 50%; monthly: 54%). The mean monthly number of days CM pts used any acute headache medication decreased from BL to Months 6 (quarterly: -6.9 days; monthly: -7.8 days) and 12 (quarterly: -8.1 days; monthly: -8.2 days). The mean change in HIT-6 score decreased from BL to Months 6 (quarterly: -6.2 ; monthly: -7.5) and 12 (quarterly: -6.9 ; monthly: -8.1).

Conclusion: Long-term fremanezumab treatment maintains efficacy, reduces the use of acute headache medication and improves headache-related disability for up to 1 year in CM pts with AMO.

Disclosure of Interests: Stephen D. Silberstein: Provides consultation to Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Curelator Inc., Depomed, Dr. Reddy's Laboratories, Ensured Inc., ElectroCore Medical LLC, eNeura Therapeutics, INSYS Therapeutics, Lilly USA LLC, Supernus Pharmaceuticals Inc., Teva Pharmaceuticals, Theranica, and Trigemina Inc.

David Kudrow: Advisor to Eli Lilly, Amgen, Alder. Research support from Amgen, Alder, Eli Lilly, Teva, Zosano, Allergan, Genentech, VM Biopharma, and Co-Lucid.

Joshua M. Cohen: Employee of Teva Pharmaceuticals.

Sanjay K. Gandhi: Employee of Teva Pharmaceuticals.

Ronghua Yang: Employee of Teva Pharmaceuticals.

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Cory Blaiss: Employee of Teva Pharmaceuticals.

IHC-PO-143

Sustained Response to Erenumab Over Time in Patients with Episodic Migraine

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Objective: Erenumab (erenumab-aooe in the US) is a fully human anti-Calcitonin Gene-Related Peptide (CGRP)

Abstract number: IHC-PO-143**Table 1.** Initial responders who maintained or achieved good or excellent response

	Erenumab 70 mg	Erenumab 140 mg
A $\geq 50\%$ MMD reduction from baseline was maintained at Month 2 by	72 (73/102)	70 (79/113)
A $\geq 50\%$ MMD reduction from baseline was maintained at Month 2 or Month 3 by	84 (86/102)	84 (95/113)
An excellent response ($\geq 75\%$ reduction from baseline in MMD) was achieved at Month 2 or Month 3 by	54 (55/102)	54 (61/113)
A good or excellent response was maintained through Month 6 based on mean MMD change over Months 4 to 6	78 (80/102)	74 (84/113)

Data represented as % (n/N1) unless otherwise stated.

n = Responders.

N1 = Number of subjects who did not achieve at least 50% reduction in MMD at Month 1.

MMD, monthly migraine days.

receptor monoclonal antibody approved for migraine prevention. While many patients treated with erenumab experience onset of efficacy as early as one week, details about the maintenance of these clinical responses have not been reported. The objective of this analysis was to evaluate patterns of sustained response with continued erenumab treatment in patients with episodic migraine (EM).

Methods: We conducted a post hoc analysis of data from STRIVE (ClinicalTrials.gov NCT02456740), a 6-month, randomised, double-blind, placebo-controlled, phase 3 study of erenumab in patients with EM (N = 955). Patients were categorised as initial responders if they achieved a $\geq 50\%$ reduction in monthly migraine days (MMD) at Month 1. During the following months of treatment, patients with initial response were classified as having an 'excellent' ($\geq 75\%$ reduction in MMD) or 'good' ($\geq 50\%$ to 75% reduction in MMD) subsequent response. This analysis was limited to those randomised to erenumab treatment.

Results: At Month 1, 33% (102/312) of patients in the erenumab 70 mg group and 36% (113/318) of patients in the erenumab 140 mg group achieved an initial response of $\geq 50\%$ reduction from baseline in MMD, and 11% and 14% achieved $\geq 75\%$. Initial responders who maintained or achieved a good or excellent response at Month 2 or Month 3 is represented in the table. Of the patients who initially responded but did not maintain a $\geq 50\%$ response through Month 2, 45% (13/29) and 47% (16/34) regained a $\geq 50\%$ response at Month 3.

Conclusion: Most patients with EM who achieved a response after one month of erenumab treatment maintained or further improved their response following continued treatment.

Disclosure of Interests: This study was supported by Amgen Inc., Thousand Oaks, CA, USA. Erenumab is co-developed by Novartis and Amgen. Abstract has been accepted as Poster presentation at AHS 2019. Peter McAllister— received consulting fees, (honoraria) for

advisory boards: Alder; Independent Contractor (Including Contracted Research, Honoraria): Amgen, Biohaven, Eli Lilly and Company and Teva Pharmaceuticals. Ira M. Turner—consulting fees, speaking/teaching fees, (honoraria): Alder, Allergan, Amgen, Assertio, Biohaven, Electrocore, Eli Lilly and Company, Impax, Novartis, Promius, Revance, Supernus and Teva Pharmaceuticals; research grant: Alder, Allergan, Amgen, Electrocore, Eli Lilly and Company and Teva Pharmaceuticals. Uwe Reuter— consulting fees, speaking/teaching fees: Allergan, Amgen, Autonomic Technologies, ElectroCore, Eli Lilly and Company, Medscape, Novartis, StreamMedUp, TEVA Pharmaceuticals; research grants: Alder, Allergan, Amgen, Autonomic Technologies, ElectroCore, Eli Lilly and Company, Novartis, TEVA Pharmaceuticals; board member: European Headache Federation; other activities: Frontiers in Neurology, Journal of Headache and Pain. Bert B. Vargas—consulting fees for advisory boards: Alder, Allergan, Amgen, Biohaven, Eli Lilly and Company, Novartis, Promius, Teva Pharmaceuticals, Upsher-Smith and Xoc; speaking/teaching fees: ATI; board member: American Headache Society, Headache Cooperative of the Pacific and Neurology Today. James V. Scalon, Sharon Richards, Denise E. Chou and Gabriel Paiva Da Silva Lima — employees and stocks: Amgen Inc. Jan Klatt— employee and stocks: Novartis.

IHC-PO-144**Temporal response patterns to erenumab in patients with episodic migraine**

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⁷Amgen Limited, Uxbridge, United Kingdom

Objective: To evaluate the clinical response to continued erenumab treatment in patients with episodic migraine (EM) who were not initial responders by the first month.

Methods: A *post hoc* analysis of the STRIVE (NCT02456740) study was conducted to evaluate response times to erenumab treatment. A $\geq 50\%$ reduction from baseline in monthly migraine days (MMD) was used to define a response; patients without a response were classified as having a 'modest' ($\geq 30\%$ to $< 50\%$) or 'no/limited' ($< 30\%$) reductions in MMD. Time-to-event analyses in patients who achieved a response to erenumab in any study month were performed. Additionally, the response to erenumab in subsequent months in the subset of patients who were not initial responders ($< 50\%$ reduction in MMD at the end of Month 1) was analysed.

Results: After Month 1, 33% (102/312) of patients in the 70 mg group and 36% (113/318) of the 140 mg group achieved an initial response. Of the patients who did not achieve an initial response, 29% (60/210) and 38% (78/205)

achieved a 'modest' reduction in MMD, respectively. The proportion of patients who subsequently responded after the first month increased over time with continued erenumab treatment (Table). Of patients who did not respond during the first 2 months, 22% (35/159) and 24% (34/141) responded after month 3. And of those who did not respond during the first 3 months of treatment, 34% (42/124) and 39% (42/107) responded over the last 3 months.

Conclusion: While many patients respond to erenumab within the first month, a notable proportion of patients without an initial response may respond later with continued treatment. These results are in line with recent AHS (American Headache Society) migraine treatment guidelines that recommend 3 months of assessment following initiation of a preventive treatment with new biologic treatments for migraine.

Disclosure of Interests: This study was supported by Amgen Inc., Thousand Oaks, CA, USA. Erenumab is co-developed by Novartis and Amgen. Abstract has been accepted as a Poster presentation at AHS 2019. Peter McAllister—received consulting fees, honoraria for advisory boards, and as an independent contractor (including contracted research), from Alder, Amgen, Biohaven, Eli Lilly and Company and Teva Pharmaceuticals. Ira M. Turner—received consulting fees, speaking/teaching fees, honoraria, research grant, from Alder, Allergan, Amgen, Assertio, Biohaven, Electrocore, Eli Lilly and Company, Impax, Novartis, Promius, Revance, Supernus and Teva Pharmaceuticals. Uwe Reuter—received consulting fees, speaking/teaching fees, from Allergan, Amgen, Autonomic Technologies, CoLucid, ElectroCore, Eli Lilly, Medscape, Novartis, StreamMedUp, TEVA Pharmaceuticals and research grants from Allergan, Amgen, Autonomic Technologies, CoLucid, ElectroCore, Eli Lilly, Medscape, Novartis, StreamMedUp, TEVA Pharmaceuticals. Bert B. Vargas—received consulting fees for advisory boards, from Alder, Allergan, Amgen,

Abstract number: IHC-PO-144**Table 1.** Response to erenumab in any study month in patients without initial response

	Erenumab 70 mg	Erenumab 140 mg
Patients who responded after month 2	24 (51/210)	31 (64/205)
Patients who responded by Month 3	41 (86/210)	48 (98/205)
Patients who responded by Month 6	61 (128/210)	68 (140/205)
Patients who achieved a response at least once during the 6-month study* % (n/N)	74 (230/312)	80 (253/318)

Data represented as % (n/N) unless otherwise stated.

n = responders.

NI = Analysis set.

NI = Number of subjects who did not achieve at least 50% reduction in MMD at Month 1.

*The median time to first response was 2 (1, 3) months for the patients who responded in each treatment group. 90% of patients who responded during the study period achieved a response by Month 4 (140 mg group) or Month 5 (70 mg group).

MMD, monthly migraine days.

ATI, Biohaven, Eli Lilly and Company, Novartis, Promius, Teva Pharmaceuticals, Upsher-Smith and Xoc; is a board member of American Headache Society, Headache Cooperative of the Pacific and Neurology Today. James V. Scalon, Sharon Richards, Denise E. Chou and Gabriel Paiva Da Silva Lima — employees and stocks: Amgen Inc. Jan Klatt— employee and stocks: Novartis.

IHC-PO-145

Sustained Reduction of Migraine Headache Days in Patients With Episodic Migraine During Months 4 to 6 of Treatment With Galcanezumab

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Objective: Sustained response of reduction in migraine headache days (MHD) in patients with episodic migraine treated with galcanezumab (GMB) was evaluated.

Methods: This was a post-hoc analysis of 2 double-blind, 6-month GMB studies in patients randomized (1:1:2) to monthly subcutaneous GMB 120 mg (after 240 mg initial loading dose) or 240 mg or placebo. The proportions of patients with a $\geq 50\%$, $\geq 75\%$, or 100% reduction from baseline in monthly MHD on an average month from Months 1 to 3 and Months 4 to 6 were evaluated. A generalized linear mixed model with effects for baseline MHD, treatment, month, and treatment-by-month interaction was used to estimate the mean monthly response rate.

Results: A total of 1739 patients (GMB $n = 864$ and placebo $n = 875$) were evaluated. In the GMB groups, the mean rates on an average month from Months 1 to 3 of $\geq 50\%$ (53% to 56%), $\geq 75\%$ (29% to 32%), and 100% (9% to 12%) responses were greater ($p < 0.001$) than placebo rates of $\geq 50\%$ (30% to 34%), $\geq 75\%$ (13% to 15%), and

100% (5%) response. The mean response rates on an average month in the GMB groups were sustained in Months 4 to 6 and greater ($p < 0.001$) than placebo (Table 1). The average reduction of 5 MHD/month in the GMB groups was greater than the reduction of 3 MHD/month with placebo ($p < 0.001$).

Conclusion: More GMB-treated patients achieved $\geq 50\%$ response; this was sustained during Months 4 to 6. The odds of achieving $\geq 50\%$ response was double for GMB, despite the high placebo response; the number of MHD/month with GMB was nearly half that of placebo.

Disclosure of Interests: Michel D. Ferrari – Grants and Consultancy or Industry support: Medtronic, Novartis, Lilly and TEVA and independent support from NWO, ZonMW, NIH, European Community, and the Dutch Heart Foundation.

Stewart J. Tepper – Grants for research (no personal compensation): Alder, Allergan, Amgen, ATI, Dr. Reddy's, ElectroCore, eNeura, Neuroief, Scion Neurostim, Teva, Zosano; Consultant and/or Advisory Boards: Acorda, Alder, Alexsa, Allergan, Alphasights, Amgen, ATI, Axsome Therapeutics, Biohaven, Cefaly, Charleston Labs, DeepBench, Dr. Reddy's, ElectroCore, Eli Lilly, eNeura, ExpertConnect, GLG, Guidepoint Global, GSK, Impel, Magellan Rx Management, Navigant Consulting, Neuroief, Nordic BioTech, Novartis, Pfizer, Reckner Healthcare, Satsuma, Scion Neurostim, Slingshot Insights, Sorrento, Sudler and Hennessey, Supernus, Teva, Theranica, Trinity Partners, XOC, Zosano; Stock Options: ATI; Royalties: Springer.

Salary: Dartmouth-Hitchcock Medical Center, American Headache Society.

Dustin Ruff and Linda Wietecha are employees of Eli Lilly and Company and/or one of its subsidiaries.

Abstract number: IHC-PO-145

Response, OR (95% CI)	EVOLVE-1			EVOLVE-2		
	GMB 120 mg (N = 191)	GMB 240 mg (N = 186)	PBO (N = 373)	GMB 120 mg (N = 212)	GMB 240 mg (N = 209)	PBO (N = 399)
$\geq 50\%$	67.8% 2.7 (2.0, 3.6)*	67.9% 2.7 (2.0, 3.6)*	44.2%	65.2% 2.5 (1.9, 3.4)*	60.2% 2.0 (1.6, 2.7)*	42.4%
$\geq 75\%$	46.2% 2.5 (1.9, 3.4)*	47.1% 2.6 (1.9, 3.5)*	25.5%	38.2% 2.1 (1.5, 2.8)*	40.0% 2.2 (1.6, 3.0)*	23.1%
100%	19.0% 2.1 (1.4, 3.0)*	21.3% 2.4 (1.6, 3.5)*	10.1%	14.8% 2.1 (1.4, 3.1)*	18.3% 2.7 (1.8, 3.9)*	7.7%

Abbreviations: CI = confidence interval; GMB = galcanezumab; OR = odds ratio; PBO = placebo.

* $p < 0.001$ versus placebo.

IHC-PO-146

Erenumab usage patterns and side effects reported by patients in a tertiary headache center: A retrospective cohort study

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Objective: We sought to describe medication usage patterns among patients in a tertiary headache clinic population who received erenumab for preventive treatment of migraine. Secondary outcomes were to identify side

effects, discontinuation rate and reason(s), and perceived benefits.

Methods: We performed an IRB-approved retrospective cohort study at the John R. Graham Headache Center at Brigham and Women’s Hospital, a tertiary headache center with over 10,000 patient visits per year. Using our electronic medical record, we obtained a report of patients who received a prescription for erenumab from a headache specialist/fellow from May to December 2018 and who had a diagnosis of migraine. We obtained patient demographics from chart review and the remainder of information was obtained via a phone survey. Questions

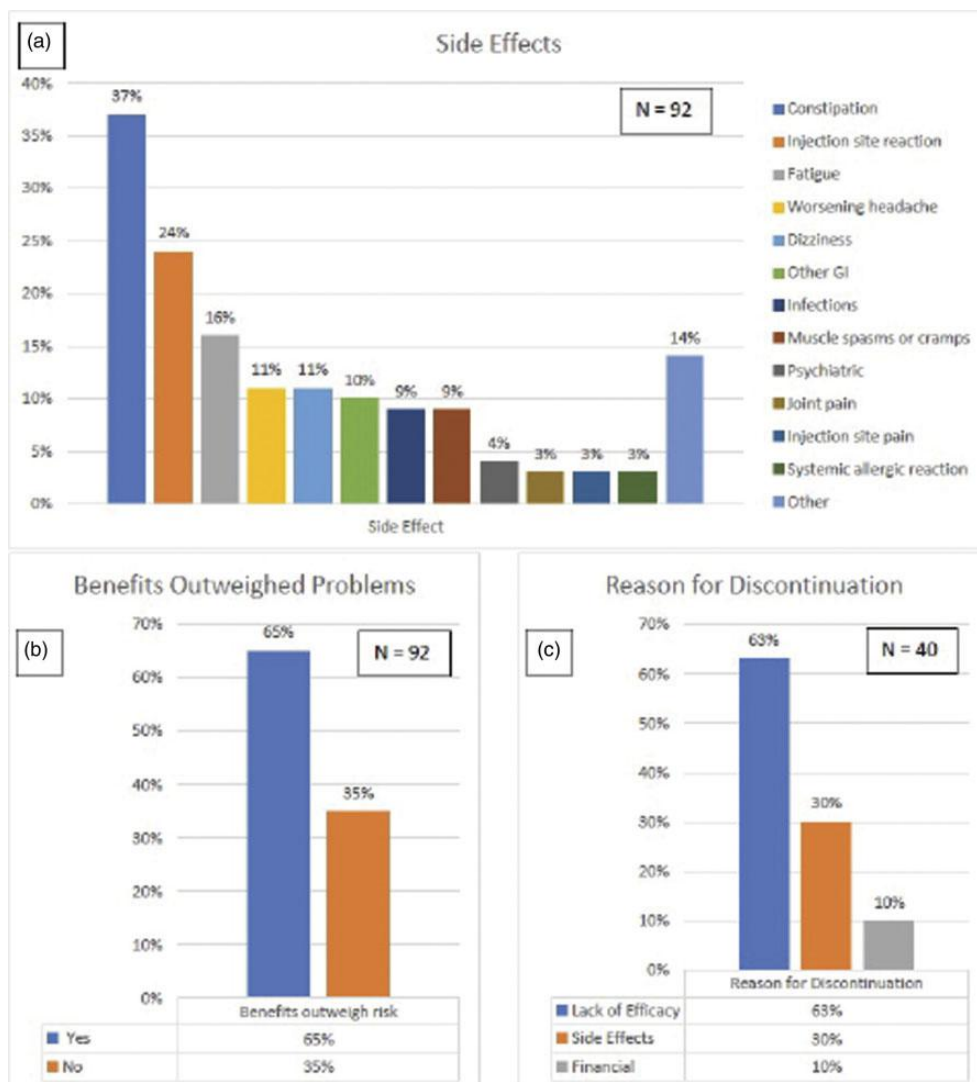


Figure 1: (A) Demonstrates the side effects reported by patients by frequency of occurrence. Other category includes side effects reported by 2 or less patients. (B) Illustrates whether patients thought the benefits of taking erenumab outweighed any problems they had with it. (C) Illustrates the reasons behind discontinuing erenumab, more than one option was allowed.

covered erenumab use, side effects (open-ended followed by checklist), and perceived benefits in comparison to drawbacks. Of those who discontinued the use of erenumab, we asked about the reason(s) for discontinuation. Here we report descriptive statistics.

N = 102	Number	Percentage
Gender:		
Female	83	81.6
Male	18	17.5
Gender Fluid	1	1
Race:		
White	96	94
Black or African American	1	1
Hispanic/Latino	2	2
American Indian or Alaska Native	1	1
Multiple Race/Ethnicities	2	2
	Mean	Range
BMI	27.5	17.9–44.8
Age	50	20–74

Results: A total of 350 patients were identified as eligible for the study. Of 175 patients contacted to date, 6 did not meet inclusion criteria. Of the remaining 169 patients, 109 completed the survey (response rate 64%). Demographic information of responders is shown in table 1. 17 patients received the prescription but never used the medication, mostly due to financial reasons. 62% of the 92 patients who used erenumab reported one or more side effects (Fig 1-A). Constipation, injection site reaction, and fatigue were the most commonly reported side effects. 65.2% of users thought the benefits outweighed any problems they had with it (Fig 1-B). 40 patients (43.5% of users) discontinued erenumab and the reason for discontinuation is shown in Fig. 1-C. The mean number of doses received before discontinuation was 3.88 (1–7).

Conclusion: Erenumab usage and side effect patterns in our clinic population differed from those described in phase 2 and 3 clinical trials. We found higher rates of discontinuation and a higher burden of side effects than was reported in the clinical trials. Our study provides valuable information for clinicians and patients who are considering erenumab as a treatment option.

Disclosure of Interest: None Declared.

IHC-PO-147

Benefit-Risk Assessment of Galcanezumab versus Placebo for the Treatment of Episodic and Chronic Migraine: Results from EVOLVE-1, EVOLVE-2, and REGAIN Clinical Trials

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Objective: To evaluate the benefit-risk profile of galcanezumab (GMB) versus placebo (PBO) for the treatment of episodic (EM) and chronic migraine (CM) in adults.

Methods: Data from three pivotal phase 3 trials of GMB were used to estimate response rates (RR), a clinically meaningful outcome for decision makers, based on monthly migraine headache day (MHD) reductions in patients with EM (EVOLVE-1 and EVOLVE-2; 6-month treatment duration) and patients with CM (REGAIN; 3-month treatment duration). Corresponding numbers needed to treat (NNT) for one patient to benefit from drug and numbers needed to harm (NNH) for one patient to be harmed by drug based on discontinuation due to adverse events (DCAE) were estimated for each trial separately.

Results: Table 1 displays NNT for 30%, 50%, and 75% RRs and NNH for DCAE. In all trials, the proportion of patients achieving these RRs was significantly higher in patients treated with GMB 120 mg and 240 mg versus those treated with PBO. Corresponding NNTs were similar across trials (5 to 9) with the exception of those obtained for $\geq 75\%$ RR in REGAIN (24 to 40). Across all trials, NNH based on DCAE ranged from 46 to 295.

Conclusion: In all trials, GMB showed a favorable benefit-risk profile versus PBO based on low NNTs for RR and higher NNH for DCAE. Higher NNTs observed in patients with CM may be due to higher disease burden (higher baseline MHD and greater disability) of these patients and shorter treatment duration (3 vs. 6 months).

Disclosure of Interests: All authors are full-time employees of Eli Lilly and Company or one of its subsidiaries and are minority holders of company stock.

Abstract number: IHC-PO-147**Table 1.** Response rates, numbers needed to treat, and numbers needed to harm for EVOLVE-1, EVOLVE-2, and REGAIN phase 3 clinical trials

	EVOLVE-1 ^a			EVOLVE-2 ^a			REGAIN ^b		
	PBO	LY120mg	LY240mg	PBO	LY120mg	LY240mg	PBO	LY120mg	LY240mg
30% RR	56.8	77.1	74.3	52.7	73.4	72.6	32.3	44.8	46.4
NNT ^c		5	6		5	5		8	8
50% RR	38.6	62.3	60.9	36.0	59.3	56.5	15.4	27.6	27.5
NNT ^c		5	5		5	5		9	9
75% RR	19.3	38.8	38.5	17.8	33.5	34.3	4.5	7.0	8.8
NNT ^c		6	6		7	6		40	24
DCAE	2.3	3.4	4.1	1.7	2.2	3.9	1.1	0.4	1.4
NNH ^c		92	57		213	46		NR	295

Abbreviations: CI, confidence interval; DCAE, discontinuations due to adverse events; LY, galcanezumab; NNT, numbers needed to treat; NNH, numbers needed to harm; NR, not relevant as higher risk with placebo; RR, response rate.

^aIncluded patient population with episodic migraine; based on data from Months 1–6.

^bIncluded patient population with chronic migraine; based on data from Months 1–3.

^cComparison versus placebo.

IHC-PO-148

Impact of fremanezumab on disability in migraine patients with medication overuse and documented inadequate response to 2–4 classes of preventive treatments: subgroup analysis of the randomised, double-blind FOCUS study

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²Teva Pharmaceuticals Industries, Frazer, PA, United States

Objective: Fremanezumab is a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP). The FOCUS study of fremanezumab was the first and largest study of a migraine preventive treatment in adults with both chronic and episodic migraine (CM and EM) and documented inadequate response to 2–4 classes of migraine preventive medications. Headache-related disability, per the 6-item Headache Impact Test (HIT-6) and Migraine Disability Assessment (MIDAS), was evaluated in a subgroup of patients (pts) with medication overuse (use of any acute medication on ≥ 15 days/month or triptans/ergots/combination medications on ≥ 10 days/month) at baseline (BL).

Methods: Pts were randomised (1:1:1) to quarterly (qtlly) fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), monthly (mthly) fremanezumab (Month 1: CM,

675 mg; EM, 225 mg; Months 2 and 3: 225 mg), or matched monthly placebo (PBO) for 12 weeks (wks). Changes in HIT-6 and MIDAS scores from BL were compared with a mixed-effects model for repeated measures.

Results: Of 838 randomised pts, 427 had medication overuse. Reductions from BL in HIT-6 scores were significantly greater with both fremanezumab regimens vs placebo at 4 wks (LSM[SE] change: qtlly, $-3.6[0.75]$; mthly, $-5.6[0.68]$ vs $-0.8[0.76]$; both $P \leq 0.0019$) and over 12 wks (qtlly, $-5.9[0.83]$; mthly, $-6.5[0.75]$ vs $-1.4[0.84]$; both $P < 0.0001$). Reductions from BL in MIDAS scores were also significantly greater with mthly fremanezumab vs placebo at 4 wks (mthly, $-13.9[4.36]$ vs $-0.6[4.80]$; $P = 0.0163$; qtlly, $-11.5[4.76]$) and with both fremanezumab regimens vs placebo over 12 wks (qtlly, $-24.4[5.45]$; mthly, $-29.6[4.99]$ vs $-8.2[5.59]$; both $P \leq 0.0194$).

Conclusion: Fremanezumab significantly reduced headache-related disability vs placebo in migraine pts with medication overuse and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: M. Ashina has received personal fees from Alder BioPharmaceuticals, Allergan, Amgen, Alder, Eli Lilly, Novartis and Teva. Dr. Ashina participated in clinical trials as the principal investigator for Alder, Amgen, Electro-Core, Novartis and Teva trials. Dr. Ashina has no ownership interest and does not own stocks of any pharmaceutical company. Dr. Ashina serves as associated editor of Cephalalgia, co-editor of the Journal of Headache and Pain. Dr. Ashina is President-elect of the International Headache Society and General Secretary of

the European Headache Federation. J. M. Cohen, V. Ramirez-Campos, and L. Janka are employees and/or stockholders of Teva Pharmaceuticals.

IHC-PO-149

Impact of fremanezumab on migraine-specific quality of life in patients with medication overuse and documented inadequate response to 2–4 classes of migraine preventive treatments: subgroup analysis of the international, multicentre, randomised, double-blind FOCUS study

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Objective: Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for preventive treatment of migraine in adults. The FOCUS study of fremanezumab was the first and largest study of a migraine preventive treatment in adults with both chronic and episodic migraine (CM and EM) and documented inadequate response to 2–4 classes of migraine preventive medications. Migraine-specific quality of life (MSQOL) was evaluated in a subgroup of patients with medication overuse (use of any acute medication on ≥ 15 days/month or triptans/ergots/combo medications on ≥ 10 days/month) at baseline (BL).

Methods: Patients were randomised (1:1:1) to quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), monthly fremanezumab (Month 1: CM, 675 mg; EM, 225 mg; Months 2 and 3: 225 mg), or matched monthly placebo for 12 weeks. Changes from BL in MSQOL domain scores were compared using a mixed-effects model for repeated measures.

Table. Change From BL in MSQOL Domain Scores at 12 Weeks

LSM(SE) change from BL	Placebo (n = 133)	Quarterly fremanezumab (n = 148)	Monthly fremanezumab (n = 146)
Role function-restrictive	4.2 (2.32)	13.6 (2.28) ^a	18.1 (2.08) ^a
Role function-preventive	5.0 (2.13)	10.0 (2.10) ^b	14.7 (1.91) ^a
Emotional function	4.5 (2.74)	11.9 (2.69) ^c	16.3 (2.45) ^a

^a $P \leq 0.0009$ vs placebo.

^b $P = 0.0569$ vs placebo.

^c $P = 0.0297$ vs placebo.

Results: Of 838 randomised patients, 427 had medication overuse. Improvements from BL in all MSQOL domain scores were significantly greater with both fremanezumab dosing regimens versus placebo at 12 weeks (all $P \leq 0.0297$; **Table**), except role function-preventive with quarterly fremanezumab ($P = 0.0569$). Significant improvements were observed by 4 weeks with both fremanezumab regimens vs placebo (all $P < 0.0001$).

Conclusion: Fremanezumab was associated with significant improvements in migraine-specific quality of life outcomes versus placebo in patients with medication overuse at BL and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: L. Mechtler has received honoraria as a speaker from Avanir, Allergan, Teva, and Promius. Dr. Mechtler has received research funding from Allergan, Teva, Boston Biomedical, Inc., and Autonomic Technologies, Inc. V. Ramirez-Campos, J. M. Cohen, and L. Janka are employees and/or stockholders of Teva Pharmaceuticals.

IHC-PO-150

Early onset of efficacy with fremanezumab in patients with medication overuse and documented inadequate response to 2–4 classes of migraine preventive treatments: subgroup analysis of the randomised, double-blind FOCUS study

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Objective: The FOCUS study of fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), was the first and largest study of a migraine preventive treatment in adults with either episodic or chronic migraine (EM and CM) and documented inadequate response to 2–4 classes of migraine preventive medications. Early response was evaluated in a subgroup of patients (pts) with EM or CM and medication overuse (use of any acute medication ≥ 15 days/month [mo] or triptan/ergot/combo medication ≥ 10 days/mo) at baseline (BL).

Methods: Pts were randomised (1:1:1) to quarterly (qly) fremanezumab (Mo 1: 675 mg; Mo 2 and 3: placebo), monthly (mthly) fremanezumab (Mo 1: EM, 225 mg; CM, 675 mg; Mo 2 and 3: 225 mg), or matched mthly placebo

(PBO) for 12 weeks (wks). Changes from BL in weekly (wkly) migraine headache days and headache days and responder rates ($\geq 50\%$ reduction in wkly migraine days) were evaluated at Wks 1–3.

Results: Of 838 randomised pts, 427 had medication overuse. Reductions from BL in wkly migraine headache days were significantly greater with fremanezumab vs PBO by Wk 1 (qly, $-0.9[0.20]$; mthly, $-1.1[0.19]$ vs $-0.1[0.21]$; $P \leq 0.0018$), as were reductions in wkly headache days of at least moderate severity (qly, $-1.0[0.20]$; mthly, $-1.4[0.18]$ vs $-0.1[0.20]$; $P \leq 0.0003$). Significantly higher proportions of pts achieved $\geq 50\%$ reductions in migraine headache days with fremanezumab vs PBO at Wk 1 (qly, 39%; mthly, 37% vs 14%; $P < 0.0001$). Significant differences were maintained through Wks 2 and 3 (all $P \leq 0.0003$).

Conclusion: Both qly and mthly fremanezumab demonstrated early onset of action, with greater response rates within 1 wk and significantly greater reductions in wkly migraine headache days and headache days as early as Wk 1 vs PBO, in pts with medication overuse and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: Z. Katsarava has served as a speaker and received honoraria from Allergan, Novartis, Teva, Lilly and Merck. None of these were related to the current manuscript. M. Machkova was an investigator in the study and, as such, received payment from Teva Pharmaceuticals. V. Ramirez-Campos, J. M. Cohen, and L. Janka are employees and/or stockholders of Teva Pharmaceuticals. E. L. H. Spierings was an investigator in the study and, as such, received research grants from Teva Pharmaceuticals.

IHC-PO-151

Reversion from chronic to episodic migraine in patients with documented inadequate response to 2–4 classes of migraine preventive treatments: results of the randomised, placebo-controlled FOCUS study

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Objective: The FOCUS study of fremanezumab, a fully-humanised monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide (CGRP), was the first and largest study of a migraine preventive treatment in adults with both episodic and chronic migraine (EM and CM) and documented inadequate response to 2–4 classes

of migraine preventive treatments. Reversion from CM at baseline (BL) to EM during study treatment and reductions in headache days among patients (pts) reverting from CM (≥ 15 headache days/month [mo] at BL) to EM (< 15 headache days/mo in all 3 mo) were evaluated in this post-hoc analysis.

Methods: Pts were randomised (1:1:1) to quarterly (qly) fremanezumab (Mo 1: 675 mg; Mo 2 and 3: placebo), monthly (mthly) fremanezumab (Mo 1: EM, 225 mg; CM, 675 mg; Mo 2 and 3: 225 mg), or matched mthly placebo for 12 weeks (wks). Overall headache days at BL and Mo 3 and percent change in headache days from BL in Mo 3 were evaluated for pts with CM at BL who reverted to EM in Mo 1, 2, and 3.

Results: In the placebo, qly fremanezumab, and mthly fremanezumab groups, respectively, 167, 167, and 172 pts had CM at BL; of those, 18(11%), 59(35%), and 59(34%) reverted to EM in Mo 1, 2, and 3. Among pts who reverted, mean(SD) mthly headache days at BL were 16.9(2.34), 17.4(2.37), and 17.4(2.57) days in the placebo, fremanezumab qly, and fremanezumab mthly groups, respectively; mean(SD) headache days at Mo 3 were 9.9(3.70), 8.6(3.60), and 8.3(3.72) days, representing reductions of 39%, 50%, and 52% days from BL. Similar reductions were observed at Mo 1 and 2.

Conclusion: Higher proportions of pts with CM reverted to EM with fremanezumab treatment vs placebo in this population of pts with inadequate response to 2–4 classes of migraine preventive treatments. On average, pts in the fremanezumab groups reverting from CM to EM experienced clinically meaningful $\geq 50\%$ reductions in monthly headache days during the 3-mo double-blind treatment period.

Disclosure of Interests: J. Ailani reports the following conflicts of interest: consulting: Amgen, Alder, Allergan, Alpha Sites Consulting, Biohaven, Electrocore, Eli-Lilly and Company, Promius, Impel, Satsuma, Supernus, Teva; speaker's Bureau: Allergan, Amgen, Eli-Lilly and Company, Electrocore, Promius, Teva; content development/delivery (CME/Non-CME): Aptus, Peer View, Medscape, Miller Medical, Medical Education International, Neurology Live; clinical trials: ARMR Registry (American Migraine Foundation); other: Section Editor Current Pain and Headache. V. Ramirez-Campos, J. M. Cohen, R. Yang, M. Galic, and X. Ning are employees of Teva Pharmaceuticals. R. H. Singh has received honoraria from Biohaven and Amgen for serving on advisory boards.

IHC-PO-152**Impact of fremanezumab on migraine-associated symptoms in patients with documented inadequate response to 2–4 classes of migraine preventive medications in the international, multicentre, randomised, placebo-controlled FOCUS study**

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Objective: Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for preventive treatment of migraine in adults. Migraine-related symptoms (nausea or vomiting and photophobia and phonophobia) were evaluated as exploratory endpoints in the FOCUS study of fremanezumab. the first and largest study of a migraine preventive treatment in adults with both episodic and chronic migraine (EM and CM) and documented inadequate response to 2–4 classes of migraine preventive medications.

Methods: During 12 weeks of double-blind treatment, patients were randomised (1:1:1) to quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), monthly fremanezumab (Month 1: CM, 675 mg; EM, 225 mg; Months 2 and 3: 225 mg), or matched monthly placebo. Changes in monthly days with nausea or vomiting and photophobia and phonophobia from baseline during 12 weeks were compared using analysis of covariance models.

Results: 838 patients were randomised. Reductions from baseline in monthly average days with nausea or vomiting and with photophobia and phonophobia were significantly

greater with both fremanezumab regimens versus placebo over 12 weeks (all $P < 0.0001$; **Table**).

Conclusion: Fremanezumab significantly reduced migraine-related symptoms versus placebo in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: P. McAllister has received research support from Amgen/Novartis, Lilly, Teva and Alder Pharmaceuticals. Dr. McAllister serves as a consultant for Amgen/Novartis, Lilly, Teva and Alder. X. Ning, M. Galic, J. M. Cohen, and R. Yang are employees of Teva Pharmaceuticals.

IHC-PO-153**Clinically meaningful responses to fremanezumab in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive medications in the international, multicentre, randomised, placebo-controlled FOCUS study**

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Objective: Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for preventive treatment of migraine in adults. Responder rates were evaluated as secondary or exploratory endpoints in the FOCUS study of fremanezumab, the first and largest study of a migraine preventive treatment in adults with both episodic and chronic migraine (EM and CM) and

Abstract number: IHC-PO-152

Table. Change From Baseline in Monthly Average Number of Days With Nausea or Vomiting and Photophobia and Phonophobia During 12 Weeks of Double-blind Treatment

	Placebo (n = 278)	Quarterly fremanezumab (n = 276)	Monthly fremanezumab (n = 283)
Monthly average days with nausea or vomiting			
LSM (SE) change from baseline	−0.5 (0.27)	−2.5 (0.27)	−2.6 (0.27)
LSMD (SE) vs placebo	–	−1.9 (0.29) ^a	−2.1 (0.29) ^a
Monthly average days with photophobia and phonophobia			
LSM (SE) change from baseline	−0.4 (0.32)	−2.6 (0.32)	−3.1 (0.32)
LSMD (SE) vs placebo	–	−2.2 (0.34) ^a	−2.8 (0.34) ^a

^a $P < 0.0001$ versus placebo.

Abstract number: IHC-PO-153**Table 1.** Proportions of Patients With $\geq 50\%$ and $\geq 75\%$ Reductions in Monthly Average Number of Migraine Days

Responder rates, n (%)	Placebo (n = 278)	Quarterly fremanezumab (n = 276)	Monthly fremanezumab (n = 283)
$\geq 50\%$ reduction at 4 weeks	28 (10)	105 (38) ^a	101 (36) ^a
$\geq 50\%$ reduction during 12 weeks after first dose	24 (9)	95 (34) ^a	97 (34) ^a
$\geq 75\%$ reduction at 4 weeks	5 (2)	40 (14) ^a	39 (14) ^a
$\geq 75\%$ reduction during 12 weeks after first dose	6 (2)	23 (8) ^b	35 (12) ^a
Sustained $\geq 50\%$ reduction from the first 4 weeks throughout the 12-week treatment period	8 (3)	56 (20) ^a	54 (19) ^a

^a $P < 0.0001$ vs placebo.^b $P < 0.005$ vs placebo.

documented inadequate response to 2–4 classes of migraine preventive medications.

Methods: For 12 weeks of double-blind treatment, patients were randomised (1:1:1) to quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), monthly fremanezumab (Month 1: CM, 675 mg; EM, 225 mg; Months 2 and 3: 225 mg), or matched monthly placebo. Proportions of responders ($\geq 50\%$ and $\geq 75\%$ reduction in migraine days) were evaluated as secondary and exploratory endpoints, respectively.

Results: 838 patients were randomised. Higher proportions of patients achieved $\geq 50\%$ and $\geq 75\%$ reductions in migraine days within 4 weeks and sustained $\geq 50\%$ reductions through the 12-week treatment period with fremanezumab versus placebo (**Table**).

Conclusion: Clinically meaningful response rates within 4 weeks and sustained $\geq 50\%$ response rates over 3 months were significantly greater with fremanezumab versus placebo in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: E. L. H. Spierings was an investigator on the study and received research grants from Teva Pharmaceuticals. X. Ning, M. Galic, J. M. Cohen, and R. Yang are employees of Teva Pharmaceuticals.

IHC-PO-154

Impact of fremanezumab on headache-related disability in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive medications in the multicentre, randomised, placebo-controlled FOCUS study

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Objective: Fremanezumab, a fully-humanised monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for preventive treatment of migraine in adults. Headache-related disability was an exploratory endpoint of the FOCUS study of fremanezumab, the first and largest study of a migraine preventive treatment in adults with both episodic and chronic migraine (EM and CM) and documented inadequate response to 2–4 classes of migraine preventive medications.

Methods: During 12 weeks of double-blind treatment, patients were randomised (1:1:1) to quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), monthly fremanezumab (Month 1: CM, 675 mg; EM, 225 mg; Months 2 and 3: 225 mg), or matched monthly placebo. Changes in 6-item Headache Impact Test (HIT-6) and Migraine Disability Assessment (MIDAS) scores from baseline (BL) during the 4 weeks after the third dose of study drug were compared using analysis of covariance models.

Results: 838 patients were randomised. With both fremanezumab regimens, reductions from BL in HIT-6 and MIDAS disability scores during the 4 weeks after the

Abstract number: IHC-PO-154**Table.** Changes from BL in HIT-6 and MIDAS During the 4 Weeks After the Third Dose

	Placebo (n = 278)	Quarterly fremanezumab (n = 276)	Monthly fremanezumab (n = 283)
Disability score measured by HIT-6			
LSM (SE) change from BL	-2.2 (0.54)	-5.2 (0.55)	-6.1 (0.54)
LSMD (SE) vs placebo		-3.0 (0.58) ^a	-3.8 (0.58) ^a
Disability score measured by MIDAS			
LSM (SE) change from BL	-7.0 (3.24)	-19.7 (3.29)	-24.7 (3.24)
LSMD (SE) vs placebo		-12.7 (3.45) ^b	-17.7 (3.43) ^a

^aP < 0.0001 vs placebo.^bP = 0.0002 vs placebo.

third dose were significantly greater vs placebo (all $P \leq 0.0002$; **Table**).

Conclusion: Both fremanezumab dosing regimens were associated with significant improvements in headache-related disability vs placebo in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: M. Ashina has received personal fees from Alder BioPharmaceuticals, Allergan, Amgen, Alder, Eli Lilly, Novartis and Teva. Dr. Ashina participated in clinical trials as the principal investigator for Alder, Amgen, Electro-Core, Novartis and Teva trials. Dr. Ashina has no ownership interest and does not own stocks of any pharmaceutical company. Dr. Ashina serves as associated editor of Cephalalgia and co-editor of the Journal of Headache and Pain. Dr. Ashina is President-elect of the International Headache Society and General Secretary of the European Headache Federation. M. D. Ferrari served as an investigator on this study for Teva Pharmaceuticals. X. Ning, M. Galic, J. M. Cohen, and R. Yang are employees of Teva Pharmaceuticals.

IHC-PO-155**Genetic Assessment of Eptinezumab Response in the Prevention of Migraine**

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Objective: The genetic basis of response to anti-CGRP monoclonal antibody treatment within the migraine patient population is not well understood and is an emerging area. Eptinezumab is a humanized anti-CGRP IgG1

monoclonal antibody under investigation for the migraine prevention. Here we present a post hoc analysis to investigate any genetic link to the eptinezumab response in patients with chronic migraine. The carefully controlled patient response evaluation and high sample set completeness provided a compelling opportunity to investigate this topic.

Methods: Patients in the ALD403-005 clinical trial (NCT02275117) consented and provided blood samples at baseline from which genomic DNA was extracted. Samples from patients in the 30, 100, and 300 mg treatment groups were selected for genetic analysis. Only patients that received a therapeutically meaningful dose of eptinezumab were included. A total of 299 samples were analyzed. Whole-genome genotyping was undertaken, using the Illumina Infinium Omni5Exome SNP array. Targeted gene sequencing was also conducted based on 8 genes centrally related to CGRP biology. Statistical analysis was undertaken to evaluate any association of genotype or copy number to protocol-based clinical response (50%, 75%, 100% responders and change in migraine day) as well as other subgroups of interest. The positive hypothesis assumed that a skewed distribution of a particular allele frequency or copy number variant (CNV) in responders would be observed when compared to non-responders.

Results: No statistically significant relationship was identified between any level of clinical response and genotype/copy number status.

Conclusion: There were no clear associations identified between any level of anti-CGRP clinical response and patient phenotype, genotype, or copy number. Two caveats of this study are: A) the sample size limits the power to detect moderate to weak signals, and B) the design limits the ability to detect complex multigenic contributions to the response. Based on this post hoc evaluation, we have

been unable to conclude a genetic link to any level of anti-CGRP response.

Disclosure of Interests: Kira Misura: Full time employee of Alder Biopharmaceuticals.

Yanyu Song: Full time employee of Alder Biopharmaceuticals.

Anup Madan: Employed at Covance Genomics Laboratory, 9911 Willows Rd #175, Redmond, WA 98052.

Claire Olson: Employed at Covance Genomics Laboratory, 9911 Willows Rd #175, Redmond, WA 98052.

Jeff Smith: Received compensation from Alder Biopharmaceuticals.

Within the past year, Dr. Smith or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value in Alder Biopharmaceuticals.

John Latham: Full time employee of Alder Biopharmaceuticals.

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Efficacy of fremanezumab in migraine patients with medication overuse and documented inadequate response to 2–4 migraine preventive medications: subgroup analysis of the randomised, placebo-controlled FOCUS study

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Objective: The FOCUS study of fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), was the

first and largest study of a migraine preventive treatment in adults with both chronic and episodic migraine (CM and EM) and documented inadequate response to 2–4 classes of migraine preventive medications. Efficacy in a subgroup of patients with medication overuse (use of any acute medication on ≥ 15 days/month or triptans/ergots/combo combination medications on ≥ 10 days/month) at baseline (BL) was evaluated.

Methods: Patients were randomised (1:1:1) to quarterly (qtl) fremanezumab (Month [Mo] 1: 675 mg; Mo 2 and 3: placebo), monthly (mthly) fremanezumab (Mo 1: CM, 675 mg; EM, 225 mg; Mo 2 and 3: 225 mg), or matched mthly placebo for 12 weeks. Changes from BL in mthly migraine days and headache days of at least moderate severity at 4 weeks and during 12 weeks of treatment were compared using a mixed-effect model for repeated measures.

Results: Of 838 randomised patients, 427 had medication overuse. Reductions from BL in mthly average migraine days and headache days of at least moderate severity at 4 weeks and during 12 weeks of treatment were significantly greater with both fremanezumab regimens vs placebo (all $P \leq 0.0001$; **Table**).

Conclusion: Qtl and mthly fremanezumab provided early and sustained reductions in migraine and headache days vs placebo in patients with medication overuse and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: As a consultant and/or advisory panel member, S. Silberstein receives, or has received, honoraria from Abide Therapeutics; Alder Biopharmaceuticals; Allergan, Inc.; Amgen; Avanir Pharmaceuticals, Inc.; Biohaven Pharmaceuticals; Cefaly; Curelator, Inc.; Dr. Reddy's Laboratories; Egalet Corporation; GlaxoSmithKline Consumer Health Holdings, LLC.; eNeura Inc.; electroCore Medical, LLC; Impel NeuroPharma, Inc.; Lilly USA, LLC; Medscape, LLC; Novartis, Inc.; Satsuma Pharmaceuticals; Supernus

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Table 1. Change From BL in Mthly Average Migraine and Headache Days

Least squares mean (SE) change from BL	Placebo (n = 133)	Qtly fremanezumab (n = 148)	Mthly fremanezumab (n = 146)
Migraine days			
At 4 weeks	−0.0 (0.62)	−3.7 (0.62) ^a	−4.5 (0.57) ^a
Over 12 weeks	−0.5 (0.62)	−3.3 (0.62) ^a	−4.5 (0.57) ^a
Headache days of at least moderate severity			
At 4 weeks	−0.2 (0.62)	−4.3 (0.62) ^a	−5.1 (0.56) ^a
Over 12 weeks	−0.8 (0.62)	−4.0 (0.62) ^a	−5.0 (0.56) ^a

^a $P \leq 0.0001$ vs placebo.

Pharmaceuticals, Inc.; Teva Pharmaceuticals; Theranica; and Trigemina, Inc. J. M. Cohen, V. Ramirez-Campos, R. Yang, M. Galic, and X. Ning are employees of Teva Pharmaceuticals. A. Jann has no conflicts to report.

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Clinically meaningful responses to fremanezumab in migraine patients with medication overuse and documented inadequate response to 2–4 migraine preventive medications in the randomised, placebo-controlled FOCUS study

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Objective: The FOCUS study of fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), was the first and largest study of a migraine preventive treatment in adults with episodic or chronic migraine (EM or CM) and documented inadequate response to 2–4 classes of migraine preventive medications. We aimed to evaluate responder rates in a subgroup of patients (pts) with medication overuse (use of any acute medication on ≥ 15 days/month or triptans/ergots/combo medications on ≥ 10 days/month [mo]) at baseline (BL).

Methods: For 12 weeks (wks) of double-blind treatment, pts were randomised (1:1:1) to quarterly (qly) fremanezumab (Mo 1: 675 mg; Mo 2 & 3: placebo [PBO]), monthly (mthly) fremanezumab (Mo 1: EM, 225 mg; CM, 675 mg; Mo 2 & 3: 225 mg), or matched mthly PBO. Proportions of pts with $\geq 50\%$ and $\geq 75\%$ reductions from BL in mthly average migraine days at 4 wks and during 12 wks were compared using logistic regression.

Results: Of 838 randomised pts, 427 had medication overuse. At 4 wks and during 12 wks, a significantly greater proportion achieved $\geq 50\%$ and $\geq 75\%$ reduction in mthly migraine days with both qly and mthly fremanezumab regimens vs PBO (all $P < 0.05$; **Table**).

Conclusion: In this population of migraine pts with medication overuse and documented inadequate response to 2–4 classes of migraine preventive medications, significantly more pts treated with fremanezumab achieved 50–75% reductions in migraine days vs PBO. Fremanezumab provided early and sustained clinically meaningful results in this subgroup, suggesting medication

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Table. Pts With $\geq 50\%$ and $\geq 75\%$ Reductions in Mthly Average Migraine Days

n (%)	PBO (n = 133)	Qly fremanezumab (n = 148)	Mthly fremanezumab (n = 146)
$\geq 50\%$			
At 4 wks	9 (7)	45 (30) ^a	44 (30) ^a
Over 12 wks	10 (8)	38 (26) ^a	46 (32) ^a
$\geq 75\%$			
At 4 wks	2 (2)	14 (9) ^b	17 (12) ^c
Over 12 wks	2 (2)	7 (5)	16 (11) ^c

^a $P \leq 0.0001$ vs placebo.

^b $P < 0.05$ vs placebo.

^c $P < 0.005$ vs placebo.

overuse is not an impediment to effective preventive treatment.

Disclosure of Interests: S. Ashina is a consultant for Allergan, Eli Lilly, Promius, Alder and Novartis. V. Ramirez-Campos, J. M. Cohen, L. Janka are employees and/or stockholders of Teva Pharmaceuticals. As an investigator involved in the study, E. L. H. Spierings received research grants from Teva Pharmaceuticals.

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What Proportion of Anti-CGRP Antibody Therapy for Migraine is Contextual (Placebo) Effect?

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Objective: To estimate Effect Sizes and Proportion Contextual Effects of anti-CGRP and anti-CGRP-Receptor antibodies (CGRPABs) for adults with migraine in randomized, placebo-controlled trials (RCTs) registered at clinicaltrials.gov between 2013–2018.

Methods: Descriptive review of data extracted from peer-reviewed publications, conference abstracts and company websites. The primary outcome measure was calculation of Effect Size (standardized mean difference) for reduction in Monthly Migraine Days. Proportion Contextual Effects calculated from ratio of placebo to active group Effect Sizes for each dose in episodic and chronic migraine.

Results: 28 RCTs identified, 18 eligible trials with 13350 adult participants tested 28 different doses of CGRPABs. 10 non-eligible trials were ongoing (8) or in children (2). Effect Sizes were small (between 0.2 and 0.49) in 12/19 episodic migraine doses (63%) and 7/9 chronic migraine doses (78%). The Proportion Contextual Effect was

between 50 and 70% in 13/19 episodic migraine (68%) and 8/9 chronic migraine doses (89%). Proportion Contextual Effects of >70% were observed in 5/19 (26%) episodic migraine and 2/9 chronic migraine doses (22%).

Conclusion: Effect Sizes for CGRPABs in migraine are small. The Proportion Contextual Effect is greater than 50% of observed benefit – similar to approved therapies such as Onabotulinum Toxin Type A for chronic migraine. A limitation of our analysis is that we only searched one register, but we estimate that most of the benefit from CGRPABs is from existing healthcare infrastructure, not a specific effect of the drug's mechanism of action.

Disclosure of Interests: Dr Forbes has received payments amounting to GBP1800 from Allergan for speaking services, and has received hospitality from the following companies – Novartis, Cyberonics, Pfizer, Janssen-Cilag, Ipsen. DR Forbes is owner and director of Forbes Neurology Services Ltd which owns and maintains the severe-headache-expert.com website and earns income from supporting private neurology practice and publishing self-help books.

DR McCarron has received royalties from UpToDate for writing review articles on vascular neurology.

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Patients With Prophylactic Treatment Failure: Evidence From the BECOME Study

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Objective: To evaluate the proportion of migraine patients who failed any prophylactic treatment and were attending European specialist headache centres.

Methods: BECOME was a prospective, multicentre, non-interventional study in adults, conducted in 2 parts. In Part 1, 12,957 (62.2%) patients had ≥ 1 prior prophylactic treatment failure (PPTF). For Part 2, patient-specific data from patients with ≥ 1 PPTF and ≥ 4 monthly migraine days was collected, along with prophylactic treatment history and

reasons for discontinuation: lack of efficacy and/or poor tolerability.

Results: Part 2 included 2419 patients; mean (SD) age 43.0 (11.6) years, females (87%), and patients with migraine without aura (53%). As per Anatomical Therapeutic Chemical Classification System level 3, three categories of prophylactic treatments were used in migraine management: pharmacological, herbal and dietary. The three most commonly reported pharmacological prophylactics failed by patients included antiepileptics, 52.1% (primarily topiramate, 45.2%), β -blockers, 39.8% (primarily propranolol, 23.6%), and antidepressants, 37.8% (primarily amitriptyline, 29.8%) (Table). Antiinflammatories and antirheumatics (2.0%) were also used and failed; normally used acutely, these were classified by treating physicians as used for prophylaxis. Dietary/herbal agents that failed, included magnesium, riboflavin, *Petasites hybridus* and *Ginkgo biloba*, with majority of patients reporting efficacy failure.

Conclusion: Migraine is a disabling neurological disease and its management is complex. Almost two-thirds (62%) of patients visiting European specialist headache centres during Part 1 of the study had ≥ 1 PPTF. Individual data from Part 2 show that patients tried and failed a wide variety of substances to prevent their disease, including herbal/dietary and acute agents, in addition to the commonly used prophylactic treatments.

Disclosure of Interests: Patricia Pozo-Rosich – received honoraria as a consultant and speaker during the last 5 years from Allergan, Almirall, Chiesi, Eli Lilly, Novartis and Teva. Her research group has received research grants from Allergan and has received funding for clinical trials from Alder, Boehringer Ingelheim, MSD, electroCore, Eli Lilly, Janssen Cilag, and Novartis. She is a trustee member of the board of the International Headache Society and a Member of the Council of the European Headache Federation. She is on the editorial board of *Revista de Neurologia*. She is an editor for *Frontiers of Neurology* and *Journal of Headache and Pain*. She is a member of the Clinical Trials Guidelines Committee of the International Headache Society. She has edited the Guidelines for the Diagnosis and Treatment of Headache of the Spanish Neurological Society. She does not own stocks from any pharmaceutical company. Christian Lucas – collaboration as an expert, investigator or coordinator of clinical trials with Novartis, Teva, Sanofi, Grunenthal, Eli Lilly, Biogen, and Ethypharm. David Watson — received honoraria from Novartis, Teva and Allergan in the last 12 months for consultancy and educational work. Charly Gaul – received honoraria for consulting and lectures within the past 3 years from Allergan Pharma, Ratiopharm, Boehringer Ingelheim Pharma, Eli Lilly, Novartis Pharma, Desitin Arzneimittel, Cerbotec, Bayer Vital, Hormosan Pharma, electroCore, Grünenthal, Reckitt Benckiser, and Teva.

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Table. Number of patients with prior prophylactic treatment failures ($\geq 1\%$) according to the reason for failure with pharmacological classes used as prophylactic treatments in Part 2 of the BECOME study, population set (N = 2419).

ATClevel3		Overall	Tolerability failure	Overall Tolerability failure	Other failure (e.g. not suitable)
Pharmacological agents-prophylactic treatments	Antiepileptics	1260 (52.1%)	637 (26.3%)	700 (28.9%)	15 (0.6%)
	β blockers	962 (39.8%)	407 (16.8%)	567 (23.4%)	18 (0.7%)
	Antidepressants	914 (37.8%)	397 (16.4%)	556 (23.0%)	7 (0.3%)
Pharmacological agents-acute treatments used as prophylactics	Antiinflammatory and antirheumatic products, non-steroids	49 (2.0%)	17 (0.7%)	33 (1.4%)	–
Dietary supplements	Mineral supplements (magnesium, nicotina-made, silicon dioxide)	81 (3.3%)	15 (0.6%)	66 (2.7%)	–
Herbal agents	Uncoded (petasites hybridus, ginkgo biloba)	8 (0.3%)	–	8 (0.3%)	–

Most important pharmacological classes/categories failed by patients listed. All values are presented as n (%). ACE, angiotensin-converting-enzyme; ATC, Anatomical Therapeutic Chemical Classification System.

He does not hold any stocks of pharmaceutical companies or medical device companies. Emma Ramsden – provides services to Novartis Pharma AG. Paolo Martelletti – Section Editor, Medicine, SpringerNature Comprehensive Clinical Medicine; Editor-in-Chief, The Journal of Headache and Pain; Headache Books Series Editor, Springer; EU Expert, European Medicine Agency. Past-President of European Federation, Chairman of School of Advanced Studies of European Headache Federation. He does not hold any stocks of any pharmaceutical companies or medical device companies. Shannon Ritter and Josefin Snellman – employees and stocks: Novartis.

IHC-PO-160**Inversed Lasagna's law: the ethics of overbooking study sites in clinical trials**

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Objective: To highlight the ethical implications of raising patients' expectations and availability (inversed Lasagna's law) and overbooking study sites with competitive enrolment in recent trials.

Methods: To speed-up patient recruitment in clinical trials, study sponsors are (i) intensively promoting their new treatment raising patient awareness and availability and (ii) heavily overrecruiting study sites and patients with competitive enrolment. As a result, patient inclusion is frequently stopped well before the planned target date.

Many patients who were already pre-screened and excited to participate, are left in despair, comparable to airline passengers being told at the very last minute their flight is overbooked. While understandable from a commercial viewpoint to complete studies ASAP, such an “hyping, overbooking and disappointing strategy” is disrespectful to patients and study physicians.

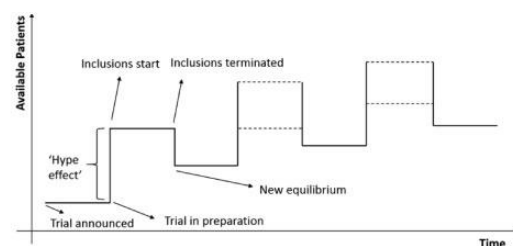


Figure 1. The inversed Lasagna's law; patient availability is plotted as a function of time. From the moment a clinical trial starts, the created "hype" among patients causes a steep increase. Only a fraction of these patients is included. Many however are still willing to participate. This results in a new equilibrium of patient availability at a higher setpoint for next trials.

Results: We experienced “unexpected early study termination” in three anti CGRP trials. Many patients were extremely disappointed and understandably angry. Most, however, remained motivated to participate in next trials, not rarely to experience the same. As a result, more and more patients were anxious to participate in trials, inverting Lasagna's law, according to which patients' availability usually drops sharply at the onset of a clinical trial, to restore again after completion. While patients and investigators are unhappy, study sponsors are delighted with the significant reduction in trial duration.

Remarkably, companies apparently weren't quite so understanding what the impact was to patients and the challenge study physicians face explaining this to furious patients.

Conclusion: While we understand the need of shortening trial inclusion times, we are seriously questioning the ethics of (i) creating hypes around a new treatment, dramatically raising patient's expectations and availability, and (ii) at the same time, significantly overbooking trial sites with competitive enrolment, leading to early termination of patient inclusion and disrespectful last minute exclusion of many "overbooked" patients who were eager and ready to participate. Possible solutions will be discussed.

Disclosure of Interest: None Declared.

IHC-PO-161

Long term actions of a recombinant advanced Botulinum toxin (BiTox-AA) molecule in migraine animal models

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Objective: Botulinum toxin A (BoNT-A) is an established preventive treatment for migraine, however its toxicity can be a major limitation in achieving higher efficacy. Recombinant BoNT that have advanced binding properties and reduced toxicity, have been recently developed. BiTox-AA is a recombinant BoNT-A toxin with double binding domains. In this project we aimed to investigate the long-term actions of BiTox-AA in the trigeminal ganglia and trigeminocervical system (TCC) in migraine animal models.

Methods: In male rats, Bitox-AA (20 ng) or saline were injected over the peri-orbital areas (100nl). Seven days later, mechanical (von Frey) and electrical trigeminovascular activation thresholds were assessed bilaterally on first order neurons in the trigeminal ganglia by means of extracellular electrophysiology, by a researcher blinded to experimental groups. In a separate set of experiments, seven days following injections, the superior sagittal sinus was electrically stimulated and TCC tissue was collected and processed for the presence of Fos-positive cells, using a standard immunohistochemistry protocol. Cell counting was performed by a researcher blinded to experimental groups.

Results: In first order neurons in the trigeminal ganglia, BiTox-AA significantly increased the mechanical thresholds of A δ -fibers compared to saline ($P < 0.005$). Electrical activation thresholds, assessed as the minimum voltage required to induce evoked action potentials, were significantly increased in the BiTox-AA treated group compared to saline in both A δ - and C-fibers ($P < 0.005$). The number of Fos-positive cells was significantly lower in the TCC tissue collected from animals treated with BiTox compared to the saline treated group ($P < 0.05$).

Conclusion: BiTox-AA is an advanced BoNT-A molecule that can significantly modulate trigeminovascular nociceptive processing, offering a promising and significant advance in the preventive therapeutic options for migraine patients.

Disclosure of Interest: None Declared.

IHC-PO-162

Administration of BoNT/A, in a population of patients with chronic refractory migraine with painkillers overuse, linked to change in Plasma levels of oxidative Stress Biomarkers

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Objective: Our aims would be: a) To investigate the different levels of plasmatic oxidative stress biomarkers AOPP (Advanced Oxidation Protein Products), FRAP (Ferric Reducing Antioxidant Power), and Thiolic Groups between chronic migraineurs (CM) and healthy controls (HC), b) To measure modifications of baseline plasmatic concentrations of oxidative stress biomarkers in CM after a 6-month prophylactic treatment with BoNT/A, c) To report plasmatic biomarkers modifications related to migraine outcomes after a 6-month prophylactic treatment with BoNT/A.

Methods: Patients were subjected to 3 visits 3 months apart from each other, as normal clinical practice in the Protocol of BoNT/A administration according to PREMP protocol (31 sites of injections)+7 additional points according to "Follow the pain" protocol.

Results: The comparison of the oxidative stress biomarkers measured in the group of CM patients with symptomatic overuse and in the HC group, the difference between AOPP values and the Thiolic Groups was significant ($p < 0.001$), and also the difference between FRAP ($p = 0.005$) values between the two groups of patients was significant. From the comparison of the quantitative

variables at T0 and T1 it was found that after six months from the beginning of BoNT/A therapy, FRAP ($p < 0.001$) and Thiolic Groups ($P = 0.04$) significantly increased, and also AOPP significantly decreased ($p = 0.003$). The frequency of cephalgic attacks, the number of symptomatic intake/month, the scores at the FSS, VNS, HIT-6, ASC-12, GAD-7 and PHQ-9 scales in the group of 27 CM, decreased significantly ($p < 0.001$) from T0 to control after six months at T1.

Conclusion: It could be hypothesized that BoNT/A, going to inhibit the expression of TRPA1 and TRPV1 receptors, at the level of nociceptive terminations at multiple levels, and also by inhibiting the release of CGRP and other pro-inflammatory molecules from pre and post-synaptic vesicles. Thanks to the block of SNAP-25, it causes itself a reduction of the oxidative and nitrosactive stress, blocking the sensitization of the Trigemino-Vascular system, Trigemino-Cervical system, thalamus and cerebral cortex. The toxin is also capable of exerting action at central level by blocking the release of CGRP and Glutamate.

Disclosure of Interest: None Declared.

IHC-PO-163

CGRP antagonists for chronic migraine: early results

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Objective: This was a retrospective review to evaluate patients with chronic migraine treated over 6 months with erenumab. 3 studies were done, evaluating: 1. efficacy and side effects of the erenumab, 2. poor responders vs. excellent responders, and 3. efficacy over a full 6 months.

Methods: Study Design.— This retrospective study was accomplished at our headache center, conducted during November and December, 2018.

Results: We evaluated the results of erenumab after the first 6 months of treatment. The first study involved 220 consecutive chronic migraine patients, after 3 months. 43% experienced 0 to 30% relief. 34% reported 30 to 70% relief, while 24% described 70 to 100% relief. 10% of patients reported almost complete relief. There were a considerable number of side effects reported by the 220 patients. Constipation was the most prevalent, at 20%. 3 patients suffered serious side effects. The 2nd study assessed poor responders vs. excellent responders. We looked at 20 variables. Patients on frequent opioids tended to be poor responders. The other variables did not hold up to statistical significance.

The third study evaluated those 50 patients who had completed 6 months of therapy. The average relief started with

36% and 35% for the initial 2 months, but slowly declined to 27% by the end of the 6th month. Patients who averaged 0 to 15% relief for the first 2 months generally continued to do poorly. Similarly, most of the patients ($N = 9$) who did very well (70% to 100% relief) for the first 2 months continued to have success.

Conclusion: Erenumab for CM has reasonable efficacy over time. The response for the initial 2 months generally predicts later response, but at times the erenumab ceases being effective. Side effects are a major concern.

Disclosure of Interests: Speaker for Teva. Speaker for Amgen. Speaker for Lilly.

IHC-PO-164

Long-term impact of fremanezumab on response rates, acute headache medication use, and disability in patients with chronic migraine who have failed at least one prior preventive migraine medication: results of a 1-year study

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Objective: Fremanezumab, a fully humanized monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide (CGRP), is approved in the US and the EU for the preventive treatment of migraine in adults. Herein we evaluated the long-term effect of fremanezumab on response rates, acute headache medication use, and disability in patients with chronic migraine (CM) who had failed ≥ 1 prior preventive migraine medication.

Methods: In this 12-month, multicenter, randomized, double-blind parallel-group study, CM patients received subcutaneous fremanezumab either quarterly (675 mg every 3 months) or monthly (225 mg every month with a starting dose of 675 mg). This *post hoc* analysis was limited to CM patients who had failed ≥ 1 prior migraine preventive medication (defined as lack of efficacy or intolerance). The proportions of patients with a $\geq 50\%$ reduction in the monthly average number of migraine days and headache days of at least moderate severity, respectively, and the change from baseline in the monthly average number of days with acute headache medication use and in headache-related disability (assessed using the six-item Headache Impact Test [HIT-6]) were measured at Months 6 and 12.

Results: The proportion of CM patients (quarterly: $n = 247$; monthly $n = 243$) with a $\geq 50\%$ reduction in monthly migraine days was maintained at Months 6 (quarterly: 34%; monthly: 48%) and 12 (quarterly: 48%; monthly: 51%). A $\geq 50\%$ reduction in the monthly number of

headache days of at least moderate severity was also maintained at Months 6 (quarterly: 40%; monthly: 51%) and 12 (quarterly: 48%; monthly: 52%). The monthly average number of days of acute headache medication use decreased from baseline to Months 6 (quarterly: -4.7 days; monthly: -6.2 days) and 12 (quarterly: -5.8 days; monthly: -6.2 days). The mean HIT-6 disability score decreased from baseline to Months 6 (quarterly: -5.5; monthly: -7.3) and 12 (quarterly: -6.5; monthly -8.0).

Conclusion: Long-term treatment with fremanezumab maintained efficacy, reduced acute headache medication use, and improved headache-related disability in CM patients who had failed ≥ 1 prior preventive migraine medication.

Disclosure of Interests: Peter McAllister: Receives research support from Alder, Allergan, Avanir, Autonomic Technologies, Lilly, Teva, Tian and serves on speakers' bureau and/or as a consultant for Allergan, Alder, Amgen, Lilly, Teva, ElectroCore, Depomed, and Avanir.

Joshua M. Cohen: Employee of Teva Pharmaceuticals.

Ronghua Yang: Employee of Teva Pharmaceuticals.

Xiaoping Ning: Employee of Teva Pharmaceuticals.

Shawn Elms: Employee of Teva Pharmaceuticals.

IHC-PO-165

Eptinezumab Increased Days Free from Canonical Migraine-Associated Symptoms Within 1 Month of Treatment in Patients with Chronic Migraine

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Objective: Migraine is diagnosed based on headache frequency accompanied by ≥ 2 of unilateral location, pulsating quality, moderate or severe pain intensity, or avoidance of physical activity, and presence of ≥ 1 of nausea and/or vomiting, or photophobia and phonophobia. Eptinezumab, a humanized anti-CGRP monoclonal antibody, demonstrated significant migraine reduction and acceptable safety in PROMISE-2, a phase 3 trial in chronic migraine (CM) (NCT02974153). We evaluated changes in canonical migraine symptom-free days in patients with CM during the first month (28 days) after treatment in PROMISE-2.

Methods: Adults with CM were randomized to eptinezumab 100 mg, 300 mg, or placebo, with quarterly

intravenous administration for 2 infusions. Migraine symptoms were assessed using daily eDiary entries. Baseline was the daily average (mean) over the 28-day screening period.

Results: Baseline days free from moderate or severe pain were 10.3 (100 mg), 10.4 (300 mg), and 10.4 (placebo), increasing to 18.1, 19.1, and 15.8 days, respectively, by Month 1. Baseline nausea-free days were 14.6 (100 mg), 14.6 (300 mg), and 14.9 (placebo), increasing to 21.4, 21.7, and 19.5 days, respectively, by Month 1. Baseline vomiting-free days were 25.1 (100 mg), 24.7 (300 mg), and 24.6 (placebo), increasing to 26.9, 26.8, and 26.2 days, respectively, by Month 1. Baseline days free from photophobia and phonophobia were 13.4 (100 mg), 14.0 (300 mg), and 13.2 (placebo), increasing to 20.0, 21.3, and 17.8 days, respectively, by Month 1. Baseline days free from avoidance of physical activity were 12.4 (100 mg), 12.2 (300 mg), and 12.1 (placebo), increasing to 19.0, 20.0, and 16.6 days, respectively, by Month 1.

Conclusion: Within the first month after treatment with eptinezumab, canonical migraine symptom-free days increased by approximately 1 week compared with baseline for most symptoms; this increase was greater than in placebo-treated patients.

Disclosure of Interests: Peter J. Goadsby: Has received personal compensation for consulting, serving on a scientific advisory board, speaking, or other activities with Amgen Eli-Lilly and Company, Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Novartis, Scion, Teva Pharmaceuticals, and Trigemina Inc. Dr. Goadsby has received personal compensation in an editorial capacity for Journal Watch- Massachusetts Medical Society. Dr. Goadsby has received research support from Amgen and Eli-Lilly and Company.

Jack Schim: Received compensation from Allergan, Amgen, Acorda, Avanir, Depomed, ElectroCore, Eli-Lilly, Novartis, Pernix, Promius, Supernus, Teva Pharmaceuticals, Upshire-Smith.

Alder – Dr. Schim or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value in a company sponsoring research with which he was involved as an investigator.

Eric Kassel: Alder Biopharmaceuticals employee. Received research support from Alder.

David Biondi: Former fulltime employee of Alder Biopharmaceuticals, Inc. Involved in the conduct of the study, data analyses and final clinical study report.

Alder BioPharmaceuticals; Johnson & Johnson – Within the past year, Dr. Biondi or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value in a company

whose medical equipment or other materials related to the practice of medicine.

Joe Hirman: Received compensation from Alder Biopharmaceuticals.

Roger Cady: Full time employee of Alder Biopharmaceuticals.

IHC-PO-166

Long-term impact of fremanezumab on response rates, acute headache medication use, and disability in patients with episodic migraine who have failed at least one prior preventive migraine medication: results of a 1-year study

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Objective: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), is approved in the US and the EU for the preventive treatment of migraine in adults. Herein we evaluated the long-term effect of fremanezumab on response rate, use of acute headache medication, and disability in patients with episodic migraine (EM) who had failed to respond to ≥ 1 prior preventive migraine medication.

Methods: In this 12-month, randomized, double-blind, parallel-group study, EM patients received subcutaneous fremanezumab quarterly (675 mg every 3 months) or monthly (225 mg monthly). This *post hoc* analysis included EM patients who had failed ≥ 1 prior migraine preventive medication (defined as lack of efficacy or intolerability; $n = 206$). The proportions of patients achieving a $\geq 50\%$ reduction in the monthly average number of migraine days and in headache days of at least moderate severity, respectively, and the change from baseline in the monthly average number of days with acute headache medication use and in headache-related disability (assessed by the Migraine Disability Assessment [MIDAS] questionnaire) were measured at Months 6 and 12.

Results: EM patients maintained a $\geq 50\%$ reduction in the monthly average number of migraine days at Months 6 (quarterly: 60%; monthly: 50%) and 12 (quarterly: 59%; monthly: 64%). A $\geq 50\%$ reduction in the monthly average number of headache days of at least moderate severity was also maintained at Month 6 (quarterly: 61%; monthly: 54%) and Month 12 (quarterly: 59%; monthly: 60%). The monthly average number of days of acute headache medication use decreased from baseline to Month 6 (quarterly -4.6 days; monthly: -3.6 days) and Month 12 (quarterly: -4.7 days; monthly: -4.5 days). The mean MIDAS score decreased from baseline to Month 6 (quarterly: -28.4 ;

monthly: -26.8) and Month 12 (quarterly: -30.7 ; monthly: -30.3).

Conclusion: Long-term treatment with fremanezumab maintained efficacy, reduced acute headache medication use, and improved headache-related disability in EM patients who had failed ≥ 1 prior preventive migraine medication.

Disclosure of Interests: Jan Lewis Brandes: Receives research support from Amgen, Eli Lilly and Company, CoLucid Pharmaceuticals, Teva Pharmaceuticals, Zosano, Allergan, and Biohaven Pharma and serves on the advisory boards and/or speaker's bureau for Amgen, Eli Lilly and Company, Depomed, Avanir Pharmaceuticals, Promius Pharma, Supernus Pharmaceuticals, and Teva Pharmaceuticals.

Timothy R. Smith: Served on speaker's bureaus for Amgen, Novartis, Lilly, and Promius and serves on advisory boards and/or as a consultant for Biohaven, Amgen, Lilly, Alder, Promius, and Zosano. Receives research support from Amgen, Alder, Lilly, Teva Pharmaceuticals, Allergan, Biohaven, Dr Reddy's, Zosano, Electrocore, Scion Neurostim, Novartis, Novo Nordisk, Ionis, and Impel.

Joshua M. Cohen: Employee of Teva Pharmaceuticals.

Ronghua Yang: Employee of Teva Pharmaceuticals.

Xiaoping Ning: Employee of Teva Pharmaceuticals.

Karen Carr: Employee of Teva Pharmaceuticals.

IHC-PO-167

Patient Global Impression of Change Related to Improvement in Most Bothersome Symptom Following Treatment With Eptinezumab

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Objective: Eptinezumab, a humanized anti-CGRP monoclonal antibody, demonstrated significant migraine reduction and acceptable safety in PROMISE-2, a phase 3 clinical trial of chronic migraine (CM) (NCT02974153). Here, we evaluated the impact of eptinezumab treatment on patient global impression of change (PGIC) and most bothersome symptom (MBS) in patients with CM.

Methods: Adults with CM ($N = 1072$) were randomized to eptinezumab 100 mg, 300 mg, or placebo, with quarterly intravenous administration for 2 infusions. Patients identified an MBS associated with migraines (other than headache) at screening. MBS options included physical, sensory, autonomic, and psychological symptoms during ictal and interictal phases of migraine. PGIC and MBS improvement

were assessed at 4-week intervals using a 7-point rating scale (from “very much improved” to “very much worse”).

Results: Eptinezumab 100 mg and 300 mg resulted in statistically significant reductions in mean monthly migraine days vs placebo ($p < 0.0001$, both doses). The most frequently identified MBSs were light sensitivity, pain with activity, and nausea. MBS was unchanged during the 28-day screening period in $>90\%$ of patients in all treatment arms. At Month 1, MBS was much or very much improved in 45.0% (100 mg), 56.9% (300 mg), and 28.9% (placebo) of patients; PGIC was much or very much improved in 45.0%, 59.0%, and 32.3%, respectively. MBS was minimally improved in 30.1% (100 mg), 22.2% (300 mg), and 29.7% (placebo) of patients; PGIC was minimally improved in 31.6%, 22.3%, and 24.0%, respectively. MBS was rated from unchanged to very much worse in 24.9% (100 mg), 21.0% (300 mg), and 41.4% (placebo) of patients; PGIC was rated from unchanged to very much worse in 23.4%, 18.8%, and 43.6%, respectively. Improvements were maintained or further increased at Months 3 and 6.

Conclusion: Eptinezumab improved MBS rapidly, beginning Month 1. Trends in MBS improvement and PGIC were similar across time points, suggesting MBS improvements are highly correlated with PGIC.

Disclosure of Interests: Richard B. Lipton: Serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta.

eNeura, Biohaven – Received compensation, that could include stock, stock options or expense compensation for serving on a board of directors for a commercial entity (for-profit business).

Biohaven– Within the past year, Dr. Lipton or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value in a company sponsoring research with which he was involved as an investigator.

Biohaven – Within the past year, Dr. Lipton or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value (which ever dollar value is lowest) in a company whose medical equipment or other materials related to the practice of medicine.

Within the past year received research support from the Migraine Research Foundation, the National Headache Foundation and Amgen.

Lora McGill: Received compensation from: Abbvie, Aevi, Alder, Alkermes, Allergan, Amgen, Aptinyx, Arbor, Axsome, AZ Therapies, Bayer, Biogen, Biohaven, Bionomics, BlackThorn, CoLucid, Daiichi, Dr. Reddy's, Eli Lilly, Esperion, Intra-Cellular, Intarcia, Ironshore, Janssen,

Labrys Biologic, Lundbeck, Mitsubishi, Mylan NLS Pharma, Nektar, Nestle Pamlab, Neuralstem, Neurocrine, Novartis, Novo Nordisk, ObsEva, Otsuka, Palatin, Pfizer, Regeneron, Rhodes, Shionogi, Shire, Sunovion, Supernus, Takeda, TauRx, Teva.

Joe Hirman: Received compensation from Alder Biopharmaceuticals.

David Biondi: Former fulltime employee of Alder Biopharmaceuticals, Inc. Involved in the conduct of the study, data analyses and final clinical study report.

Alder BioPharmaceuticals; Johnson & Johnson – Within the past year, Dr. Biondi or an immediate family member held stock or stock options greater than 5 percent of the company or greater than \$10,000 in value in a company whose medical equipment or other materials related to the practice of medicine.

Roger Cady: Full time employee of Alder Biopharmaceuticals.

IHC-PO-168

Long-Term term efficacy of fremanezumab in chronic and episodic migraine patients with acute medication overuse at baseline: results of a 1-year study

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Objective: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), is approved in the US and the EU for the preventive treatment of migraine in adults. We assessed the long-term efficacy of fremanezumab in migraine patients with baseline acute medication overuse (AMO).

Methods: This 12-month, multicenter, randomized, double-blind, parallel-group study evaluated two subcutaneous dose regimens of fremanezumab in patients with chronic (CM) or episodic (EM) migraine. The study included patients rolled over from two placebo-controlled studies and 312 new patients. Patients were assigned to either quarterly (675 mg every 3 months) or monthly (225 mg monthly; CM: starting dose of 675 mg) dosing. The mean change from baseline in monthly average number of migraine days and in headache days of at least moderate severity was measured in patients with or without baseline AMO (defined as acute headache medication use $[\geq 15$ days], migraine-specific acute medication use $[\geq 10$ days], or use of combination medications for headache $[\geq 10$ days]).

Results: At baseline, 599/1103 (54%) CM patients and 100/775 (13%) EM patients had AMO. At Month 12, reductions in the monthly number of migraine days were sustained in patients with CM (quarterly [mean change]: -7.5 days; monthly: -8.2 days) and EM (quarterly: -5.9 days; monthly: -5.1 days) and baseline AMO. Reductions in migraine days were also seen in patients without baseline AMO (CM: quarterly: -6.9 days; monthly: -7.9 days; EM: quarterly: -5.1 days; monthly: -5.1 days). At Month 12, reductions in the monthly number of headache days of at least moderate severity were sustained in CM (quarterly: -7.0 days; monthly: -7.4 days) and EM (quarterly: -6.1 days; monthly: -4.6 days) patients with baseline AMO. Reductions in headache days of at least moderate severity were also seen in patients without baseline AMO (CM: quarterly: -5.5 days; monthly: -6.2 days; EM: quarterly: -4.1 days; monthly: -4.2 days).

Conclusion: Fremanezumab demonstrated efficacy over 12 months in migraine patients regardless of AMO at baseline.

Disclosure of Interests: Stephen D. Silberstein: Provides consultation to Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Curelator Inc., Depomed, Dr. Reddy's Laboratories, Ensured Inc., ElectroCore Medical LLC, eNeura Therapeutics, INSYS Therapeutics, Lilly USA LLC, Supernus Pharmaceuticals Inc., Teva Pharmaceuticals, Theranica, and Trigemina Inc.

Messoud Ashina: Speaker fees from Allergan, Amgen, Novartis and Teva Pharmaceuticals.

Joshua M. Cohen: Employee of Teva Pharmaceuticals.

Michael J. Seminerio: Employee of Teva Pharmaceuticals.

Ronghua Yang: Employee of Teva Pharmaceuticals.

Xiaoping Ning: Employee of Teva Pharmaceuticals.

Cory Blaiss: Employee of Teva Pharmaceuticals.

IHC-PO-169

Healthcare Resource Utilization in Adult Patients Treated With OnabotulinumtoxinA for Chronic Migraine: Results From the COMPEL Study

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Objective: To evaluate healthcare resource utilization (HRU) by patients treated with onabotulinumtoxinA for chronic migraine (CM) in a subanalysis of the COMPEL study.

Methods: The single-arm, open-label, multicenter, post-authorization, prospective COMPEL study (NCT01516892) enrolled adults with CM receiving onabotulinumtoxinA 155 U approximately every 12 weeks (9 treatments). Patients recorded headache (HA) days in a daily diary to assess mean change from baseline in the number of HA days/28-day period up to 108 weeks. HRU data, including total HA-related visits to a healthcare professional (HCP), emergency room (ER)/urgent care (UC) visits, overnight stays, and number of HA-related diagnostic tests, were collected at baseline (over the previous 6 months) and at each treatment session (since the last visit). *P*-values and 95% confidence intervals were based on t-test or Wilcoxon signed rank test.

Results: Patients (N = 716 enrolled) were, on average, aged 43 years, 85% were female, and 63% had a family history of migraine. At baseline, 557 patients reported a mean (SD) of 7.0 (15.4) and a minimum-maximum of 0–198 HA-related visits to an HCP. Visit frequency was significantly reduced at all time points. At each visit, the majority of patients reported seeing a neurologist/HA specialist, followed by a primary care physician. At baseline, 690 patients reported a mean (SD) of 0.5 (2.0) HA-related ER/UC visits, and 691 patients reported 0.2 (1.5) HA-related overnight hospital stays. Following onabotulinumtoxinA treatment, HA-related ER/UC visits and overnight hospital stays were significantly reduced at all time points. At baseline, 193 patients reported a total of 487 HA-related diagnostic tests. A total of 334 HA-related diagnostic tests were reported from weeks 24 to 96. Commonly reported diagnostic tests at baseline included blood tests (21.0%), MRI (18.7%), and CAT/CT scans (10.9%).

Conclusion: Real-world findings from the COMPEL study show that onabotulinumtoxinA treatment is associated with HRU reductions. These data support the long-term benefits associated with the use of onabotulinumtoxinA for the treatment of CM in clinical practice.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

IHC-PO-170

Smartphone Based Migraine Behavioral Therapy in the Neurology Office

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Objective: Progressive Muscle Relaxation (PMR) is an under-utilized Level A evidence-based treatment for

migraine prevention. We studied the feasibility and acceptability of smartphone application (app) based PMR for migraine in a neurology setting, explored whether app based PMR might reduce headache (HA) days, and examined potential predictors of app and/or PMR use.

Methods: In this single-arm pilot study, adults with ICHD3 migraine, 4+ HA days/month, a smartphone and no prior behavioral migraine therapy in the past year were asked to complete a daily HA diary and do PMR for 20 minutes/day for 90 days. Outcomes were: adherence to PMR (# and duration of audio plays) and frequency of diary

Table 1. Participant Demographics and Headache Characteristics and Duration and Frequency of PMR Use

Participant	N = 51
Female	48 (94%)
Age:	Mean = 39 ± 13 [19,66]
Current (Mean, SD, Range)	Median 35, IQR = 21
Age when headache began (mean, SD, Range)	Mean = 21 ± 12 [5,55] Median = 17, IQR = 18
Race/Ethnicity	
White/Caucasian	38 (75%)
African American	4 (8%)
Other	8 (16%)
Missing	1 (2%)
Positive Family History of Headache	39 (76%)
Headache Characteristics	Mean = 13 ± 8 [4,31]
Average number of Headache Days/month:	Median = 10, IQR = 2
(Mean, SD, Range)	Mean = 6 ± 2 [3,10]
Average pain intensity (0–10 pain scale):	Median = 6, IQR = 4
(Mean, SD, Range)	Mean = 2 ± 2 [0,7]
Current pain intensity (0–10 pain scale):	Median = 2, IQR = 5
(Mean, SD, Range)	Mean = 53 ± 64 [0, 350]
MIDAS (Sum of the first 5 questions)	Median = 26, IQR = 2
Little or no Disability (Grade I: 0–5)	0–5 = 6
Mild Disability (Grade II: 6–10)	6–10 = 7
Moderate Disability (Grade III: 11–20)	11–20 = 6
Severe Disability (Grade IV: 21+)	21+ = 32
Psychiatric Screens	
PROMIS Depression (Sum)	Mean = 50 ± 10 [31,73]
PROMIS Anxiety (Sum)	Mean = 50 ± 10 [31,75]
Average Days PMR Played During the Study	22 ± 21
Mean PMR Session Duration (minutes)	11 ± 7

use. Predictors in the models were baseline demographics, HA history (age at first HA, # of HA days/past month, average HA intensity, current HA intensity, migraine disability (MIDAS), prior migraine therapies), PROMIS depression and anxiety scores, and presence of overlapping pain conditions studied and app satisfaction scores at enrollment.

Results: See table. There was a decline in use/week; most users of the app/PMR used it in the first 6 weeks of the 90-day period. On average, high users (PMR 2+ days/week in the first month) had 4 fewer days of reported HAs in month 2 vs. month 1, whereas low PMR users (PMR less than 2 days/week in the first month) had only 2 fewer HA days in month 2. PROMIS depression score was negatively associated with the log odds of using the diary at least once (vs. no activity) in a week (OR = 0.70, 95% CI = [0.55,0.85]) and of doing the PMR at least once in a week (OR = 0.77, 95% CI = [0.68, 0.91]). PROMIS anxiety was positively associated with using the diary at least once every week (OR = 1.33, 95% CI = [1.09, 1.73]) and with doing the PMR at least once every week (OR = 1.14 [95% CI. = [1.02, 1.31]).

Conclusion: About half of participants used smartphone PMR intervention based upon a brief, initial introduction to the app. App use was associated with reduction in HA days. Higher depression scores were negatively associated with diary and PMR use while higher anxiety scores were positively associated.

Disclosure of Interests: Dr. Seng has received research support from the NINDS (NS096107: PI Seng), consulting fees from GlaxoSmithKline and Eli Lilly, and contributor fees from Haymarket Media.

Dr. Richard B. Lipton is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. He receives research support from the NIH: 2PO1 AG003949 (mPI), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), IRF1 AG057531 (Site PI), RFI AG054548 (Investigator), IRO1 AG048642 (Investigator), R56 AG057548 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor), IK01AG054700 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation. He serves on the editorial board of Neurology, senior advisor to Headache, and associate editor to Cephalalgia. He has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva,

Trigemina, Vector, Vedanta. He receives royalties from Wolff's Headache 7th and 8th Edition, Oxford Press University, 2009, Wiley and Informa.

Thomas Berk: Honoraria from Medscape Neurology. Advisory Board participation from Amgen/Novartis and Biohaven.

IHC-PO-171

A Pharmacokinetic Bioequivalence Study of Fremanezumab Administered Subcutaneously Using an Autoinjector and a Prefilled Syringe

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Objective: To demonstrate pharmacokinetic bioequivalence of fremanezumab administered subcutaneously (sc) using 2 presentations: a newly developed autoinjector (AI, test) and the currently marketed prefilled syringe (PFS, reference) in healthy volunteers. Safety and tolerability were also evaluated.

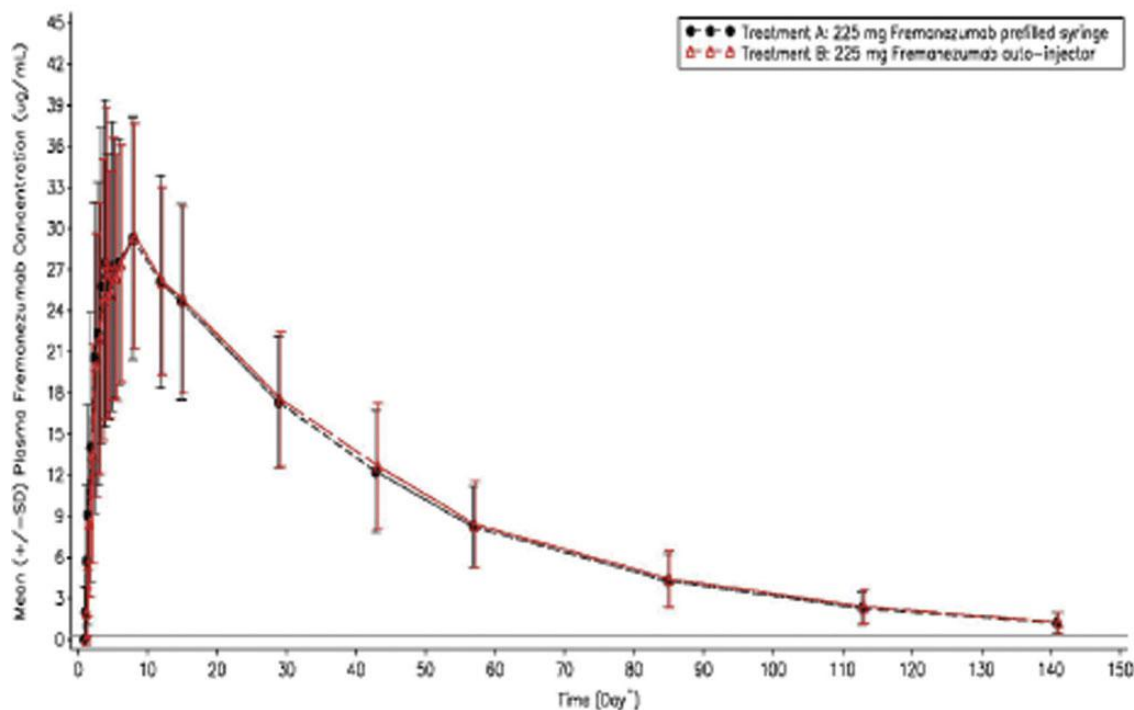
reference) in healthy volunteers. Safety and tolerability were also evaluated.

Methods: Healthy male and female volunteers received a single sc injection of 225 mg to the abdomen via AI or PFS in a parallel group design. Blood samples for pharmacokinetics (PK) and anti-drug antibodies (ADA) were collected pre- and post-dose. Sample size was calculated to provide a minimum of 90% power for showing bioequivalence for the following primary PK parameters: C_{max} , AUC_{0-t} , $AUC_{0-\infty}$. Safety and tolerability assessments included vital signs, physical examinations, adverse event reporting, laboratory evaluations and immunogenicity.

Results: Mean concentration-time profiles for the two treatment groups (AI n = 106 and PFS n = 110) were similar (Figure 1). Correspondingly the point estimates for the back transformed ratio of geometric least squares (LS) means of C_{max} , AUC_{0-t} , and $AUC_{0-\infty}$ (test/reference) were 1.03, 1.04, and 1.05, respectively. The 90% CIs of geometric LS means ratio for all primary PK parameters were entirely contained within bioequivalence margins of 0.8 to 1.25. In addition, for both groups, median t_{max} was 5 days and mean $t_{1/2} \sim 29$ days.

The safety profile was similar to other fremanezumab studies. The incidence of treatment-related adverse events (AEs) was reported by 39 [36%] subjects in the AI group and 26 [24%] in the PFS group. The most frequently

Figure 1: Plots of Mean Plasma Concentration—Time Profiles of Fremanezumab by Treatment on a Linear Scale



Abstract number: IHC-PO-171

occurring AEs were injection site reactions which were comparable between AI and PFS groups and resolved 4 hours post-dose in 99% of subjects. The incidence of treatment-emergent ADA response was low and evenly distributed between AI (n = 3 [3%]) and PFS (n = 4 [4%]) groups.

Conclusion: The AI presentation of fremanezumab provides a bioequivalent PK profile to that of the PFS. Safety and tolerability were comparable between the two administration presentations and similar to the safety reported in prior studies.

Disclosure of Interests: Authors are employees of Teva Pharmaceutical Industries Ltd.

IHC-PO-172

Impact of fremanezumab on any acute headache medication use in migraine patients with medication overuse and documented inadequate response to 2–4 migraine preventive medications in the multicentre, randomised, placebo-controlled FOCUS study

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Objective: The FOCUS study of fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), was the first and largest study of a migraine preventive treatment in adults both chronic and episodic migraine (CM and EM) and documented inadequate response to 2–4 classes of migraine preventive medications. Changes in use of any acute headache medication were evaluated in a subgroup of patients (pts) with medication overuse (use of any acute medication on ≥ 15 days/month or triptans/ergots/combination medications on ≥ 10 days/month [mo]) at baseline (BL).

Methods: For 12 weeks of double-blind treatment, pts were randomised (1:1:1) to quarterly fremanezumab (Mo 1: 675 mg; Mo 2 and 3: placebo), monthly fremanezumab (Mo 1: CM, 675 mg; EM, 225 mg; Mo 2 and 3: 225 mg), or matched monthly placebo. Changes from BL in monthly average days with acute headache medication use at 4 and 8 weeks (wks) and during the 12 wks after the first dose were compared using analysis of covariance.

Results: Of 838 randomised pts, 427 had medication overuse. Reductions from BL in monthly days with any acute headache medication use at 4 and 8 wks and during the 12 wks after the first dose were significantly

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Table. Change From BL in Monthly Average Days of Use of Any Acute Headache Medication at Wks 4 and 8 and During 12 Wks

LSM change (SE) from baseline	Placebo (n = 133)	Quarterly fremanezumab (n = 148)	Monthly fremanezumab (n = 146)
Wk 4	−0.3 (0.61)	−4.2 (0.61) ^a	−4.9 (0.56) ^a
Wk 8	−1.1 (0.71)	−3.8 (0.71) ^b	−4.8 (0.65) ^a
Wk 12	−0.8 (0.62)	−3.9 (0.62) ^a	−4.8 (0.57) ^a

^aP < 0.0001 vs placebo.

^bP = 0.0021 vs placebo.

greater with both fremanezumab regimens versus placebo (all P \leq 0.0021; **Table**).

Conclusion: Fremanezumab provided early and consistent reductions in the use of any acute headache medication versus placebo in pts with medication overuse at BL and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: L. Newman is on an Advisory Board for Teva Pharmaceuticals. J. M. Cohen, V. Ramirez-Campos, and L. Janka are employees and/or stockholders of Teva Pharmaceuticals. In the last 3 years, H. C. Diener has received honoraria for participation in clinical trials, contribution to advisory boards, or oral presentations from: Alder, Allergan, Amgen, Autonomic Technology, Bristol-Myers Squibb, CoLucid, Electrocore, Ipsen Parma, Lilly, Medtronic, MSD, Novartis, Pfizer, Schaper and Brümmer, Teva and Weber & Weber. Dr. Diener has received financial support for research projects from Allergan, Electrocore, MSD and Pfizer. Dr. Diener's headache research at the Department of Neurology in Essen is supported by the German Research Council (DFG), the German Ministry of Education and Research (BMBF) and the European Union. Dr. Diener has no ownership interest and does not own stocks of any pharmaceutical company. Dr. Diener serves on the editorial boards of Cephalalgia and Lancet Neurology. Dr. Diener chairs the Clinical Guidelines Committee of the German Society of Neurology and is member of the Clinical Trials Committee of the IHS.

IHC-PO-173

Can OnabotulinumA Be Stopped? Prognosis Following Discontinuation of OnabotulinumA Therapy in “Super-responding” Chronic Migraine Patients

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Objective: To determine whether successful treatment of chronic migraine (CM) with onabotulinum A (BotoxA) may be followed by a continued respite from headache once therapy has been discontinued.

Methods: We prospectively evaluated a series of patients with CM, all of whom were treated according to a uniform protocol involving serial injection of BotoxA. We followed all positively responding patients who met our stopping rule for a minimum of 6 months after discontinuation of BotoxA, and we assessed the incidence of clinical worsening in that group.

Results: Over 80% of our CM patients who achieved the stopping rule reported no clinical worsening or need to resume prophylactic therapy over the 6 months following discontinuation of BotoxA therapy. Patients with pre-treatment baseline chronic daily headache of greater than 6 months duration or a greater number of BotoxA treatments required to achieve our stopping rule were more likely to report clinical deterioration within 6 months of stopping treatment.

Conclusion: In many CM patients who experience an especially positive response to serial BotoxA injection therapy, clinical improvement may be sustained for a period of at least 6 months following discontinuation of prophylactic therapy.

Disclosure of Interest: None Declared.

IHC-PO-174

Effect of fremanezumab on quality of life and health status in migraine patients with documented inadequate response to 2–4 classes of migraine preventive medications in the randomised, placebo-controlled FOCUS study

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Objective: The FOCUS study of fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), was the

first and largest study of a migraine preventive treatment in adults with both episodic and chronic migraine (EM and CM) and documented inadequate response to 2–4 classes of migraine preventive medications. Exploratory endpoints included migraine-specific quality of life (MSQOL) domain and EuroQol-5 Dimension (EQ-5D-5L) visual analogue scale (VAS) scores.

Methods: During 12 weeks of double-blind treatment, patients were randomised (1:1:1) to quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), monthly fremanezumab (Month 1: CM, 675 mg; EM, 225 mg; Months 2 and 3: 225 mg), or matched monthly placebo.

Table. Change From Baseline in MSQOL Domain and EQ-5D-5L VAS Scores During 4 Weeks After Third Study Drug Dose

LSM(SE) change from BL	Placebo (n = 278)	Quarterly fremanezumab (n = 276)	Monthly fremanezumab (n = 283)
MSQOL domain			
Role function-restrictive	6.9(1.48)	15.7(1.50) ^a	17.5(1.48) ^a
Role function-preventive	6.2(1.37)	11.9(1.39) ^a	14.4(1.37) ^a
Emotional function	4.4(1.70)	13.4(1.72) ^a	15.6(1.70) ^a
EQ-5D-5L VAS	1.6(1.39)	4.7(1.41) ^b	7.2(1.39) ^b

^aP < 0.0001 vs placebo.

^bP < 0.05 vs placebo.

Mean changes from baseline (BL) in MSQOL domain and EQ-5D-5L VAS scores during the 4 weeks after the third dose of study drug were evaluated.

Results: 838 patients were randomised. Improvements from BL in all MSQOL domain and EQ-5D-5L VAS scores were significantly greater with fremanezumab vs placebo (all P < 0.05; **Table**).

Conclusion: Fremanezumab was associated with significant improvements vs placebo in MSQOL domain and EQ-5D-5L VAS scores in migraine patients with documented inadequate response to 2–4 classes of migraine preventative medications.

Disclosure of Interests: L. Mechtler has received honoraria as a speaker from Avanir, Allergan, Teva, and Promius. Dr. Mechtler has received research funding from Allergan, Teva, Boston Biomedical, Inc., and Autonomic Technologies, Inc. P. Pozo Rosich has received honoraria as a consultant and speaker for: Allergan, Almirall, Chiesi, Eli Lilly, Novartis and Teva. Dr. Pozo Rosich's research group has received research grants from Allergan and has received funding for clinical trials from Alder, Electrocore, Eli Lilly, Novartis and Teva. Dr. Pozo Rosich does not own stocks from any pharmaceutical company. X. Ning, M. Galic, J. M. Cohen, and R. Yang are employees of Teva Pharmaceuticals.

IHC-PO-175

Long-term Efficacy of Erenumab in Patients With Chronic Migraine Who Failed ≥ 3 Prior Prophylactic Treatments

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Objective: Erenumab is a fully human monoclonal antibody that selectively binds to and inhibits the canonical CGRP receptor. Patients (pts) with chronic migraine (CM) were randomly assigned (3:2:2) to receive placebo, sc erenumab 70 mg/140mg once every 4wks in a 12-wk double-blind treatment phase (DBTP; parent study) of a placebo-controlled study (NCT02066415). A subsequent 52-wk open-label extension (OLE) study (NCT02174861) assessed long-term efficacy and safety of erenumab. Here, we report the long-term efficacy of erenumab in a subgroup of pts in the OLE who failed ≥ 3 prior prophylactic treatments (TF) due to the lack of efficacy and/or poor tolerability before enrolment in the parent study.

Methods: The parent study enrolled 667 adult pts with CM (≥ 15 headache days/month; ≥ 8 migraine days/month). Pts completed 12wks of the DBTP to be eligible for the 52-wk OLE, during which they received erenumab every 4wks. Following a protocol amendment, pts who had not reached wk28, had a dose increase to 140 mg to allow them to receive the higher dose for ≥ 6 months; pts completing wk28 visit remained on 70 mg throughout OLE. OL treatment phase data were summarised by visit for all pts (combined treatment groups), irrespective of DB treatment received and for ≥ 3 (TF) subgroup of pts. Outcomes assessed in the subgroup analyses included change in MMD from baseline to wk52 and proportion of pts achieving $\geq 50\%$ reduction in MMD.

Results: Of 605 pts enrolled in the OLE, 226 had ≥ 3 prior prophylactic TFs. Mean (SD) MMD at baseline for the TF subgroup was 18.95 (4.2); overall, 18.11 (4.5). At wk52, erenumab treatment resulted in a sustained reduction in MMD from baseline (TF, -7.94 [6.5]; overall, -9.29 [6.6]) and 47% of pts in the ≥ 3 TF subgroup achieved $\geq 50\%$ response (Table). Treatment with erenumab also showed further reductions in MMD from wk12 to 52. At wks 40 and 52, pts in the 140 mg erenumab treated group had numerically greater reductions from baseline in MMD and a higher proportion of pts achieved $\geq 50\%$ response vs the erenumab 70 mg group.

Conclusion: Erenumab treatment resulted in sustained efficacy in pts with ≥ 3 TF, a difficult-to-treat population, with greater efficacy for 140 mg vs 70 mg.

Disclosure of Interests: Mark Weatherall has received honoraria and fees for lecturing from Allergan,

Abstract number: IHC-PO-175

Outcome measures	Erenumab 70 mg/140 mg (OLE)					
	Week 12		Week 40		Week 52	
	≥ 3 TF n = 214	Overall n = 560	≥ 3 TF n = 161	Overall n = 430	≥ 3 TF n = 136	Overall n = 383
Change from parent study baseline in MMD	-6.39 (6.48)	-7.63 (6.49)	-7.13 (6.17)	-8.72 (6.53)	-7.94 (6.47)	-9.29 (6.64)
Change from parent study Week 12 in MMD	-1.31 (5.36)	-1.76 (5.29)	-1.65 (6.06)	-2.66 (5.9)	-2.73 (6.33)	-3.33 (5.95)
Responder rate $\geq 50\%$ reduction ^a in MMD from parent study baseline, ^b n' (%)	73 (34.1)	256 (45.7)	67 (41.6)	239 (55.6)	64 (47.1)	226 (59.0)

Data expressed as mean (SD), unless specified, are combined results for active treatment groups (erenumab 70 mg and 140 mg).

ⁿ = Number of patients with observed data at each time point.

^a $\geq 50\%$ reduction in MMD from parent study (NCT02066415) baseline determined at corresponding visit.

^b % = $n'/n \times 100$, where n' = Number of responders at corresponding visit.

MMD, monthly migraine days; SD, standard deviation; TF, treatment failure.

Novartis, and Teva Pharmaceuticals. Andreas R Gantenbein has received honoraria for consulting or lecturing in the past 3 years from the following companies: Allergan, Ammirall, Curatis, Eli Lilly, Mepha, Novartis, Pfizer, Roche and TEVA Pharmaceuticals. Shannon Ritter, Josefina Snellman and Jan Klatt are employees and stockholders of Novartis. Daniel D Mikol is an employee and stockholder of Amgen.

IHC-PO-176

Changes in anxiety, sleep, and need for rescue medications in migraine patients on fremanezumab therapy: patient survey results following completion of a 1-year extension study

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Objective: Long-term safety and efficacy of fremanezumab, a monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), were evaluated in a 52-week extension study. Perceived impact of fremanezumab treatment on anxiety, sleep, and need for rescue medication (med) were evaluated as a part of a retrospective, web-based questionnaire in a subpopulation from the extension study.

Methods: In the extension study, adults with chronic (CM) or episodic migraine (EM) were randomised to quarterly or monthly dosing with fremanezumab. 253 patients (pts) from US study sites completed a retrospective survey 1–24 months (mo) after completing the extension study. 134 pts had received fremanezumab during a preceding phase 3 study; all 253 received active treatment during

Table. Patient-reported Change in Anxiety, Sleep Quality, and Acute Med Use With Fremanezumab

Change, %	Overall
Improvement in anxiety (n = 109 ^a)	67
Improvement in sleep quality (n = 253)	57
Reduction in acute med use (n = 253)	70

^aPatients with self-reported anxiety prior to studies.

the extension study. Pts who had started another CGRP-targeted treatment after the extension study were excluded. Pts' self-reported perception of change in anxiety, sleep, and acute (OTC and prescription) med use

from the 3-mo period before the clinical trials to the period during active fremanezumab treatment were evaluated retrospectively with questions on a 0–10-point response scale (0 = significantly worse/less; 10 = significantly better/more).

Results: > 50% of pts reported improvements in anxiety or sleep quality and decreases in acute med use during fremanezumab treatment (**Table**). Results were consistent across CM (n = 134) and EM (n = 119) pt subgroups and across groups taking monthly (n = 122) and quarterly (n = 131) fremanezumab dosing.

Conclusion: Migraine pts reported improvements in anxiety and sleep quality and a reduction in acute med use during fremanezumab treatment for ≥ 1 year compared to before starting treatment. Results may be limited by recall and participation bias.

Disclosure of Interests: D. C. Buse has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Lilly, Promeius and Teva. She is on the editorial board of Current Pain and Headache Reports. S. Gandhi, J. M. Cohen, and V. Ramirez-Campos are employees of Teva Pharmaceuticals. B. Cloud had no conflicts of interest to report. R. B. Lipton is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. He receives research support from the NIH: 2PO1 AG003949 (mPI), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), IRF1 AG057531 (Site PI), RF1 AG054548 (Investigator), IRO1 AG048642 (Investigator), R56 AG057548 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor), IK01AG054700 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation. He serves on the editorial board of Neurology, senior advisor to Headache, and associate editor to Cephalgia. He has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. He receives royalties from Wolff's Headache 7th and 8th Edition, Oxford Press University, 2009, Wiley and Informa.

IHC-PO-177**Can OnabotulinumtoxinA be successfully stopped in Chronic Migraine responders?**

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Objective: OnabotulinumtoxinA (OBT-A) is an important preventive treatment for chronic migraine (CM). Its efficacy is well demonstrated, however little is known about resistance and about patients that successfully stop this treatment. The aim of the study is to evaluate long-term follow-up of CM patients that were responders to OBT-A in real life.

Methods: We retrospectively review the medical records of 267 CM patients unresponsive to at least 3 preventive oral medications that were treated between 2015 and 2018 in our Headache Center. OBT-A was administered at 3-month intervals according with PREEMPT protocol (155–190 U including the “follow the pain” paradigm).

Results: 139/267 (52%) patients were responders to the first two OBT-A administrations (reduction of >30% of headache days). 9% of responders (12/139 patients: 10 female, 2 male; mean age 58 ± 12 years) had successfully stopped OBT-A. Mean CM duration was of 13 ± 11 years and frequency of attacks before treatment was 22 ± 7 days/month. Episodic pattern of migraine (<15 headache days/month) was achieved between the first and the second session of treatment. OBT-A was stopped after 5 ± 1 sessions, when patients had a migraine frequency of 8 ± 3 days/month. Of these patients, seven had still an episodic pattern of migraine at 33 ± 5 months of follow-up, five relapsed to chronic migraine after 9.6 ± 9 months. 6,5% of responders (9/139 patients: 6 female, 3 male; mean age 51 ± 8 years) relapsed to CM during treatment after 5.8 ± 3.0 administrations, becoming resistant to the successive injections.

Conclusion: Our case series suggested that OBT-A could be successfully stopped after one-year of treatment with long-term remission of CM in selected patients. Moreover, we evidenced the development of OBT-A resistance in a

relative small sample of responder subjects. These results needs to be confirmed in a larger sample of patients.

Disclosure of Interest: None Declared.

IHC-PO-178**Botox in chronic migraine; predicting response to treatment based on headache days at baseline**

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Objective: To establish whether the number of headache days at the baseline predict response to treatment with OnabotulinumtoxinA in adult patients with chronic migraine (CM).

Methods: Adult patients receiving OnabotulinumtoxinA for CM at the Hull Migraine Clinic were followed up prospectively.

All patients had tried and failed at least one preventive migraine therapy.

OnabotulinumtoxinA was delivered using PREEMPT protocol.

Patients were asked to maintain a headache diary for 30 days prior to and continuously after receiving OnabotulinumtoxinA.

Data were extracted for headache days, migraine days, crystal clear days before and after treatment at cycle 1.

Patients were divided into three frequency groups based on the number of headache days pre-treatment, low frequency (16–20 days), Moderate frequency (21–25 days) and high frequency (26–30 days). The response to treatment in the three groups were compared.

Responder rate was assessed applying the HULL criteria defined as those with:

- 50% reduction of headache or migraine days or/and.
- An increment in the number of crystal clear (headache-free days) twice that of the baseline provided they had at least 3 clear days before treatment. Those with less than 3 days had to achieve at least 6 crystal clear (headache free days).

The outcomes were all categorised as response or no response. As a result, the Chi-Square test was used to compare the three groups.

Results: Of a series of 972 patients treated between July 2010 and February 2019 and received 5745 cycles; full data was available on 846 patients.

152 (18%) had low frequency headache days (16–20); 157 (19%) had moderate frequency headache days (21–25) and 537 (63%) had high frequency headache days (26–30).

The results suggested that patients with low or moderate frequency of headache days tend to have more chances of response than those with high frequency headache days.

Applying Hull criteria to define responder fulfilling one of the three parameters; patients with moderate frequency of headache days are more likely to respond. Achieving all three primary outcome was also better in patients with moderate frequency headache days, although the results did not reach statistical significance.

Conclusion: Our results indicate a better response in those with moderate frequency headache than those with low or high frequency headaches in most of the responder parameters.

Disclosure of Interests: M. Khalil Conflict with: Received honorarium from Allergan for delivering talks at Migraine Masterclass, A. Buture: None Declared, F. Ahmed Conflict with: Received honoraria from Allergan which were forwarded to the British Association for the Study of Headache.

IHC-PO-179

Triptan Exposure During Pregnancy and the Risk of Post-Partum Hemorrhage: A Meta Analysis

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Objective: Triptan medications are commonly used to treat migraines in pregnancy. The usage of triptans may have adverse effects on delivery outcomes, mainly postpartum hemorrhage. However, there exist a menial number of studies in support of the same hypothesis. The aim of this study was to determine the reproductive safety of triptan medications in the light of its influence on postpartum hemorrhage by performing a meta-analysis.

Methods: Available publications regarding pregnancy outcomes following exposure to triptans during pregnancy were identified and reviewed according to the inclusion criteria. A meta-analysis model was implemented to combine two studies, viz. a Norwegian population registry study of pregnant women living in Norway between 2004 and 2007 and Norwegian Mother and Child Cohort Study: an observational, prospective cohort study of pregnant women between 1999 and 2007 conducted by the Norwegian Institute of Public Health, with available pregnancy outcome data for 3000 women who redeemed triptans during pregnancy in comparison to 1470 women who redeemed triptans prior to pregnancy only.

Results: Triptan therapy was found to be significantly associated with postpartum blood loss (OR: 1.48; 95% CI 1.25–1.73, SE: 0.120). The model related computations were done using Statistical Analysis Software(SAS v9.2).

Conclusion: Our data suggest slight increase in the risk of hemorrhage was associated with triptan usage during

pregnancy. Although the present findings are reassuring, confirmation in independent studies is warranted.

Disclosure of Interest: None Declared.

IHC-PO-180

OnabotulinumtoxinA Is Safe and Effective in Patients Who Discontinue Topiramate: Results of the FORWARD Study

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Objective: To evaluate effectiveness of onabotulinumtoxinA among patients discontinuing topiramate and switching to onabotulinumtoxinA.

Methods: Adults with chronic migraine (CM) were randomized 1:1 to onabotulinumtoxinA 155 U every 12 weeks (3 treatment cycles) or topiramate 25 mg/day (first week), titrated to 50–100 mg/day (up to 36 weeks). Patients discontinuing topiramate between weeks 12 and 36 could switch to onabotulinumtoxinA; their final/exit visit was week 48. Using baseline-observation-carried-forward methods, crossover exploratory endpoints of $\geq 30\%$, $\geq 50\%$, and $\geq 70\%$ responder rates and changes from baseline in headache days/28 days and total Headache Impact Test (HIT-6) scores were assessed descriptively.

Results: 80 of 144 randomized patients discontinued topiramate and switched to onabotulinumtoxinA (89% by week 12). From week 16 to study end, reductions in headache days/28 days of $\geq 30\%$ were observed in up to 52.5% of patients (weeks 29–32), $\geq 50\%$ in up to 43.4% of patients (weeks 17–20), and $\geq 70\%$ in up to 22.5% of patients (weeks 37–40). Mean (SD) changes from baseline in 28-day headache day frequency were -6.5 (7.8; week 36) and -5.3 (7.9; week 48). Reductions from baseline in mean (SD) HIT-6 scores occurred at week 18 (-3.0 [5.3]), week 30 (-4.0 [4.7]), and week 42 (-2.9 [6.0]). Adverse events (AEs) incidence in crossover patients (47.5%) and those initially receiving onabotulinumtoxinA (47.7%) was similar and differed from topiramate (78.9%). No crossover patient discontinued treatment with onabotulinumtoxinA because of AEs.

Conclusion: OnabotulinumtoxinA treatment was associated with reductions in monthly headache days and was safe and well tolerated in patients with CM who switched from topiramate treatment.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

John F. Rothrock, MD, has served on advisory boards and/or has consulted for Allergan, Lilly, Amgen, and Supernus. He also has received funding for travel and speaking from Supernus and has received honoraria from Allergan plc for participating as a speaker and preceptor at Allergan-sponsored educational programs.

Richard B. Lipton, MD, serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta.

William B. Young, MD, is a consultant or acts on an advisory board for Alder, Allergan, Avanir, and Supernus; is a speaker for Amgen; and has conducted research for Amgen, Autonomic Technologies, CoLucid, Cumberland, Dr. Reddy's Laboratories, Eli Lilly, Novartis, PCORI, Scion, Teva, and Zosano.

Aubrey Manack Adams, PhD and Esther Jo, MPH, are full-time employees of Allergan plc and owns stock in the company.

Andrew M. Blumenfeld, MD, has served on advisory boards and/or has consulted for Allergan, Avanir, Depomed, Pernix, Supernus, Amgen, Alder, Novartis, Lilly, Promius, and Teva, and has received funding for travel, speaking, and/or royalty payments from Allergan.

IHC-PO-181

Clopidogrel can be an effective complementary prophylactic for drug-refractory migraine with patent foramen ovale

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Objective: To determine the potential prophylactic effect of clopidogrel for migraine with patent foramen ovale (PFO), who were poorly responded to two or more common prevent medications.

Methods: Migraineurs who met diagnosis criteria of the international classification of headache disorders, 3rd edition (ICHD-3 beta version) were enrolled. All eligible patients underwent contrast-enhanced transcranial Doppler (cTCD) examination to confirm the presence of PFO and right-to-left shunts (RLS) degree. Then the migraine patients with PFO and drug-refractory were included for further study. Clopidogrel 75 mg daily was added to the existing prophylactics regimen for 3 months and 6 months. The variances of headache attack frequency(/M), headache duration of each onset(/H),

MIDAS scores and headache severity bases on headache diary have been enrolled in details.

Results: The presence of PFO was found in 56.8%(151/266) of all migraine patients, in which 65 cases presented with large shunt. The presence of PFO was found in 70.2%(59/84) of all migraine with aura and 36 cases with large shunt. While the PFO was found in 50.5%(92/182) of the migraine without aura and large shunt in 29 cases. 27 migraine patients with drug-refractory were initially, added clopidogrel 75 mg/d for 3 months with existing preventing medications. Finally 22 patients had completed this study. Comparing with baseline, the headache frequencies was significantly decreased [(5.48 ± 3.01)/M vs. (3.00 ± 2.06)/M; P < 0.001]. Each attack duration of headache was obviously decreased either [(12.57 ± 14.16) h vs. (7.66 ± 8.26) h; P = 0.004]. VAS score remarkably reduced from (5.78 ± 1.88) at baseline to (4.52 ± 0.93) 3 months later (P = 0.001). MIDAS score decreased from baseline (22.14 ± 7.13) to (15.82 ± 4.98) at 3 months later (P < 0.001). These improvement had extended to 6 months with 8 patients with drug refractory migraine presented as the headache frequency, headache duration of each attack and MIDAS scores better than before clopidogrel addition (P = 0.019; P = 0.041; P = 0.002), but the headache severity didn't indicate this continuous benefit (P = 0.225).

Conclusion: PFO is closely correlated with migraine, especially in migraine with aura. Clopidogrel may act as an effective complementary prophylactic for migraine with PFO who are poorly respond to routine prophylactics.

Disclosure of Interest: None Declared.

IHC-PO-182

Improvement in Cumulative Migraine Pain and Severity in Patients Treated with Erenumab

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Objective: To evaluate the impact of erenumab on the change from baseline in cumulative monthly migraine pain and pain severity independent of migraine frequency.

Methods: This was a post-hoc analysis of 2 pivotal studies of erenumab in patients with episodic migraine (EM, NCT02456740) and chronic migraine (CM, NCT02066415). Cumulative monthly migraine pain was derived to account for migraine frequency and pain severity as sum of patient-reported daily worst migraine pain intensity scores (0 = non-migraine day, 1 = mild migraine day, 2 = moderate migraine day, or 3 = severe migraine day) for each monthly interval. The mean change in cumulative monthly migraine pain from baseline was reported by treatment group. An additional analysis was performed to assess proportion of patients achieving ≥ 0.5 -point reduction from baseline in monthly average migraine pain severity (using the above scale from 0–3).

Difference in LSM change from baseline in cumulative monthly migraine pain versus placebo in episodic migraine over Months 4–6 and chronic migraine at Month 3.

	Erenumab 70 mg	Erenumab 140 mg
Difference in LSM (95% CI) Episodic migraine	–2.5 (–3.5, –1.4)	–3.2 (–4.3, –2.2)
Difference in LSM (95% CI) Chronic migraine	–4.3 (–6.8, –1.9)	–4.8 (–7.3, –2.4)

CI, confidence interval; LSM, least squares means.

Results: The mean (SD) cumulative monthly migraine pain at baseline for EM patients was 19.7 (7.3) and 41.4 (13.5) for those with CM and was balanced between both groups. The difference in LSM is shown in **Table**. Examining the proportion of patients achieving ≥ 0.5 -point reduction in monthly average migraine pain severity, for both EM and CM, a greater proportion of erenumab-treated patients achieved this threshold response compared with placebo (odds ratios range: 1.5 to 1.8). These findings further support the beneficial effect of erenumab in reducing migraine pain severity.

Conclusion: In patients with EM or CM, treatment with erenumab led to a reduction in monthly cumulative migraine pain as well as a greater proportion of patients with a ≥ 0.5 -point reduction from baseline in average migraine pain severity compared with placebo. This suggests erenumab reduces migraine pain independent of its effect on reducing frequency of monthly migraine days. To better assess the impact of treatment on residual migraine pain severity, future studies should consider the use of a broader rating scale (e.g. 0–10) than that used here (0–3).

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Table. IRT Item Slope (a), Thresholds (b), and Standard Error (SE) Estimates for a Unidimensional Model of the HIT-6 at Baseline

Item	Content	a (SE)	b ₁ (SE)	b ₂ (SE)	b ₃ (SE)	b ₄ (SE)
1	Severe pain	1.12 (0.09)	-3.72 (0.29)	-0.68 (0.08)	2.86 (0.21)	
2	Limits daily activities	2.33 (0.14)	-2.07 (0.10)	-0.31 (0.05)	1.62 (0.08)	
3	Lie down	1.34 (0.09)	-3.37 (0.23)	-1.67 (0.11)	0.32 (0.06)	
4	Too tired	3.28 (0.23)	-2.67 (0.14)	-1.46 (0.06)	-0.14 (0.04)	1.63 (0.08)
5	Felt fed up or irritated	1.45 (0.09)	-3.47 (0.23)	-1.99 (0.12)	-0.43 (0.06)	1.35 (0.09)
6	Limits concentration	3.52 (0.27)	-2.72 (0.15)	-1.59 (0.07)	-0.31 (0.04)	1.39 (0.06)

Abstract number: IHC-PO-183

IHC-PO-183

Item Response Theory Analysis of the HIT-6 in a Chronic Migraine Population

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Objective: The short-form Headache Impact Test (HIT-6) was derived from a larger item bank using item response theory (IRT) and validated in general headache and migraine patients. Here, we evaluated HIT-6 conceptual framework and assess the performance of individual items in a chronic migraine (CM) population.

Methods: The conceptual framework of HIT-6 was evaluated using latent variable modeling and baseline data from PROMISE-2 (NCT02974153; N = 1072). A unidimensional graded response model within the IRT framework assessed dimensionality. The overall IRT model fit was assessed using the root mean square error of approximation (RMSEA) based on the limited information goodness-of-fit test statistic and Tucker-Lewis index (TLI); individual item fit was assessed via $S-X^2$. Evaluating the *a priori* hypothesis that a single construct or disease state (eg, migraine) underlies HIT-6 item responses.

Results: The overall model fit was acceptable (RMSEA = 0.04; TLI = 0.95), supporting existing unidimensional conceptual framework. All item slopes and thresholds were statistically significant and of reasonable magnitude (**Table**). Individual item fit results suggested that items were generally modeled well by the unidimensional graded model.

Conclusion: HIT-6 was successfully calibrated using IRT and data from PROMISE-2. All items provide good coverage over the range of the latent construct. Each item contains unique information and contributes reliable information to the total score. HIT-6 appears well suited

for measuring the impact of CM and clinical use in the CM population.

Disclosure of Interests: Rj Wirth: Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

James S. McGinley: Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

Joe Hirman: Received compensation from Alder BioPharmaceuticals.

Steve Snapinn: Full time employee of Alder BioPharmaceuticals.

Carrie R. Houts: Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

Roger Cady: Full time employee of Alder BioPharmaceuticals.

IHC-PO-184

Validity Evidence of the HIT-6 Total Score in a Sample of Patients with Chronic Migraine

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Objective: The short-form Headache Impact Test (HIT-6) has been validated in the headache and migraine populations. The current analyses were conducted to provide evidence of the validity of the HIT-6 specifically in patients with chronic migraine (CM).

Methods: Cross-sectional assessments of convergent/discriminant and known-groups (KGs) validity were conducted using data from the PROMISE-2 trial (NCT02974153; N = 1072). Convergent and discriminant validity correlations were examined between HIT-6 total

scores and reference patient-reported outcome (migraine days, Short-Form Health Survey [SF-36], EuroQOL 5-dimensions 5-level scale [EQ-5D-5L]) at baseline and Month 3. Expectations with respect to direction and magnitude were specified *a priori*. Classes for KGs analyses were defined by Patient Global Impression of Change (PGIC) response (very much improved/much improved vs minimally improved/worse) and frequency of headaches (≥ 15 days/month [chronic] vs < 15 days [not chronic]). KGs analyses were conducted using only Month 3 data.

Results: For the convergent and discriminant analyses, all observed correlations conformed to expectations of direction. The magnitudes of the correlations were generally consistent with expectations at baseline and Month 3 (eg, SF-36 Physical Role Function, expected $r = -0.30$ to -0.50 ; baseline $r = -0.42$) although, in some cases, observed values fell just outside the expected range (eg, frequency of migraine days in the past month [expected $r = 0.30$ to 0.50 ; Month 3 $r = 0.51$] and EQ-5D-5L mobility [expected $r = 0.00$ to 0.10 ; baseline $r = 0.12$; Month 3 $r = 0.14$]). For the KGs analyses, HIT-6 total scores conformed to expectations, both in terms of reported mean values and with respect to the outcome of formal tests of difference between the groups. Improved and non-chronic groups had lower HIT-6 total scores, indicating lesser impact, with effect sizes large in magnitude.

Conclusion: HIT-6 total scores behaved as was theorized and distinguished between clinically meaningful groups in a CM population. Findings suggest that the HIT-6 total score is a valid and useful outcome for assessing migraine impact in patients with CM.

Disclosure of Interests: Carrie R. Houts: Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

RJ Wirth: Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

James S. McGinley: Employee of Vector Psychometric Group, LLC (VPG). VPG was hired by Alder BioPharmaceuticals, Inc. to complete the analyses for this abstract submission.

Chad Gwaltney: Nothing to disclose.

Roger Cady: Full time employee of Alder BioPharmaceuticals.

IHC-PO-185

Long-term impact of fremanezumab on response rate, acute headache medication use, and disability in episodic migraine patients with acute medication overuse at baseline: results of a 1-year study

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Objective: Fremanezumab, a fully humanized monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide (CGRP), is approved in the US and the EU for migraine preventive treatment in adults. Herein we evaluated the long-term impact of fremanezumab on response rates, acute headache medication use, and disability in episodic migraine (EM) patients with acute medication overuse (AMO) at baseline.

Methods: In this 12-month, randomized, double-blind, parallel-group study, EM patients received subcutaneous fremanezumab quarterly (675 mg every 3 months) or monthly (225 mg monthly). This *post hoc* analysis was limited to EM patients with AMO (defined as acute headache medication use on ≥ 15 days, migraine-specific acute medication use on ≥ 10 days, or combination medication use for ≥ 10 days) at baseline. The proportions of patients achieving $\geq 50\%$ reduction in the monthly average number of migraine days and headache days of at least moderate severity, respectively, and the change from baseline in the monthly average number of days with acute headache medication use and in headache-related disability (assessed with Migraine Disability Assessment (MIDAS) questionnaire) were measured at Months 6 and 12.

Results: At baseline, 100 EM patients (quarterly: $n = 58$; monthly: $n = 42$) had AMO. A $\geq 50\%$ reduction in monthly migraine days was maintained at Months 6 (quarterly: 47%; monthly: 34%) and 12 (quarterly: 55%; monthly: 43%). A $\geq 50\%$ reduction in the monthly number of headache days of at least moderate severity was maintained at Months 6 (quarterly: 49%; monthly: 29%) and 12 (quarterly: 59%; monthly: 43%). The monthly number of days of acute headache medication use decreased from baseline to Months 6 (quarterly: -5.5 days; monthly: -3.7 days) and 12 (quarterly: -6.1 days; monthly: -5.3 days). The mean MIDAS score decreased from baseline to Months 6 (quarterly: -21.3 ; monthly: -19.1) and 12 (quarterly: -20.8 ; monthly: -28.2).

Conclusion: Long-term treatment with quarterly and monthly fremanezumab showed sustained efficacy, reduced acute headache medication use, and improved

headache-related disability in EM patients with AMO at baseline.

Disclosure of Interests: Richard B. Lipton: Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. He receives research support from the NIH: 2PO1 AG003949 (Program Director), 5U10 NS077308 (PI), ROI NS082432 (Investigator), IRFI AG057531 (Site PI), RFI AG054548 (Investigator), IROI AG048642 (Investigator), R56 AG057548 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor), IK01AG054700 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation. He serves on the editorial board of *Neurology*, as senior advisor to *Headache*, and as associate editor of *Cephalalgia*. He has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. He receives royalties from Wolff's *Headache* 7th and 8th Edition, Oxford Press University, 2009, Wiley and Informa. Ira Turner: He has received research support from Alder, Allergan, Amgen, Teva, Eli Lilly, electroCore and Biohaven. He has also served as a consultant to, served as an advisory board member for, or received honoraria from Alder, Allergan, Amgen, Teva, Eli Lilly, Assertio, Promius, Supernus, electroCore, Novartis, Revance and Impax. Joshua M. Cohen: Employee of Teva Pharmaceuticals. Sanjay K. Gandhi: Employee of Teva Pharmaceuticals. Ronghua Yang: Employee of Teva Pharmaceuticals. Xiaoping Ning: Employee of Teva Pharmaceuticals. Shawn Elms: Employee of Teva Pharmaceuticals.

IHC-PO-379

The Aimovig "Wear-Off": A Retrospective Case Series of Response to 14 day Dosing

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Objective: As demonstrated in collaborative research, a small cohort of patients on Aimovig 140 mg once monthly injections have been found to have a "wear-off" effect where the medication was found to be not as effective by the end of the month as it was at the beginning of the month.

The primary objective of this study was to identify if changing dosing in patients taking Aimovig 140 mg with "wear-off" effect, to 70 mg injections every 14 days would decrease monthly headache frequency and/or severity.

Methods: Through retrospective chart review, we identified patients that were started on Aimovig 140 mg monthly injections that had, per patient report, an initial response to medication at the beginning of the month, followed by an increase in frequency and severity of headaches by the end of the month. Patients were offered a change in dosing to Aimovig 70 mg to be taken every 14 days. Response to change in dosing was measured per patient report in respect to frequency and severity at next clinical visit or by phone call interview at least 1 month after making dosing frequency change.

Results: Of the 190 patients started on Aimovig in this outpatient headache specialty clinic, 17 were identified as having a "wear-off" effect. Of these 17 patients, 6 opted to switch to every 14 day dosing. By study start date, 5 of these 6 patients had been seen for follow up or had been contacted for phone interview. Three patients (60%) had a reduction in both headache frequency and severity. One patient (10%) had a reduction in severity alone. One patient (10%) had no change in monthly headache frequency or severity. Monthly headache frequency ranged from 0 to 50% reduction with 14 day dosing. Monthly headache severity ranged from 0 to 41% reduction with 14 day dosing. Side effects were noted to be increased constipation in one patient (10%), injection site reaction

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Patient	Headache Frequency	Headache Severity	New Headache Frequency	New Headache Severity	Percent Frequency Reduction	Percent Severity Reduction
1	14	8.5	14	5	0%	41%
2	9.5	5	9.5	5	0%	0%
3	21	7	10.5	5.5	50%	21%
4	6	7.5	4	5	33%	33%
5	6	6	4	4	33%	33%

that resolved fairly quickly in one patient (10%), and vertigo when supine in one patient (10%).

Conclusion: For patients with Aimovig “Wear-Off”, switching therapy from Aimovig 140 mg single monthly injections to 70 mg injections every 14 days is an option that can potentially reduce monthly headache frequency and severity, while maintaining mild side effect profile. Further study must be done to assess the efficacy of dosing every 14 days in patients with Aimovig “wear-off”.

Disclosure of Interests: Deborah Reed has been a speaker for Teva, Amgen, and Lilly, and is on ad board for Lilly.

IHC-PO-380

Trajectory of Response to Migraine Preventive Interventions: A Meta-Analysis

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Objective: To pool randomized controlled trial data on the trajectory of response to migraine preventive interventions.

Methods: PubMed, Embase and the Cochrane database were searched from inception through 2017 for randomized controlled trials or meta-analyses of preventive interventions for patients with migraine that included data on headache or migraine frequency over at least three separate time points. To be eligible, all studies were required to have a PMID. Eligible trials were reviewed and raw data for the trajectory of clinical response were entered into a database. For the initial comparison, the time course of response to placebo was compared to all active treatment arms. Further analysis will compare individual active treatments. In this initial analysis, absolute reduction in frequency was analyzed.

Results: A total of 112 full-text articles were screened and 55 trials met criteria, with 48 included in this analysis. Thirty-five articles presented the results graphically, 20 by table or text, with 57 rejected. Twenty-three treatments for chronic headache (11), non-chronic headache (29) and combined (8) were analyzed. Due to the historical nature of the review, they were all migraine, but some would not meet the current ICHD criteria. Studies included adult only (39), pediatric only (5) and combined populations (5). The mean participant sample size was 117 (standard deviation = ± 145 , range: 15–696). At baseline the mean frequency of headaches was 7.7 ± 5.2 days per month (placebo: 7.8 ± 5.4 , active: 7.6 ± 5.1). The largest improvement was seen within 30 days, with a reduction to

4.3 ± 2.9 (placebo: 4.7 ± 3.3 , active: 4.1 ± 2.7). There was continued, though minimal improvement after this point (180 days – all: 3.0 ± 1.2 , placebo: 3.1 ± 1.3 , active: 3.0 ± 1.1).

Conclusion: The time course of response to preventive treatment for migraine is rapid with the greatest improvement occurring within 30 days. In a combined analysis, active treatment was similar to placebo. Further analysis may separate outliers. This study is important clinically, as efficacy of a preventive treatment may be assessed rapidly and may help patients achieve efficacy sooner than the traditionally held assumptions.

Disclosure of Interests: Serena L. Orr: Receives royalties from Cambridge University Press.

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Andrew Hershey: Dr. Hershey serves on advisory boards for Alder, (funds to Cincinnati Children’s), Amgen, Lilly, Teva, Biohaven, Curelator, Electrocore, Supernus, Upsher-Smith, Impax. He has contracts with Amgen, Lilly, Impax, Avanir (all to institution). Dr. Hershey has NIH grants and also receives honoraria from UpToDate.

IHC-PO-381

Effects of yoga therapy in migraine: A meta-analysis

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Objective: Yoga therapy has been used to reduce the physical symptoms of migraine for a long time. This study was performed to evaluate the effects of yoga therapy on migraine-frequency, duration, and severity.

Methods: MEDLINE/PubMed, IndMED, Cochrane Library [Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Methodology Register], and International Clinical Trials Registry Platform and ClinicalTrials.gov were searched until 28 February, 2019. Interventional studies that have evaluated the effects of yoga therapy on migraine-frequency, duration, and severity were included.

Pooled standardized mean difference was calculated using a random effects model (Revman 5.3).

Results: Forty-six studies were screened and three interventional trials were included in the analyses. Yoga therapy was not found to cause any improvement in migraine frequency [mean difference: -1.07 (95% CI: $-5.64, 3.49$)], duration [mean difference: 0.03 h (95% CI: $-4.50, 4.56$)], and severity [mean difference: -0.53 (95% CI: $-2.03, 0.98$)] (moderate GRADE evidence).

Conclusion: Yoga therapy did not improve migraine frequency, duration, and severity.

Disclosure of Interest: None Declared.

IHC-PO-382

Adherence to treatment and its related factors among a sample of Egyptian migraineurs

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Objective: Poor adherence to medications has long been identified as a considerable cause of treatment suboptimal response and disease progression among different health conditions including migraine. Migraine is prevalent in Egypt. Even though, there is a lack of data about adherence to migraine treatment and the adherence-related factors in the country. Thus, the objective of this research was to explore the compliance to treatment and factors related to it among a sample of Egyptian migraineurs.

Methods: A cross-sectional study was conducted on migraineurs attending an outpatient neurology clinic in Alexandria, Egypt. A translated and validated Arabic form of the Brief Adherence Rating Scale (BARS) was distributed among patients for self-reporting, and they were asked about possible aetiologies for poor compliance to prophylactic therapy during the past two months.

Results: Seventy patients participated in this study, with females constituting 70% of the sample. The mean age of the patients was 30.31 ± 7.25 years, and 22.9% of them were on polytherapy. Only 17% of the patients reported that they did not miss any day of treatment during the past two months, and 34.3% reported taking inadequate doses on other days. On regression analysis, dosing frequency ($r=0.6$), number of drugs administered ($r=0.6$), drug adverse events ($r=0.7$), drug cost ($r=0.5$), patient education about migraine ($r=0.49$) and patients' level of education ($r=-0.7$) were significantly correlated to poor drug adherence ($P < 0.001$).

Conclusion: Poor adherence is common among Egyptian migraineurs. Drug adverse events, cost, dosing regimen, and level of education are the main causes of poor adherence. Patient education about their illness can contribute significantly to improving compliance.

Disclosure of Interest: None Declared.

IHC-PO-383

A systematic review of RCTs evaluating probiotic interventions in adult migraine sufferers

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Objective: To evaluate the effectiveness of probiotics in managing migraines in adult patients.

Methods: A review of the literature (in English) was performed (January 2019), using multiple search terms for "probiotics & migraine" in databases: EMBASE, MEDLINE, PubMed, Cochrane library, ClinicalTrials.gov. Citation lists of relevant papers were checked.

Results: 97 titles were retrieved with 67 original papers remaining after removing duplicates. 57 papers were excluded during screening (different conditions or interventions, paediatric or healthy populations) and 10 full-text articles were assessed. 8 full-text papers were excluded (non-RCT, abstract only, open label) with 2 papers included in the final analysis.

A total of 163 patients were enrolled and 139 (113 women) completed trials; with 74 patients in probiotic groups and 65 in placebo. Trials used different multistrain probiotic formulations with similar doses (5×10^9 vs 4×10^9 colony forming units). Interventions were 12 or 8–10 weeks long with daily supplementation. The identified trials were not suitable for meta-analysis (due to small numbers and different reporting styles). One study demonstrated no change in migraine symptoms after the intervention, while the other study reported significant improvement in the migraine symptoms in both chronic and episodic migraine sufferers.

Studies reported over 30 clinical parameters each, with only 5 outcome parameters reported in the same manner. This inconsistency of reporting prevented direct comparison of results, including the number of migraine days per month, frequency of headaches and use of medications. Other parameters (depression score, migraine duration, gastrointestinal symptoms), were reported in only one of the two papers. The only results reported in the same manner were inflammatory markers (TNF α , CRP) and migraine intensity.

Conclusion: With nearly 70 trials of probiotics in migraine, there is a clear lack of consistency in the reporting of results. Results to date do not allow for effective meta-analysis. One of the two eligible RCTs demonstrated no significant effect on migraine frequency while the other showed a statistically significant improvement. There is a clear need for well-designed large scale RCTs with

standardised reporting looking at the effectiveness of probiotics in managing migraine.

Disclosure of Interests: One of the studies in this review used a product manufactured by ADM Protexin.

IHC-PO-384

Efficacy of fremanezumab in male patients with migraine and documented inadequate response to 2–4 classes of migraine preventive treatments: results of the randomised, placebo-controlled FOCUS study

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Objective: There is a lack of strong efficacy results for migraine preventive treatments in male patients (pts). The FOCUS study of fremanezumab was the first and largest study of a migraine preventive treatment in adults with both episodic and chronic migraine (EM and CM) and documented inadequate response to 2–4 classes of migraine preventive treatments. Efficacy was evaluated in a subgroup of male pts.

Methods: Pts were randomised (1:1:1) to quarterly (qtl) fremanezumab (Month [Mo] 1: 675 mg; Mo 2 and 3: placebo), monthly (mthly) fremanezumab (Mo 1: EM, 225 mg; CM, 675 mg; Mo 2 and 3: 225 mg), or matched mthly placebo for 12 weeks (wks). Changes from baseline (BL) in mthly average migraine days and headache days of at least moderate severity and proportions of pts achieving $\geq 50\%$

reduction in mthly average migraine days over 12 wks were evaluated for male pts.

Results: Of 838 randomised pts, 138 were male. Reductions in mthly average migraine and headache days and proportion of pts achieving $\geq 50\%$ reduction in mthly average migraine days from BL over 12 wks were significantly greater with fremanezumab vs placebo in male pts (all $P < 0.05$; **Table**).

Conclusion: This subgroup analysis demonstrated statistically significant improvements in efficacy outcomes due to the strong effect size vs placebo in male pts, a group for whom the impact of migraine is often underestimated and undertreated.

Disclosure of Interests: A. MaassenVanDenBrink reports receipt of grants/research supports from CoLucid/Lilly, Amgen/Novartis, and ATI and receipt of honoraria or consultation/speaker fees from CoLucid/Lilly, Amgen/Novartis, and Teva. G. M. Terwindt reports consultancy or industry support from Teva, Novartis, Lilly, and independent support from Netherlands Organization for Scientific Research (NWO); European Community; the Dutch Heart Foundation; and the Dutch Brain Foundation. J. M. Cohen, R. Yang, V. Ramirez-Campos, M. Galic, and X. Ning are employees of Teva Pharmaceuticals. M. Kärppä has received compensation from Teva, Eisai, and Amgen for being investigator in their studies.

IHC-PO-385

Safety and tolerability of fremanezumab in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive medications in the international, multicentre, randomised, placebo-controlled FOCUS study

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Abstract number: IHC-PO-384

Table. Efficacy Outcomes Over 12 Wks in Male Pts

	Placebo (n = 46)	Qtl Fremanezumab (n = 47)	Mthly Fremanezumab (n = 45)
LSM(SE) change from BL			
Mthly average migraine days	−0.4(0.74)	−4.2(0.73) ^a	−4.6(0.78) ^a
Mthly headache days of at least moderate severity	−0.5(0.74)	−4.2(0.75) ^a	−4.5(0.80) ^a
$\geq 50\%$ reduction in mthly average migraine days, n(%)	4(9)	14(30) ^b	17(38) ^b

^a $P < 0.0001$ vs placebo.

^b $P < 0.05$ vs placebo.

Abstract number: IHC-PO-385**Table.** AEs With an Incidence $\geq 5\%$ in Any Treatment Group; AEs Leading to Discontinuation; and SAEs

AE incidence, n (%)	Placebo (n = 277)	Quarterly fremanezumab 675 mg/placebo/placebo (n = 276)	Monthly fremanezumab	
			675 mg/ 225mg/225mg (n = 174)	225 mg/ 225mg/225mg (n = 111)
Any AE	134 (48)	151 (55)	85 (49)	44 (40)
AEs with incidence $\geq 5\%$ in any treatment group				
Injection-site erythema	15 (5)	19 (7)	12 (7)	4 (4)
Injection-site induration	12 (4)	12 (4)	10 (6)	3 (3)
Nasopharyngitis	11 (4)	13 (5)	6 (3)	1 (<1)
AEs leading to discontinuation	3 (1)	1 (<1)	3 (2)	1 (<1)
SAEs	4 (1)	2 (<1)	3 (2)	1 (<1)

Objective: Fremanezumab, a fully-humanised monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for the preventive treatment of migraine in adults. Safety and tolerability outcomes are presented here for the FOCUS study of fremanezumab, the first and largest study of a migraine preventive treatment in adults with both episodic and chronic migraine (EM and CM) and documented inadequate response to 2–4 classes of migraine preventive medications.

Methods: In the 12-week, double-blind treatment period, patients were randomised (1:1:1) to quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), monthly fremanezumab (Month 1: CM, 675 mg; EM, 225 mg; Months 2 and 3: 225 mg), or matched monthly placebo. Adverse events (AEs) and serious adverse events (SAEs) were summarised descriptively.

Results: 838 patients were randomised. AEs were reported for similar proportions of patients across treatment groups. AEs leading to discontinuation and SAEs were infrequent ($\leq 1\%$) across treatment groups (**Table**). No SAEs were considered to be treatment-related by investigators, and no safety signals were identified.

Conclusion: Fremanezumab administered quarterly or monthly was generally safe and well tolerated, with similar incidences of AEs compared with placebo, in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive medications.

Disclosure of Interests: M. D. Ferrari served as an investigator on this study for Teva Pharmaceuticals. J. M. Cohen, X. Ning, M. Galic, and R. Yang are employees of Teva Pharmaceuticals.

IHC-PO-386**Randomised controlled trials of preventive treatment of migraine in children: Quality of evidence as assessed against IHS guidelines**

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Objective: This study aims to assess the quality of previously published randomised control trials for the prevention of migraine against the recently published International Headache Society's (IHS) guidelines and assess the evidence for recommendations.

Methods: A complete search was performed on Medline, Embase, Psych info and Pubmed looking for clinical trials of preventive treatment of migraine in children and adolescents. We excluded trials published before the publication of the 1st edition of International headache classification in 1988. A total of 23 RCT's were identified. A full assessment of methods, results presentations, statistical analysis and adherence to international/national regulatory organisations were made. Data were collected on an excel sheet for ease of comparison against the IHS guidelines.

Results: Five trials reported on propranolol as a comparator to sodium valproate, cinnarizine, topiramate or pregabalin. None of these trials achieved enough quality as stipulated by the current guidelines especially for blinding, inclusion and exclusion criteria, or defined primary and secondary end points. Eight trials reported on the efficacy of topiramate; only one study (CHAMP trial, 2016) met, fully, the guideline recommendations. Three trials reported on efficacy of amitriptyline; 2 trials (Power et al. 2013 and CHAMP trial 2016) met most of IHS recommendations. Four studies reported on efficacy of riboflavin. Three RCTs reported on Coenzyme Q10 (as an add on),

Magnesium and Butterbur root. None of these trials met most recommendations from the guidelines.

Conclusion: The standard of randomised controlled trials was not achieved in most previously published trails on preventive treatment of migraine in children and adolescents. Current IHS guidelines, if implemented, would help to provide a reliable evidence in future RCTs.

Disclosure of Interest: None Declared.

IHC-PO-387

Patient satisfaction with fremanezumab treatment in migraine: results from a patient survey after completion of a 1-year extension study

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Objective: Long-term safety and efficacy of fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), were evaluated in a 52-week extension (ext) study. Patient (pt) satisfaction with fremanezumab treatment was evaluated using a retrospective, web-based questionnaire in a subpopulation from the ext study.

Table. Satisfaction With Efficacy Dimensions^a

Efficacy dimension, %	Overall
Reducing:	
Attack frequency	84
Migraine pain intensity	69
Attack duration	60
Migraine-associated symptoms	55
Migraine-associated disability	55
None of the above	6

^aCould check all that apply.

Methods: In the ext study, adults with chronic or episodic migraine (CM or EM) were randomised to receive quarterly or monthly fremanezumab. 253 pts from US study sites completed a retrospective survey 1–24 months after completing the ext. study. 134 pts had received fremanezumab during a preceding phase 3 study; all 253 received active treatment during the ext study. Pts who started another CGRP-targeted migraine treatment after the ext study were excluded. Pt satisfaction overall and across

different treatment dimensions were evaluated retrospectively with a series of 5 questions using a 7-point scale (1 = “extremely dissatisfied or difficult” to 7 = “extremely satisfied or easy”; 5–7 indicated satisfaction) and one satisfaction item instructing “check all that apply.”

Results: The mean overall satisfaction rating for fremanezumab among 5 items (response options 1–7) was 6.1. Mean satisfaction ratings for fremanezumab were high across all evaluated aspects of treatment: ability to prevent/treat migraines (6.1), relief of symptoms (6.1), time to start working (5.7), and ease of use (6.0). >50% of pts reported satisfaction with all efficacy dimensions of fremanezumab (**Table**).

Conclusion: Treatment satisfaction with fremanezumab was high overall and across treatment dimensions. Pts most commonly reported satisfaction with reduction in attack frequency with fremanezumab. Results may be limited by recall and participation bias.

Disclosure of Interests: R. B. Lipton is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. He receives research support from the NIH: 2PO1 AG003949 (mPI), 5U10 NS077308 (PI), ROI NS082432 (Investigator), IRFI AG057531 (Site PI), RFI AG054548 (Investigator), IROI AG048642 (Investigator), R56 AG057548 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor), IK01AG054700 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation. He serves on the editorial board of Neurology, senior advisor to Headache, and associate editor to Cephalgia. He has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. He receives royalties from Wolff's Headache 7th and 8th Edition, Oxford Press University, 2009, Wiley and Informa. S. Gandhi, J. M. Cohen, V. Ramirez-Campos, and A. H. Ahn are employees of Teva Pharmaceuticals. B. Cloud has no conflicts of interest to report. D. C. Buse has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Lilly, Promeius and Teva. She is on the editorial board of Current Pain and Headache Reports.

Disclosure of Interest: None Declared.

IHC-PO-388**Functioning and work performance after long-term treatment with fremanezumab in migraine patients: a patient survey study following completion of a 1-year extension study**

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Objective: The perceived impact of treatment with fremanezumab, a fully humanised monoclonal antibody (IgG2Δa) that selectively targets the calcitonin gene-related peptide (CGRP), on social interactions, work and/or school performance, and leisure activities was evaluated as part of a web-based questionnaire in a subpopulation from a 52-week extension study in migraine patients (pts).

Methods: In the extension study, adults with chronic (CM) or episodic migraine were randomised to receive quarterly (675 mg every 3 months [mo]) or monthly (225 mg/mo; starting 675-mg dose for CM pts) fremanezumab for 52 weeks. 253 pts from US study sites completed a retrospective survey 1–24 mo after completing the extension study. 134 pts received fremanezumab during a preceding phase 3 study; all 253 received active treatment during the extension study. Pts who started another CGRP-targeted treatment after the extension study were excluded. Changes in pts' interactions with family/friends, work/school performance, and leisure or household activities pre- and post-study treatment were queried retrospectively on a 10 point-scale (from "significantly worse/less" to "significantly better/more") in the survey.

Results: When asked about their experience while taking fremanezumab compared with the baseline period before the trial, 71% of pts reported spending more time with family/friends; 83% reported better quality of time spent with family/friends. 69% of pts reported spending more time at work/school; 76% reported better performance at work/school. 76% of pts reported spending more time participating in leisure activities, 81% reported more enjoyment of leisure activities, and 74% reported better performance of household activities.

Conclusion: Approximately three-quarters of pts surveyed reported that longer-term treatment with monthly or quarterly fremanezumab was associated with improvements in social functioning (quality and amount of time spent with family/friends), leisure activities, and performance at work/school.

Disclosure of Interests: D. C. Buse has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Lilly, Promieus and Teva. She is on the editorial board of Current Pain and Headache Reports. B. Cloud has no conflicts of interest to disclose. S. Gandhi, J. M. Cohen, and V. Ramirez-Campos are employees of Teva Pharmaceuticals. R. B. Lipton is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. He receives research support from the NIH: 2PO1 AG003949 (mPI), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), IRFI AG057531 (Site PI), RFI AG054548 (Investigator), IRO1 AG048642 (Investigator), R56 AG057548 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor), IK01AG054700 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation. He serves on the editorial board of Neurology, senior advisor to Headache, and associate editor to Cephalalgia. He has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. He receives royalties from Wolff's Headache 7th and 8th Edition, Oxford Press University, 2009, Wiley and Informa.

IHC-PO-389**The use of a phytotherapeutic compound containing Tanacetum Parthenium and Andrographis, in combination with CoQ10 and Riboflavin, for migraine prophylaxis: a randomized double blind versus placebo clinical trial**

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Objective: The most of migraineurs patients need prophylactic treatments to reduce the burden of disease in terms of attacks, days with headache, and symptomatic drugs consumption because their headache is characterized by a middle to high frequency of migraine attacks. So far, pharmacologic prophylactic treatments are characterized by a sub-optimal efficacy due to the high number of patients that do not respond to the treatments, and the

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	Verum group			Placebo group		
	Mean T0	Mean T3	p value	Mean T0	Mean T3	p value
Attacks	4.23 ± 1.79	3.92 ± 2.31	p = 0.04	5 ± 2	5.1 ± 1.97	p = 0.72
Days	7.23 ± 3.88	4.83 ± 3.49	p < 0.01	6.7 ± 2.75	7.7 ± 4.08	p = 0.77
Doses	6.54 ± 4.16	3.67 ± 2.53	p = 0.03	5.7 ± 3.3	7.6 ± 4.9	p = 0.92
MIDAS	25.23 ± 17.55	13.25 ± 14.69	p = 0.07	22.8 ± 18.08	17.9 ± 25.08	p = 0.24
HIT-6	62.08 ± 3.5	54.61 ± 7.15	p < 0.01	60.7 ± 4.19	56 ± 11.16	p = 0.13
VAS	7.38 ± 0.96	6.31 ± 1.11	p = 0.01	7.4 ± 0.7	6.3 ± 1.64	p = 0.02

Mean values ± standard deviation of monthly number of attacks, headache days, drug doses and score of MIDAS, HIT-6 and VAS as determined at the baseline (T0) and at the end of the 3rd month of double blind treatment (T3).

elevated incidence of side effects. To match the patient needs, waiting for the next generation treatments, the use of herbal medicine is very common among migraine population. In the last years, phytoextracts of feverfew (*tanacetum parthenium*) were studied and adopted to treat migraineurs. In particular, there is a fixed combination of *Tanacetum Parthenium*, *Andrographis*, Coenzyme Q10, and Riboflavin, that is widely used in Italy. In order to verify the efficacy of that association, we designed a randomized double blind versus placebo clinical trial. Here we present the preliminary results of our study.

Methods: Forty patients were enrolled and randomly assigned to receive the verum or the placebo treatment for 3 months. Each treatment kit, blinded by a unique code that was coupled to each patient, was composed by 120 pills, enough for 3 months: (1 pill b.i.d. in the first month, 1 per day in the second and third month).

Results: When the blind was broken, 21 patients resulted to be assigned to verum group, 19 to placebo.

Eight patients out of 21 assigned to the verum arm of the study improved their headache frequency at least of 50% (responder rate of 38.1%). On the contrary, only 2/19 patients that received the placebo treatment improved their headache frequency at least of 50% (responder rate of 10.52%). No major side effects were reported.

Conclusion: The traditional use of herbal medicine is as old as the history of medicine and that ancient practice is present in almost all cultures. Our results show that the examined combination is effective in the migraine prophylaxis if compared to placebo and safe if compared with data about synthetic drugs, as they are reported in literature.

Disclosure of Interest: None Declared.

IHC-PO-390**Erenumab for the treatment of refractory chronic migraine: a UK prospective real world experience**

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Objective: Erenumab is a calcitonin gene-related peptide (CGRP) receptor antibody designed for the prevention of migraine. Its efficacy in episodic and chronic migraine has been demonstrated in clinical trials. However, data on its efficacy and tolerability in clinical practice is lacking. Furthermore, no data on the more difficult to treat subgroup of migraine have been published. We aim to assess the efficacy and tolerability of erenumab in a real world setting in a population of medically refractory chronic migraine (CM).

Methods: This is an open-label prospective clinical audit. The audit is ongoing. Seventy-five CM patients, who failed at least three preventive treatments and botulinum toxin A (BoNTA), received at least one erenumab 70 mg treatment. Audit tools for efficacy outcomes collection included a headache diary and HIT-6 questionnaire. Change in headache days, migraine days and HIT-6 at 3 months of treatment compared to baseline were analysed here. Data on adverse events and treatment compliance were also collected.

Results: Thirty-seven CM patients completed the three month trial period. At baseline, patients displayed an average of 26.7 headache days/month, 20.3 migraine days/month and average HIT-6 score of 66.8 (severe impact). Following the 3-month trial, there was an average reduction of headache days to 22.4/month (−4.3 days), a reduction in migraine days to 14.2/month (−6.1 days) and of the HIT-6 score down to 59.9 (−6.9 points) (substantial

impact). Nineteen patients (51.4%) obtained at least a 30% reduction in migraine days; ten patients (27.0%) obtained at least a 50% reduction of migraine days. Side effects were reported by 24 patients (64.9%) and they were mostly mild. No particular compliance issues were identified.

Conclusion: Refractory CM is a subset of highly disabling patients in whom there is a vast unmet need for new treatments. Erenumab may constitute an effective preventive treatment option for this group of patients in clinical practice. The proportion of patients reporting side effects was higher than the one reported in the clinical trials, although none of the 37 patients analysed had to discontinue the treatment because of tolerability issues.

Disclosure of Interests: Dr G Lambru has received honoraria for participation in Novartis advisory board. BH, MM and APA have nothing to disclose.

IHC-PO-391

The Aimovig “Wear-Off”: A Retrospective Review

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Objective: Since its release in May 2018, Aimovig (erenumab) has been used to achieve better migraine control. It has been noted that a small cohort of patients experiences a “wear-off” effect, wherein the medication’s effectiveness diminishes after multiple doses or does not last for the full cycle until the next dose is due. We attempt to review those patients in our clinic to determine what percentage of them have experienced this effect, what their demographics are, and the timing of the effect.

Methods: Through retrospective chart review, we identified patients who were started on Aimovig and had an initial response but whose response was diminished in some way after subsequent doses. This included both those who developed worsening headaches at the end of the month as well as those who, after the second or later doses, did not see as much of an effect as with the initial dose.

Results: We evaluated 190 patients in clinic who have been prescribed Aimovig. Of these, 17 described the “wear-off” effect. The median patient age was 52 with a range of 29–75. 13 were female and 4 male. The median number of headache days prior to initiation of Aimovig was 15 with a range of 2 to 30 (i. e. daily migraines). All but one patient were on a dose of 140 mg monthly, while the other was receiving 70 mg monthly. 12 patients had “wear-off” after either the second or third dose (6 patients each), 3 after the 4th dose, one after the 5th, and one after the first dose but not the second. All

patients experienced the “wear-off” in the form of pain; some had other symptoms accompanying the pain, usually components of their migraine (i. e. photophobia, nausea). One patient had a sensation as though the headache wanted to return but without the actual pain. The “wear-off” most commonly occurred between three and seven days before the next dose was due, though two patients had a breakthrough migraine within a 1–2 days after their second and third doses, respectively. Five of the patients had eventual return to baseline number of headache days.

Conclusion: Through retrospective review, it is evident that a subset of patients experience a “wear off” effect from Aimovig. Further investigation is required as to whether increased frequency of dosing (i. e. by transitioning from a 140 mg monthly dose to 70 mg biweekly) can be used to mitigate this effect.

Disclosure of Interests: Dr. Deborah Reed receives compensation as a speaker for Eli Lilly, Teva, Amgen and as an advisory board member for Eli Lilly.

IHC-PO-392

Combination of Moderate Running, Diaphragmatic Breathing, and Eye Movement Desensitization as a Novel Therapy in the Treatment of Migraine

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Objective: Exercise regulates Nitric Oxide (NO) and brain-derived neurotrophic factor (BDNF)-dependent activities. Eye movement desensitization (EMD) stimulates NO in autonomic nerve fibres in the retina. Diaphragmatic breathing (DB) stimulates NO in vascular endothelial cells. Nitric Oxide has a relaxant role in the blood vessels and has been implied as a neural messenger. Considering homeostasis, BDNF relation with oxidative stress is fundamental. Furthermore, roles of NO and BDNF in the migraine brain are known. Therefore, the present study is focusing on aerobic exercise—moderate running (MR)—EMD and DB as novel therapies in the treatment of non-chronic migraine.

Methods: A three-group, pre-post-test and single blind-randomized study in which the dependent variables, including pain frequency per month, pain duration and pain intensity per attack, in all groups, were measured and compared before and after the intervention procedures. In the present study, the targeted migraineurs population was, diagnosed according to the IHCD-III, screened

(based on including and excluding criteria) and randomly divided into two experimental (MR plus EMD, $n = 19$ and MR plus DB, $n = 22$) and a control ($n = 22$) group. MR plus EMD group was scheduled to perform 3.2 kilometers running (25 minutes; every moment two deep nasal inhalations, two seconds repose, and three deep oral exhalations) every other night, plus EMD, 30 minutes before breakfast and 30 minutes before bed, every night, for 10 consecutive weeks. The other experimental group did the same, but instead of EMD, they performed DB—three-time (every time five minutes; in an upright position, two deep nasal inhalations, two seconds repose, and three deep oral exhalations) per day, for 10 consecutive weeks.

Results: The results of a series of one-way ANOVA, MR plus EMD and MR plus DB, significantly ($p < 0.05$) showed reduction in all theorized characteristics of non-chronic migraine pain in both experimental groups compared to the control group.

Conclusion: the results of present study show that MR and EMD and MR plus DB can be performed as novel therapies or life-style modification in the treatment of non-chronic migraine.

Disclosure of Interest: None Declared.

IHC-PO-393

Greater Occipital Nerve block without the use of corticosteroids in the treatment of paediatric primary headaches

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Objective: Greater Occipital Nerve (GON) block has been used for many decades as acute treatment for a variety of primary headaches disorders in adults and children. Most regimes for nerve blocks involve the use of a local anaesthetic and a potent long acting corticosteroid. There are concerns about repeated exposure to potent corticosteroids in growing children. There has been no publications of the use of GON without corticosteroids in children. Here we describe our observation of the use of GON block without steroids for primary headaches in children.

Methods: Children less than 18 years of age who received GON block at a hospital based paediatric headache clinic from Sept 2014 to Nov 2016 were identified from a local database. Data was retrospectively obtained from their clinical notes.

Results: A total of 11 children were identified. 7 were female, 5 were male. They were age 9 years to 17 years at the time of the first injection. Their diagnoses range from episodic migraine, chronic migraine, ophthalmoplegic migraine and primary stabbing headaches. 7 children

received 2 sets of injections, one had 3 set, 3 had 5 sets of injections. The average duration of primary headache was 1.6 yrs. All patients had failed at least 2–4 headache prophylaxis previously. 2 children did not report any benefit from the injection. 7 children reported greater than 50% relieve in number of attacks from the injection for at least 3 weeks. Two children reported reduction in intensity of headache but no reduction of the number of attacks. There were no complications from the injections. Two children had minor side effects of dizzy spells lasting less than a day. All injections were performed by the author. GON was identified by bony landmarks and localised nerve sensitivity. GON was infiltrated by Lidocaine 2mls of 1% (20 mg) using a 25G needle at each injection point and had resulted in localised anaesthesia.

Conclusion: GON block without corticosteroids appears safe and feasible as a treatment modality for primary headaches in children.

Disclosure of Interest: None Declared.

IHC-PO-394

Repetitive peripheral nerve blocks as an alternative preventative therapy for chronic migraine

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Objective: We did a prospective cohort study to identify the effectiveness and safety of repetitive peripheral nerve blocks (PNBs) in a cohort of patients with chronic migraine.

Methods: Patients with a diagnosis of chronic migraine were referred for PNBs if they preferred an injectable treatment and had prominent tenderness of the occipital and/or supraorbital (SO), supratrochlear (ST) and auriculotemporal (ATN) nerves on exam. Patient data was collected between June 2017 to March 2019. Patients underwent repetitive PNBs, which included a combination of steroids and local anaesthetic or local anaesthetic alone. Patients continued on their migraine preventatives and acute medications. Primary outcome measurements were the reduction of headache days in 4 weeks following the blocks and reduction of HIT6 scores at 3 months. Patient-reported duration of improvement was gathered by a telephone survey and complication rates were collected.

Results: Outcomes for 64 patients with a diagnosis of chronic migraine were collected. Mean age at referral was 41 years (S.D 12.4), with a female to male ratio of 54:10. Mean baseline headache days per month were 17 (S.D 3.3) and HIT6 score was 67 (S.D 6.0). 37 patients (58%) had repetitive occipital nerve blocks only, and 27 patients

(42%) had occipital and trigeminal nerve blocks. 33 patients (52%) had a minimum of 2 nerve block sessions. 42 patients (66%) responded to the PNBs with at least a 30% reduction in headache days. Of the responders, mean reduction in headache days was 8 days (S.D 4.0). The mean HIT6 post block was 61 (S.D 9.0). Patient-reported mean duration of effect was 9 weeks (S.D 4.3). 13 responders with chronic migraine transformed to low frequency episodic migraine on follow-up. 22 patients (34%) showed no reduction in headache days or HIT6 scores. 27 patients were referred for botox due to suboptimal response to PNBs. 3 instances of minor post block complications were documented out of 114 PNB encounters with a total of 501 injections.

Conclusion: This study suggests that repetitive PNBs are safe and could be an effective alternative strategy in providing short-term headache prevention in patients with chronic migraine. The transformation into episodic migraine in a third of our responders is promising and needs further study.

Disclosure of Interest: None Declared.

IHC-PO-395

Adherence to prophylactic migraine therapy in a primary care hospital in India

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Objective: Medication adherence is integral to the successful treatment of migraine. The aim of this study was to evaluate the rate and factors associated with non-adherence to prophylactic migraine therapy in a resource-limited primary care hospital in India where the direct treatment cost is borne by the government.

Methods: Patients of migraine with or without aura satisfying the IHS criteria who were started on hospital-available drugs (propranolol, amitriptyline, gabapentin, and valproate) alone or in combination for migraine prophylaxis within the last 1.5 years were enrolled. Non-adherence was defined as discontinuation of the drug(s) for ≥ 6 consecutive weeks. The demographic characteristics; frequency, severity, and duration of migraine attack; and medical and treatment history of the patients were recorded. The different factors associated with non-adherence were assessed by binary logistic regression analysis.

Results: Out of 383 patients, non-adherence was documented in 91 (23.75%) patients. Although the non-adherence rate did not vary significantly across the different drugs, valproate showed the maximum non-adherence rate (34.06%). The median duration of non-adherence was 11.5 weeks (IQR 10.75). The most common cause of non-adherence was familial/personal (47.5%). The non-

adherent patients had significantly less satisfaction with the treatment and had higher attack frequency and duration as compared to the adherent patients. Educational status [adjusted OR, 3.87 (95% CI, 1.29–11.63), $P=0.002$], longer duration of disease [adjusted OR, 2.5 (95% CI, 1.14–5.46), $P=0.011$], co-medications [adjusted OR, 3.61 (95% CI, 2.15–6.32), $P=0.019$], and habit of consumption of over-the-counter analgesics [adjusted OR, 1.92 (95% CI, 1.04–3.17), $P=0.041$] were significantly associated with non-adherence.

Conclusion: The rate of non-adherence to prophylactic migraine therapy was high when the direct treatment cost factor was eliminated. The causes of non-adherence were identified. A holistic approach of treatment including psycho-social support is essential to improve adherence in these patients.

Disclosure of Interest: None Declared.

IHC-PO-396

Post-Market Observational Study of Patient Experience with Erenumab

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Objective: Erenumab, a calcitonin gene-related peptide (CGRP) receptor monoclonal antibody, has been well tolerated with good efficacy for episodic and chronic migraine in clinical trials. Limited post-market observations are available. This study aims to describe provider patient selection, patient experience, and clinical characteristics after 6 months on erenumab compared to a baseline retrospective chart review.

Methods: This is an observational study of patients in a headache clinic who received ≥ 1 erenumab injection (70 mg or 140 mg). Retrospective chart review, baseline phone call, and 6 month phone call was completed. Primary data analysis was reduction in self-reported headache days per month at baseline compared to 6 months. Secondary endpoints of adverse effects, prior preventive treatments, comorbidities, wearing off, and discontinuation are descriptive.

Results: Of the 94 patients, 87.2% were female with an average age of 49 years. There was 93.6% chronic migraine with 19.1% medication overuse headache. The average headache days per month was 24.1 ± 8.3 days. Comorbidities were depression (45.7%), anxiety (44.7%), POTS (19.1%), hypermobile EDS (8.5%), MCAS (9.6%), fibromyalgia (12.8%), other chronic pain (33%), concussion (22.3%), IBS (28.7%), gastroparesis (8.5%), strokes (6.4%), CAD with stenting (1.1%), and venous thromboembolism (6.4%). An average of 11 unique oral medications and 5.3 medication categories were tried with 83% having tried

onabotulinumtoxinA. Of the 62 patients with complete data, 40.3% discontinued due to lack of efficacy (52%) or adverse effects (48%). Rate of constipation was 25.8%. Wearing off was seen in 51.1%. At 6 months ($n = 37$), the average monthly headache days were 18.4 days or -7.35 days ($p < 0.001$, 95% CI 4.01–10.69). 50% responder rate was 31.8% for headache days and 47.6% for monthly migraine days.

Conclusion: This retrospective post-market observational study aims to describe patient selection, patient responses, and adverse events to erenumab in a tertiary Headache Clinic with a complex patient population. These patients had a significant clinical response to erenumab, but high rates of discontinuation. This study also noted wearing off and high rates of constipation. Further post-market studies are needed.

Disclosure of Interests: Robblee: No disclosures. Mendez/Potter/Slonaker: Amgen speaker.

Starling: Alder, eNeura, Amgen, Eli Lilly & Company, Novartis.

IHC-PO-397

Medication Overuse does not affect response to OnabotulinumtoxinA treatment in patients with Chronic Migraine; update from real-life data from Hull Headache Clinic

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Objective: CM affects 2% of the general population with substantial impact on quality of life. Medication overuse in CM is seen in around two third of patients in specialist headache clinics. There is lack of consensus on whether preventive treatment be initiated before or after the analgesic withdrawal. We analysed the response to OnabotulinumtoxinA in patients with CM with or without analgesic overuse treated at the Hull Migraine Clinic. To compare the efficacy of OnabotulinumtoxinA in adults with Chronic Migraine with or without medication overuse.

Methods: Adult patients with CM were offered OnabotulinumtoxinA based on clinical need and were injected based on the PREEMPT treatment paradigm. Headache diaries were maintained for 30 days prior to and continuously after treatment. Data were extracted for headache, migraine and headache-free days and responders were defined based on Hull Criteria (50% reduction of either headache or migraine days or increment in headache free days twice that of the baseline).

Results: Of 972 patients, full data for the first cycle was available on 851 patients 448 (52.6%) with analgesic

overuse and 403 (47.3%) without overuse. The responder rate based on Hull criteria was similar in both groups for headache and migraine days and 50% reduction in migraine and headache days. There was significant reduction in days with analgesic consumption in both groups.

Conclusion: Patients with CM respond equally well to OnabotulinumtoxinA irrespective of analgesic consumption at baseline.

Disclosure of Interests: Fayyaz Ahmed has served on the advisory board of Allergan, Electrocore, Eneura, TEVA and Novartis for which he receives honorarium donated to charitable organisations e.g. Migraine Trust, ADMA, BASH.

Alina Buture – None.

Taukir Tanvir – None.

Modar Khalil – None.

IHC-PO-398

Analysis of patterns of response to OnabotulinumtoxinA in Chronic Migraine in predicting long-term outcome

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Objective: The efficacy of OnabotulinumtoxinA for Chronic Migraine (CM) is established; however, long term outcome data is limited and need for ongoing treatment remains uncertain.

The study aims to identify patterns of response to OnabotulinumtoxinA that predict successful conversion to episodic migraine.

Methods: Adult patients receiving OnabotulinumtoxinA for CM at the Hull Migraine Clinic were prospectively followed. All patients maintained headache diary continuously during treatment. Data was extracted on headache and migraine days to identify patterns of response and need for ongoing treatment at two years.

Results: Of 655 patients followed up for at least two years 380 fulfilled NICE or Hull Criteria for responder and continued treatment beyond cycle 2. Of the 380 responders, 152 patients were still obtaining positive response at year 2 and 112 were successfully converted to episodic migraine. Others were either lost to follow up, relapsed, became resistant or stopped treatment for other reasons. Our study analysed patterns of response and outcome in the cohort of 264 responders. We found two distinct patterns of response with 150 (56.8%) patients having a fluctuating 'wearing off' pattern with an increase in headache frequency prior to their next treatment; 114 (43.1%) having a steady decline on headache days without significant fluctuation between treatments. We found that

the 'wearing off' pattern predicted those patients who would remain in chronic migraine with only 27/150 (18%) patients converting to episodic migraine compared to 93/114 (81.5%) with stable non-fluctuating response.

Conclusion: We observed two distinct patterns of response that help to predict long-term outcome.

Disclosure of Interests: Fayyaz Ahmed served as advisory board member for Allergan, Novartis, TEVA, Electrocore and Eneura and received honorarium donated to the charitable organisations e.g. Migraine Trust, BASH and ADMA.

Taukir Tanvir – None.

Alina Buture – None.

Modar Khalil – None.

IHC-PO-399

The impact of onabotulinumtoxinA vs placebo on efficacy outcomes in responder and nonresponder subgroups of patients with chronic migraine: PREEMPT pooled analysis

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Objective: OnabotulinumtoxinA (onabotA) reduced headache (HA) days in patients with chronic migraine (CM). HA-day reduction may not capture the full benefit for patients. We evaluated the impact of onabotA treatment on patient-reported outcomes in adults with CM according to HA responder status.

Methods: Data from the two PREEMPT clinical trials with 24-week randomized double-blind treatment phases were pooled. Patients were stratified by responder ($\geq 50\%$ reduction from baseline in HA days) and nonresponder ($< 50\%$ reduction) status after 24 weeks of treatment. Responder groups were defined using modified last observation carried forward. The Headache Impact Test (HIT-6) and the Migraine-Specific Quality of Life Questionnaire (MSQ) were used to evaluate clinical impact of treatment.

Results: Among 1384 enrolled patients, 688 were randomized to onabotA (45% [$n = 308$] responders; 55% [$n = 380$] nonresponders) and 696 to placebo (34% [$n = 238$] responders; 66% [$n = 458$] nonresponders). OnabotA-treated nonresponders compared with placebo nonresponders showed a significantly greater reduction in

HA impact as measured by change in HIT-6 scores (-2.3 vs -0.8 ; $P < 0.001$) and greater improvement in MSQ domains (Restrictive, 8.8 vs 2.9; Preventive, 6.0 vs 1.8; Emotional, 8.5 vs 2.8; all $P < 0.001$). Furthermore, HIT-6 and MSQ Restrictive and Preventive scores showed significantly greater improvement among onabotA-treated responders compared with placebo responders at week 24 ($P \leq 0.001$).

Conclusion: The results support a treatment benefit of onabotA in CM at 24 weeks that may not be fully captured by reduction in HA days as a single endpoint. OnabotA was associated with significantly greater improvements than placebo in HA-related impact and quality of life in both HA-day responders and nonresponders as typically defined by an arbitrary and binary 50% cutoff ($\geq 50\%$ reduction in HA days).

Disclosure of Interests: Support: This study was supported by Allergan plc, Dublin, Ireland.

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Richard B. Lipton, MD, serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta.

David D. Dodick, MD, reports personal fees from Acorda, Amgen, Alder, Allergan, Autonomic Technologies, Biohaven, Colucid, Eli Lilly, eNeura, Foresight Capital, Neurolief, Zosano, WL Gore, Vedanta Associates, Promius Pharma, Magellan Healthcare, CC West Ford Group, Nocira, Novartis, NuPathe, Supernus, Electrocore, Tonix, Teva, Alcobra, Insys, Ipsen, Charleston Laboratories, Biocentric, Theranica, Xenon. ZP Opco. Travel expense reimbursement and speaking fee from Sun Pharma. Anticipated income from consulting

within next 3 weeks not previously reported: Impel pharmaceuticals (currently under review by Mayo Clinic Medical Industry Relations Committee). Compensation for activities related to data safety monitoring committee from Axsome. Speaking fees, or fees related to CME content development: Healthlogix, Medicom Worldwide, Medlogix Communications, MedNet, Miller Medical Communications, PeerView Operation Services America, Web MD/Medscape, American Academy of Neurology, American Headache Society, PeerView Institute for Medical Education, Chameleon Communications, Academy for Continued Healthcare Learning, Universal Meeting Management, Haymarket Medical Education, Global Scientific Communications, UpToDate, Meeting LogiX. Consulting use agreement through employer: NeuroAssessment Systems, Myndshft.

Ronald DeGryse and Aubrey Manack Adams, are full-time employees of Allergan plc and owns stock in the company. Stephen D. Silberstein, MD, is a consultant and/or advisory panel member for and has received honoraria from Alder. Biopharmaceuticals, Allergan, Amgen, Avanir, eNeura, ElectroCore Medical, Labrys Biologics, Medscape, Medtronic, Neuralie, NINDS, Pfizer, and Teva. His employer receives research support from Allergan, Amgen, Cumberland Pharmaceuticals, ElectroCore Medical, Labrys Biologics, Eli Lilly, Merz, and Troy Healthcare.

IHC-PO-400

Non-headache benefits of onabotulinumtoxinA in chronic migraine patients: PREEMPT pooled analysis

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Objective: To assess the sensitivity and specificity of the 6-item ID-CM for Chronic Migraine (ID-CM) screener.

Method: Patients from a large medical group with at least 1 medical claim with an International Classification of Diseases 9th/10th revision (ICD-9/10) code for migraine in the 12-month prescreening period were enrolled. Those with an ICD-9/10 code for CM or a migraine-related onabotulinumtoxinA claim in the 12-month prescreening period were excluded. The 12-item

ID-CM screener was administered by e-mail, in person, or over the telephone to all enrolled. The 12-item ID-CM screener is based primarily on 30-day patient recall and comprises questions assessing headache (HA) frequency, HA symptoms, medication use for HA, interference with activities due to HA, and planning disruption due to HA. The 6-item ID-CM screener, a subset of the 12-item version, includes only questions that assess HA frequency and HA symptoms. Additionally, a Semi-Structured Diagnostic Interview (SSDI) was administered by telephone to a subset of eligible patients by a trained physician. The SSDI assesses HA symptoms, frequency, disability, and medication use based on 30- and 90-day patient recall and served as the study gold standard for determining CM status. The analysis excluded patients to whom the SSDI was not administered.

Results: The analysis included 109 patients with a migraine diagnosis who completed the ID-CM screener and the SSDI. The mean (SD) age of the patient sample was 48.7 (14.5) years; 91.7% were female. Using the SSDI as the diagnostic gold standard for CM, the 6-item ID-CM screener had a sensitivity of 70.8% (46/65) and a specificity of 93.2% (41/44).

Conclusion: Optimal treatment of CM requires accurate diagnosis. Based on the SSDI as the gold standard for CM diagnosis, the 6-item ID-CM screener demonstrated acceptable sensitivity and good specificity in determining CM status, supporting its real-world validity as a simple yet accurate tool to identify CM patients.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

Hans-Christoph Diener, MD, has received honoraria for participation in clinical trials and for contribution to advisory boards or oral presentations from Addex Pharma, Allergan, Almirall, Autonomic Technology, AstraZeneca, Bayer Vital, Berlin Chemie, Boehringer Ingelheim, Bristol-Myers Squibb, Coherex, CoLucid, GlaxoSmithKline, Grunenthal, Janssen-Cilag, Lilly, La Roche, 3M Medica, Medtronic, Menerini, Minster, MSD, Neuroscore, Novartis, Johnson & Johnson, Pierre Fabre, Pfizer, Schaper and Brümmer, Sanofi, St. Jude, and Weber & Weber. He has received financial support for research projects from Allergan, Almirall, AstraZeneca, Bayer, GSK, Janssen-Cilag, MSD, and Pfizer. Headache research at the Department of Neurology in Essen is supported by the German Research Council (DFG), the German Ministry of Education and Research (BMBF), and the European Union. Dr. Diener has no ownership interest and does not own stock in any pharmaceutical company.

Richard B. Lipton, MD, serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura

Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta.

David D. Dodick, MD, reports personal fees from Acorda, Amgen, Alder, Allergan, Autonomic Technologies, Biohaven, Colucid, Eli Lilly, eNeura, Foresight Capital, Neurolief, Zosano, WL Gore, Vedanta Associates, Promius Pharma, Magellan Healthcare, CC West Ford Group, Nocira, Novartis, NuPathe, Supernus, Electrocore, Tonix, Teva, Alcobra, Insys, Ipsen, Charleston Laboratories, Biocentric, Theranica, Xenon. ZP Opco. Travel expense reimbursement and speaking fee from Sun Pharma. Anticipated income from consulting within next 3 weeks not previously reported: Impel pharmaceuticals (currently under review by Mayo Clinic Medical Industry Relations Committee). Compensation for activities related to data safety monitoring committee from Axsome Spine. Consulting fees related to CME content development: Healthlogix, Medicom Worldwide, Medlogix Communications, MedNet, Miller Medical Communications, PeerView Operation Services America, Web MD/Medscape, American Academy of Neurology, American Headache Society, PeerView Institute for Medical Education, Chameleon Communications, Academy for Continued Healthcare Learning, Universal Meeting Management, Haymarket Medical Education, Global Scientific Communications, UpToDate, Meeting LogiX. Consulting use agreement through employer: NeuroAssessment Systems, Myndshft.

Ronald DeGryse and Aubrey Manack Adams, are full-time employees of Allergan plc and owns stock in the company. Stephen D. Silberstein, MD, is a consultant and/or advisory panel member for and has received honoraria from Alder Biopharmaceuticals, Allergan, Amgen, Avanir, eNeura, ElectroCore Medical, Labrys Biologics, Medscape, Medtronic, Neuralieve, NINDS, Pfizer, and Teva. His employer receives research support from Allergan, Amgen, Cumberland Pharmaceuticals, ElectroCore Medical, Labrys Biologics, Eli Lilly, Merz, and Troy Healthcare.

IHC-PO-401

Catastrophizing attitude changes accompanying Onabotulinumtoxin A treatment in Chronic Migraine with Medication Overuse: Interim findings

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Objective: Chronic Migraine with Medication Overuse (CM-MO) is associated with high levels of disability, lessened quality of life and high catastrophizing attitude. Onabotulinumtoxin A is helpful for alleviating pain in chronic migraine, with generally high rates of adherence. Onabotulinumtoxin A can also lead to improvements in psychological symptoms. Our ongoing trial is designed to further evaluate the efficacy of Onabotulinumtoxin A as well as to explore concurrent changes in additional key secondary outcomes, catastrophizing in particular.

Methods: Seventy-nine patients, diagnosed as CM-MO (according to IHS criteria) are being treated by Onabotulinumtoxin A according to the PREEMPT protocol, at the dosage of 195 UI, after a 5-day structured withdrawal in a day hospital setting. Patients are recording headache days and medication intake per month, the primary measure of outcome, in daily headache diaries. They are also completing secondary outcome measures for catastrophizing attitudes about pain (Pain Catastrophizing Scale), disability (MIDAS Questionnaire), and quality of life (HIT-6) at varied follow-up periods.

Results: Sixty patients (all females) have completed the third session of treatment to date. At 6 months headache days and medication intake were reduced by 38% (22.6 vs 13.9) and 36% (22.8 vs 14.6) respectively. Levels of improvements varied considerably with respect to pain catastrophizing (19%; 29.2 vs 23.6), disability (32%; 76 vs 51.7), and quality of life (5%; 65 vs 61.8), with none reaching statistical significance.

Conclusion: The dosage of 195 UI was well tolerated and revealed improvement similar to prior investigations. Changes with respect to pain catastrophizing and disability are trending in the direction of improvement, but these aspects typically take longer to manifest completely. We anticipate further improvements when all patients have completed treatment and our planned longer term followup evaluations are conducted.

Disclosure of Interest: None Declared.

IHC-PO-402

Erenumab in migraine: the first Italian real-life data

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Objective: To report the preliminary data of the first prospective observational Italian study with erenumab in

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(pts. n)	Episodic Migraine (25 pts)				Chronic Migraine (97 pts)			
	Baseline (25)	Week 4 (18)	Week 8 (9)	Week 12 (1)	Baseline (97)	Week 4 (67)	Week 8 (33)	Week 12 (8)
Monthly migraine days, mean \pm SD	10.8 \pm 1.8	7.2 \pm 5.1	7.2 \pm 7.3	3	21.8 \pm 5.8	10.6 \pm 7.2	10.8 \pm 8.5	7.1 \pm 3.3
Change in monthly migraine days, mean \pm SD		-3.5 \pm 4.7	-3.6 \pm 6.2	-4		-11.6 \pm 8.3	-11.2 \pm 9.5	-14.5 \pm 7.8
Monthly analgesic intake, mean \pm SD	12.8 \pm 5.3	7.6 \pm 5.2	7.2 \pm 7.3	3	23.6 \pm 22.5	9.9 \pm 7.2	9.2 \pm 8.1	7.1 \pm 3.3
Change in monthly analgesic intake, mean \pm SD		-6.4 \pm 5.6	-9.4 \pm 7.2	-4		-15.8 \pm 15	-12.8 \pm 11.3	-15.4 \pm 14.2
Responder rate \geq 50%		44.5%	55.5%			61.2%	66.7%	87.5%
Responder rate \geq 75%		16.7%	33.3%			31.3%	27.3%	25%
Responder rate 100%		0	11.1%			0%	0%	0%

the prevention of high frequency episodic migraine (HFEM: 9–14 days/month) and chronic migraine (CM).

Methods: We included all consecutive patients with HFEM and CM seen at our IRCCS San Raffaele Headache and Pain Unit from 20 December 2018 to 5 April 2019. Eligible patients were treated with a single erenumab 70 mg dose given subcutaneously every 28 days. We evaluated change in monthly migraine days (MMD), analgesic intake, pain intensity (VAS), headache impact test (HIT-6 TM) score and \geq 50%, \geq 75% and 100% responder rates at different time intervals compared to baseline.

Results: One-hundred-twenty-two migraineurs (F/M: 98/24; HFEM/CM: 25/97 pts) received at least 1 dose of erenumab 70 mg. Patients with HFEM and CM were comparable for gender (F/M in both groups: 4/1), age (48.7 \pm 11.9 vs 46.8 \pm 10.4 years), BMI score (22.4 \pm 2.6 vs 21.5 \pm 2.5), disease duration (28.9 \pm 12.8 vs 29.6 \pm 12 years), pain severity (VAS, 8 \pm 1.1 vs 7.8 \pm 1.1), cutaneous allodynia (56% vs 62.9%), triptan responsivity (78.3% vs 71.1%), concomitant migraine prophylaxis (56% vs 62.9%), number of prior therapeutic failures (4.8 \pm 2.1 vs 5.2 \pm 2.4) and HIT-6 score (68.2 \pm 5.3 vs 68.6 \pm 6). CM patients had more frequently bilateral pain (41.2% vs 28%) unilateral cranial autonomic symptoms (73.2% vs 60%), medication overuse (86.6% vs 40%) and used a higher number of analgesics (23.6 \pm 22.4 vs 12.1 \pm 3.9). Dopaminergic symptoms were more common in HFEM patients (60% vs 49.5%). The effects of erenumab 70 mg on monthly migraine days and analgesic intake are summarized in the table. VAS and HIT-6 scores were also progressively reduced at the different time intervals. One adverse event (injection site erythema) was reported in a single patient.

Conclusion: The preliminary findings of the first Italian real-life study confirm that erenumab is highly effective and

well tolerated in the prophylaxis of both HFEM and CM, being characterized by a very rapid onset of action and by a remarkable proportion of super-responders.

Disclosure of Interest: None Declared.

IHC-PO-403

Patient preference for dosing regimen and perception of dosing flexibility with fremanezumab for migraine: results from a patient survey following completion of a 1-year extension study

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Objective: Patient (pt) preference for the dosing regimen and perceptions of dosing options for fremanezumab, a fully humanised monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide (CGRP), were evaluated using a retrospective, web-based questionnaire in a subpopulation of a 52-week extension study in migraine pts.

Methods: In the extension study, adults with chronic or episodic migraine (CM or EM) were randomised to receive either quarterly (qtly) or monthly (mthly) fremanezumab. A sample of 253 pts from US study sites completed a retrospective survey 1–24 months after completing the extension study. 134 of these pts had received

fremanezumab during the preceding phase 3 study; all 253 received active treatment during the extension study. Pts who started another CGRP-targeted migraine preventive treatment after the extension study were excluded. Pt preference for dosing schedule (qtlly or mthly), perceived impact of flexible dosing options on prospective compliance, and perceived value of flexible dosing were evaluated retrospectively in the survey.

Results: Overall, 69% of pts expressed a preference for qtlly dosing, with a similar proportion choosing this regimen if they had been treated in the qtlly (68%) or mthly (70%) dosing arm during the extension study. 74% of pts believed having dosing flexibility makes it easier to adhere to a migraine medication, and 77% believed having dosing flexibility adds value to a migraine medication, with no differences in these perceptions between those in the qtlly or mthly dosing arms.

Conclusion: These results highlight the high value that migraine pts place on having flexible dosing options with fremanezumab therapy. The finding that more than two-thirds of pts expressed a preference for qtlly over mthly fremanezumab dosing is relevant for clinical decision makers involved in treatment selection. Results may be limited by recall and participation bias.

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IHC-PO-404

Patient preference for and satisfaction with fremanezumab following completion of a 1-year extension study

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Objective: To assess patient (pt) preference for and satisfaction with fremanezumab, a fully humanised monoclonal antibody (IgG2Δa) that selectively targets CGRP.

Methods: In a 1-year extension (ext) study, adults with migraine were randomised to quarterly or monthly fremanezumab. 253 pts from US study sites completed a

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Table. Preference and satisfaction with fremanezumab vs prior preventive

	Tricyclic antidepressant (n = 53)	Antiepileptic (n = 130)	SSRI/SNRI (n = 27)	Anti-hypertensive (n = 62)	Onabotulinum-toxinA (n = 28)
Tried prior preventive, %	24	53	11	35	13
Preferred fremanezumab, %	95	93	94	88	85
Satisfaction with prior preventive, mean (fremanezumab rating [n = 253], 6.1)	2.7	2.7	3.0	2.7	2.9

^a1–7 scale (1 = "extremely dissatisfied"; 7 = "extremely satisfied").

retrospective survey 1–24 months after the ext study. 134 pts received fremanezumab during a preceding phase 3 study; all 253 received active treatment during the ext study. Pts who started another CGRP-targeted migraine preventive treatment after the ext study were excluded. Pt preferences for prior migraine preventive treatments or fremanezumab were evaluated retrospectively. Pts also rated their satisfaction with fremanezumab and with prior preventives on a 7-point scale (1 = “extremely dissatisfied” to 7 = “extremely satisfied”).

Results: 145 (57%) pts tried ≥ 1 preventive (protocol allowed ≤ 3) before entering fremanezumab trials. Most pts reported preference for fremanezumab vs prior treatment (**Table**), primarily due to higher reduction of migraine frequency and pain intensity. Of pts with prior onabotulinumtoxinA use ($n = 32$), 91% preferred fremanezumab injection. Mean satisfaction with fremanezumab ($n = 253$) was 6.1 out of 7 and 2.7–3.0 for prior treatments ($n = 27$ to 130; **Table**).

Conclusion: Fremanezumab was consistently and highly preferred to prior preventive medicines for a range of reasons. Fremanezumab injection was preferred over onabotulinumtoxinA injection by most pts. Results may be limited by recall bias and higher likelihood of prior therapy failure and fremanezumab response.

Disclosure of Interests: R. P. Cowan has received consulting fees and honoraria from Teva, Amgen, Alder, and Lilly. S. Gandhi, J. M. Cohen, V. Ramirez-Campos, and A. H. Ahn are employees of Teva Pharmaceuticals. B. Cloud has no conflicts of interest to disclose. D. C. Buse has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Lilly, Promieus and Teva. She is on the editorial board of *Current Pain and Headache Reports*. R. B. Lipton is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. He receives research support from the NIH: 2PO1 AG003949 (mPI), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), IRF1 AG057531 (Site PI), RFI AG054548 (Investigator), IRO1 AG048642 (Investigator), R56 AG057548 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor), 1K01AG054700 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation. He serves on the editorial board of *Neurology*, senior advisor to *Headache*, and associate editor to *Cephalalgia*. He has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics,

GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. He receives royalties from Wolff's *Headache 7th and 8th Edition*, Oxford Press University, 2009, Wiley and Informa.

IHC-PO-405

Will refractory migraine patients in the real world respond to Erenumab?

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Objective: In the real world, Erenumab is being used in a less controlled and more severely affected cohort, than in the prior Randomised Controlled Trials (RCT)¹.

Methods: 109 patients from 3 Australian headache centres on Erenumab had response in monthly migraine days (MMD) and monthly headache days (MHD), correlated to their age, frequency of headache, duration of Chronic Migraine (CM), failed prophylactic medications, severity scores and medication overuse headache (MOH).

Results: After 3 months of treatment, 57.5% (61/106) had $\geq 50\%$ reduction in MMD. Mean baseline MHD was 23 and MMD was 20.2, reducing to 16.6 and 10.4 at 3 months. Migraine Disability Impact (MIDAS) scores were severe in 98%. The Headache Impact Test (HIT-6) reduced from 66 to 58. Triptan use reduced by a mean of 5 days.

In this Australian cohort, the mean age was 46.4 years (18–73 years). 40.4% (44/109) had persistent daily headache, which was excluded in the RCT. Mean duration of migraine was 28.8 years, with 64.3% (63/98) having CM ≥ 10 years. 100% had failed ≥ 3 prophylactic medications (being an exclusion for the RCT), with 18.3% (20/109) failing ≥ 10 prophylactics. 96% (105/109) had tried Onabotulinum toxin A, of which 36.2% (38/105) failed to respond, 60% (63/105) were partial responders and 3.8% (4/105) were good responders to onabotulinum toxin A. At baseline, 44.9% overused triptans and 26.2% overused codeine. Within more severe subgroups, the $\geq 50\%$ MMD responder rates were similar to the overall response rate: 50% (22/44) in persistent headache; 50% (10/20) after ≥ 10 previous prophylactic failures; 64.6% (31/61) in triptan overuse ($p = 0.02$); 53.6% (15/28) in codeine overuse; 60% (21/35) of Onabotulinum toxin-A failures; and 53.1% in the patients with HIT-6 scores ≥ 60 .

Conclusion: This early cohort of Australian patients using Erenumab represent a more severe, longstanding,

refractory and older patient group. Despite this, there were still $\geq 50\%$ responders in the more severe subgroups at similar rates to the overall rate of response after 3 months of treatment, with increased rates of responsiveness in triptan MOH. Further studies are recommended to assess if there are clinical predictors of responsiveness.

Disclosure of Interests: Dr Bronwyn Jenkins has received fees for lectures and advisory boards from Allergan, Eli Lilly, Novartis and Teva. Dr Shuli Cheng has no disclosures. Dr Nicole Limberg has received fees for travel and staffing from Allergan, and advisory board fees from Novartis. Dr Elspeth Hutton has received fees for lectures and advisory board from Allergan, Eli Lilly, Sanofi-Genzyme, Novartis and Teva.

IHC-PO-406

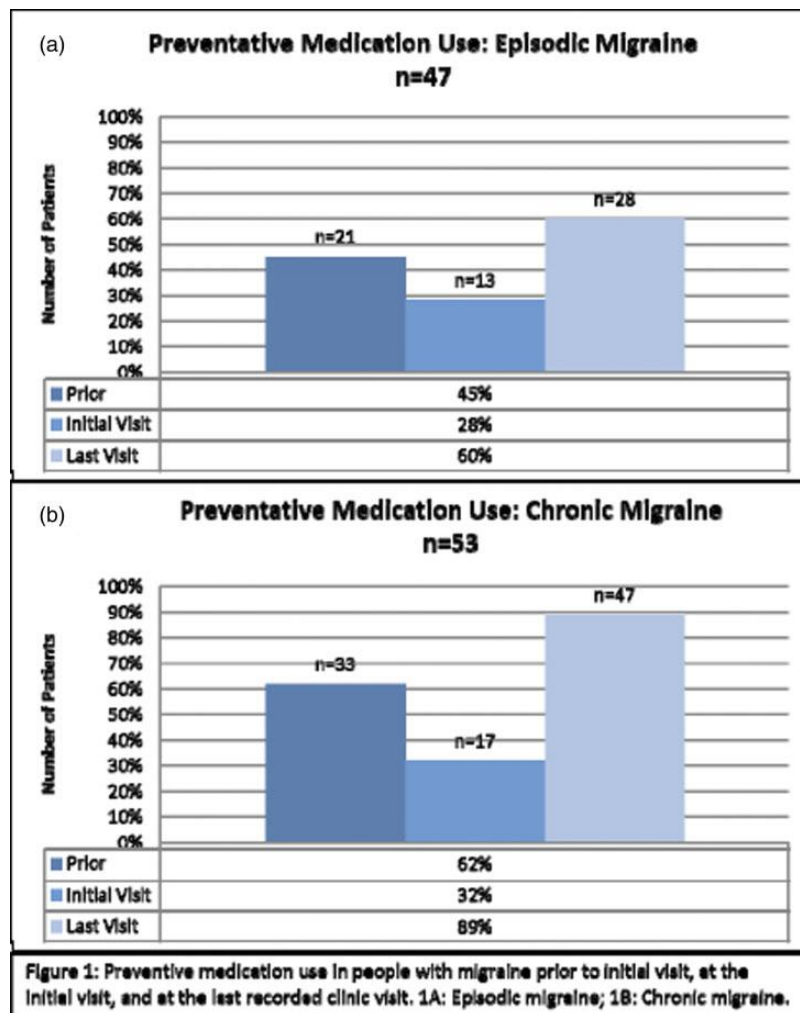
Migraine preventive medication use patterns in a tertiary headache center

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Objective: We aimed to describe longitudinal preventive medication use patterns in a tertiary headache center over a three year period. We were particularly interested in how many patients required combination preventive treatment.

Methods: We searched for all new patients seen at the John R. Graham Headache Center at Brigham and Women's Hospital for initial evaluation of migraine from May-December 2015. We recorded information for up to 3 subsequent years. We recorded current and past



Abstract number: IHC-PO-406

preventive medication use at the initial visit; any newly prescribed or recommended preventive headache medications; duration of followup; and the preventive medication regimen at the final visit.

Results: We identified 567 new patient visits and reviewed 100 charts as a pilot. The average age was 38 years old and 13% were male. 47 patients were diagnosed with episodic migraine and 53 had chronic migraine. 21 (45%) patients with episodic migraine had ever tried a preventive medication (average 2.1 medications, range 1–7) and 13 (28%) were currently taking preventative medications at the time of their initial appointment. 33 (64%) patients with chronic migraine had ever tried a preventive medication, (average 5.0 medications, range 1–19) and 17 (32%) were currently taking preventatives at the time of their initial appointment. 54/100 patients had more than one visit. Average followup time for patients with >1 visit was 18.7 months. 72 patients received a recommendation or prescription for a new preventive at some point during their care. 28 patients (60%) with episodic migraine were taking preventive treatment at their last visit. 20 were taking 1 medication, 6 were taking 2, and 2 were taking 3 medications. Of those with chronic migraine, 47 (89%) of patients were taking preventive treatment. 30 were taking 1 medication, 11 were taking 2, and 6 were taking 3 or more medications. Of the 100 patients seen for new visits for migraine, one quarter required combination preventive treatment. These findings are summarized in Figure 1.

Conclusion: About half of patients presenting to our tertiary headache center for migraine had ever tried a preventive medication. Around ¾ of patients were recommended to try preventive treatment, and 25% required combination treatment. These findings may inform clinical treatment decisions, economic modeling, and payor coverage determinations in the future.

Disclosure of Interest: None Declared.

IHC-PO-407

A randomized double-blind, cross-over trial of very low-calorie ketogenic vs. non-ketogenic diet in overweight migraine patients

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Objective: Considering the negative impact of obesity on migraine disability, we decided to determine the therapeutic effect of a very low-calorie diet in overweight/obese episodic migraine patients during a weight-loss

intervention during which they alternate randomly in a double-blind cross-over design a very low-calorie ketogenic diet (VLCKD) and a very low-calorie non-ketogenic diet (VLCnKD) each for one month. This trial protocol was intended to allow separating the effect on migraine of caloric restriction and carbohydrate restriction.

Methods: In a nutritional program, 35 overweight obese migraineurs were allocated blindly to 1-month successive VLCKD or VLCnKD in random order (VLCKD-VLCnKD or VLCnKD-VLCKD). We analyzed the clinical outcome of both diets on our patients and the possible influence of the order in which both diets were performed.

Results: Only data from the intention-to-treat cohort (n=35) will be presented. Patients who dropped out (n=6) were considered as treatment failures. All the dropout occurred when patients underwent to the VLCnKD.

The 50% responder rate for migraine days was 74.28% during the VLCKD period, but only 8.57% during VLCnKD.

Monthly headache frequency significantly decreased in VLCKD if compared to VLCnKD (p < 0.0001).

No differences emerged in terms of weight loss.

Conclusion: Our results confirm in a double-blind design that VLCKD is rapidly effective for the short-term improvement of migraine in overweight patients, while VLCnKD is not, suggesting that ketogenesis may be a useful therapeutic strategy for migraine.

Disclosure of Interest: None Declared.

IHC-PO-408

The preventive management for chronic migraine preferred by Mexican neurologists

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Objective: To know the prescription preference of the Mexican physicians for Chronic Migraine treatment.

Methods: A written survey was conducted to Neurologists, Pediatric Neurologists and Mexican physicians in two conferences of Neurology. The survey had five questions with paragraphs, where they were asked about age, gender, specialty, if they suffered from episodic or chronic migraine and which are the medications more frequently prescribed in chronic migraine.

Descriptive statistics was made. The results were expressed as percentages or means and standard deviations.

Results: The participants were one hundred thirty-eight physicians (73.9% men), with an average of age: 49.93 ± 12.7 . 93 adult neurologists (67.4%), 34 neuro-pediatrician (24.6%) and 11 general physicians or with other specialties (8%). Of the total participants, 30 (21.7%) suffer from episodic migraine, and 2 (1.5%) suffer from chronic migraine.

Their preferences for prescribing drugs for the treatment of chronic migraine were as follow: in the 76.1% of the cases, neuromodulators ($n = 105$, 65.7% adult neurologists) were the first option. In 2.9% of the cases ($n = 4$; 75% adult neurologists) the botulinum toxin was the first option. In 4.3% ($n = 6$, all adult neurologists) the combination of neuromodulator and botulinum toxin was the first choice. In 14.5% ($n = 20$, 55% adult neurologists) the first choice was other kind of medication and the 2.1% ($n = 3$) not specify their first choice.

The most prescribed neuromodulators and antidepressants were topiramate 58% ($n = 80$, 61.2% adult neurologists), valproate 10.1% ($n = 14$, 57.2% adult neurologists), amitriptyline 26.8% ($n = 37$, 83.8% adult neurologists) and 5.1% ($n = 7$) did not specify.

Conclusion: The Mexican Neurologist have similar prescription tendencies as the IHS guidelines marks. However, we need to improve the level of education in our population in the way to offer the best quality of treatment to our population.

Disclosure of Interest: None Declared.

IHC-PO-409

Endovenous in-hospital treatment for desensitization and detoxification of chronic migraine. Our experience with lacosamide

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Objective: Central sensitization and medication overuse have reached a great importance in migraine chronification in recent years. In the present study, we want to analyze our experience with lacosamide as a desensitizing treatment.

Methods: We included patients with chronic migraine who received endovenous in-hospital treatment between 2015 to 2018 in Hospital La Fe, Valencia, Spain. They

received the following protocol as treatment: Lacosamide 200 mg each 12 hours, Ketorolac 30 mg each 8 hours, Tiaprizal 100 mg each 12 hours, from 3 to 5 days.

Results: We included 48 patients, 41 female (85.4%) and 7 male (14.5%), with mean age of 48 years (range 16–77). At the time of hospital admission, 46 patients (96%) had been taken acute medication in the overuse range. 36 patients were taking triptans (77.7% took triptans daily). 4 patients were taking nonsteroidal anti-inflammatory drugs (NSAIDs) daily and finally, 6 patient were on opioids on a daily basis.

With regards to preventive treatment, 80% of the patients had failed 3 or more treatments and 66.6% of them had tried botulinum toxin.

The hospitalizations lasted an average of 7.70 days. We used corticosteroid in 33.3% of patients (subsequent to the previous protocol if it was not effective). The average VAS (Visual Analogue Scale) of pain at hospital admission was 7.81/10. At the time of discharge it was 2.81/10.

During following medical consultations (3 and 6 months after the hospitalization), 77% described an improvement in their quality of life, which lasted a median of 2 months and an average of 3.66 months. We observed a reduction in more than 50% of acute medication days in 50% of the patients taking triptans, 57% of the patients taking opioids, and 33.3% of the patients taking NSAIDs.

Conclusion: Lacosamide seems to be effective as part of this protocol. The results in the medium to long term are less satisfactory however, they do signal a symptomatic relief for refractory chronic migraine. More studies are needed to define the profile of patients who could benefit the most for this treatment.

Disclosure of Interest: None Declared.

IHC-PO-410

Postural Tachycardia Syndrome (POTS) in Migraine Patients & their Response to Erenumab

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Objective: Erenumab, a calcitonin gene-related peptide (CGRP) receptor monoclonal antibody, has FDA approval for migraine prevention in adults. Limited postmarket observations are available. Tolerability and efficacy of this medication in postural orthostatic tachycardia syndrome (POTS) is unknown. POTS has a higher frequency in migraine, and patients have difficulty tolerating medications. This study characterizes POTS in migraine and the clinical response to Erenumab.

Methods: This is an observational study of patients with migraine and POTS who received ≥ 1 erenumab injection (70 mg or 140 mg). Retrospective chart review, baseline phone call, and 6 month phone call was completed. Primary data analysis was reduction in self-reported headache days per month at baseline compared to 6 months.

Results: Eighteen patients were identified with POTS and migraine. 88.9% were female with average age of 34 years. 94.4% had chronic migraine including 13 patients with daily headache (average 26.3 headache days per month). Comorbidities were depression (55.6%), anxiety (50%), hypermobile EDS (27.8%), Mast cell activation syndrome (44.4%), fibromyalgia (11.1%), other pain syndromes (38.9%), concussion (33.3%), IBS (33.3%), and gastroparesis (22.2%). An average of 11 individual oral prophylactics including tricyclic antidepressants (77.8%), SNRI (61.1%), anti-epileptics (100%), beta-blockers (66.7%), calcium channel blocker (27.8%), and supplements (66.7%) have been tried. OnabotulinumtoxinA was tried by 88.9%, nerve blocks by 94.4%, and non-invasive neuromodulation devices in 50%. Six patients have 6 month data with -5.7 headache days per month (0 to -22 days) and -6.8 migraine days per month (0 to -24 days). Seven patients stopped erenumab early (6 ineffective, 5 adverse effects). Adverse effects included constipation (6), injection pain (1), allergic reaction (1), and negative effects on migraine (3).

Conclusion: This is a retrospective observational study of patients with migraine and POTS who received Erenumab. These are complex and often refractory patients. Headache and especially migraine days decreased in some at 6 months. Constipation and discontinuation rates were high. Further studies are needed on the diagnosis and treatment of POTS patients with migraine.

Disclosure of Interests: Robblee & Grimsrud: No disclosures.

Vanderpluym: Amgen, Teva and Healint.

Mendez/Potter/Slonaker: Speakers for Amgen.

Starling: Alder, eNeura, Amgen, Eli Lilly & Company, Novartis.

IHC-PO-411

Migraine diagnosis rate and prophylactic treatment patterns in the Czech Republic: a retrospective claims data analysis

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Objective: Limited data are available on migraine epidemiology, diagnosed and treated patients, prophylactic treatment (PT) use from real world clinical practice. The objectives of our study were to analyze health insurance (claims) data in order to estimate migraine diagnosis rate and describe PT use in migraine patients.

Methods: For this retrospective analysis, data was extracted from database of the second biggest health insurance fund in the Czech Republic (CR) equally covering 12% of the whole CR population. For the purpose of this analysis, migraine population was defined as i. patients with ICD code G43 and ii. patients with ICD code G44 on concomitant triptans therapy. Data was extracted for the reference period 2012–2016.

Results: Migraine diagnosis/ claimed rate was stable during the study period 2012–2016. Approximately 1/3 of the total migraine population represents newly diagnosed patients. Every year, 1% of patients from the total insured population had migraine related healthcare expenses/ claims in their records. By applying these figures to overall country, the number of migraine patients utilizing healthcare paid by health insurance companies would be around 110 000 every year, in the whole CR.

Mean (SD) age of all migraine patients in reference year 2016 was 42.0 (16.1) years, proportion of females was 80.8%. Mean (SD) age of migraine patients newly diagnosed in 2016 was 33.7 (16.1) years, proportion of females was 71.5%.

Considering 3-year or 7-year recall period the proportion of adult migraine patients using ≥ 2 PT was 12.2% or 23.3% in 2016, respectively.

Conclusion: In comparison with published migraine prevalence data (10% – 15%), the proportion of migraine patients utilizing healthcare covered by healthcare insurance funds is very low. From our migraine patients, 40% were on PT. Antiepileptics (26%) and beta-blockers (16%) were the most frequent PT used.

Disclosure of Interests: supported by Novartis, s.r.o.

IHC-PO-412

Effectiveness of erenumab in chronic migraine in a tertiary headache centre

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Objective: To report outcome data for erenumab in treating chronic migraine patients in a tertiary headache clinic, using the UK Free-of-Charge (FoC) scheme.

Methods: Patients with chronic migraine by the International Classification of Headache Disorders (ICHD-3) who had failed at least three previous preventive classes received erenumab 70 mg s/c monthly initially for 3 months. Patients were asked to keep headache diaries and were reviewed monthly to check their progress. We collected as part of our routine practice: headache days, migraine days, analgesics days, and HIT-6 score at baseline and one month after the third injection. We audited these clinical outcomes. We examined for differences using Wilcoxon matched pairs and paired-t tests setting $P < 0.05$ as significant. We calculated the 50% responder rate for migraine days response. We tabulated reported side effects.

Results: At writing, 60 patients fulfilled the FoC scheme criteria for starting erenumab, and a total of 179 cycles were given. Full 3 cycles data were available for 31 patients (19% male) with mean age of 46 (± 14) years. They had had an average of eight previous preventive therapies. There was a reduction in mean headache days (-4 , $p < 0.01$), mean migraine days (-5 , $p < 0.01$) and mean acute analgesics days (-5 , $p < 0.01$). There was a HIT-6 reduction of 3 points ($p = 0.03$). The 50% responder rate for migraine days was 35%. The commonest side effects were: constipation (25%), fatigue (6%), worsened headache (6%), change in aura (6%) and weight loss (3%).

Conclusion: Erenumab is a valuable, effective and well tolerated therapeutic option for patients with chronic migraine who have failed multiple previous preventive therapies. The migraine days responder rate is comparable to previously reported results.

Disclosure of Interests: M. Khalil Conflict with: Received honorarium from Allergan for delivering talks at Migraine Masterclass, D. Moreno-Ajona: None Declared, F. Greenwood: None declared, Peter J. Goadsby reports grants and personal fees from Amgen and Eli-Lilly and Company, and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Biohaven Pharmaceuticals Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Novartis, Teva Pharmaceuticals, and Trigemina Inc., and personal fees from MedicoLegal work, Massachusetts Medical Society, Up-to-Date, Oxford University Press, and Wolters Kluwer; and a patent Magnetic stimulation for headache assigned to eNeura without fee.

IHC-PO-413

Evaluating the indications for treatment with OnabotulinumtoxinA and anti-CGRP monoclonal antibodies in migraine patients attending a headache outpatient clinic

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Objective: To evaluate the prevalence of migraine patients attending a headache outpatient clinic that are candidates to start therapy with OnabotulinumtoxinA or anti-CGRP antibodies, according to the drug labelling and different definitions of refractory migraine.

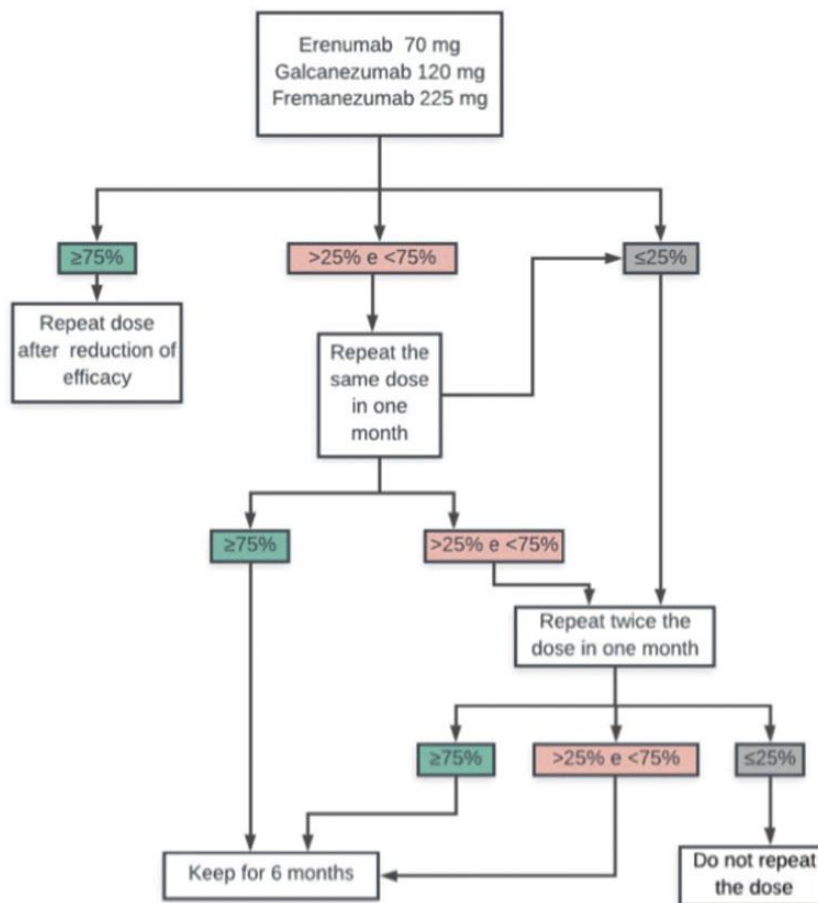
Methods: We performed a demographic analysis of a cohort of migraine patients referred to a headache outpatient clinic between June 2017 and February 2019, and evaluated which of them met the drug labelling criteria to start the abovementioned therapies. We also looked for those that could be referred to their use, according to the European Headache Federation (EHF) and American Headache Society (AHS) definitions of refractory migraine.

Results: Amongst 92 migraineurs, most were female (87.0%), and had a medium age of 39 years. There was a predominance of migraine without aura (59.3%), followed by with aura (34.1%), hemiplegic (5.5%) and other types (1.1%). The average time since the onset of symptoms was 18 years and the patients reported a medium number of 9 migraine days per month. Medication-overuse headache was present in 27.2%.

According to the drug labelling, 23 of those patients (25.0%) met criteria for the OnabotulinumtoxinA treatment, with 76 of them (82.6%) being indicated for anti-CGRP antibodies. If we consider the EHF definition for refractory headache, no patient would be indicated for any of the mentioned therapies. However, if we were to exclude the medication-overuse factor, 1 patient (1.1%) would fulfil this definition. By the AHS definition, 10 patients (11.0%) would benefit from these therapies.

Conclusion: If we consider the drug labelling alone, we find a high number of patients that could apply for the described drugs. The definitions of refractory headache, can restrict this number and help in the decision of initiating these therapies. Nevertheless, by being more restrictive, they limit the use of this therapeutic options in patients with a short follow-up time and a limited medical record of previous failure of preventive therapies.

Disclosure of Interest: None Declared.



Abstract number: IHC-PO-414

IHC-PO-414

Algorithm for preventing migraine through anti-CGRP monoclonal antibodies: a guide for real-world practice

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Objective: Anti-CGRP monoclonal antibodies have been developed for preventing migraine. We propose an algorithm in order to better assist decision-making processes on the use of these drugs.

Methods: The algorithm was proposed based on the lowest efficacious dose of each compound through different strategies according to the patient's response to treatment.

Results: The algorithm guides how to provide patients appropriate treatment according to their responses. If $\geq 75\%$, we suggest repeating the dose soon after reducing effectiveness. If $>25\%$ and $<75\%$, we also recommend repeating the same dose within a month. If $\leq 25\%$, the dose should be doubled in the next administration. If a

substantial improvement is achieved after the second administration, we recommend the same dose, but only after six months. If the patient's response is partial or there is lack of response, the dose should also be doubled.

Conclusion: This protocol should facilitate doctors' and patients' understanding about the management of these new drugs in migraine prevention treatments.

Disclosure of Interest: None Declared.

IHC-PO-415

The Effect of Aimovig on Trigeminal Neuralgia: A Retrospective Case Series

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Objective: Recently, the class of Anti-CGRP monoclonal antibodies has been approved for use in the treatment of migraine headaches. With its mild side effect profile, many chronic migraine patients have started this preventative

Abstract number: IHC-PO-415

Patient	Aimovig Effective	Post Treatment Frequency
1	1 (Definitely Not)	4 (Very Often)
2	5 (Definitely Yes)	1 (Never)
3	4 (Probably Yes)	3 (Sometimes)
4	5 (Definitely Yes)	3 (Sometimes)
5	5 (Definitely Yes)	3 (Sometimes)
6	4 (Probably Yes)	4 (Very Often)
7	5 (Definitely Yes)	4 (Very Often)
8	1 (Definitely Not)	4 (Very Often)
Mean	3.75	3.25

treatment. The first FDA approved in this class is Aimovig (erenumab). There has been limited evidence as to the efficacy of this class of medications on trigeminal neuralgia. The primary objective of this study was to identify if patients on Aimovig had any improvement in their trigeminal neuralgia pain.

Methods: Through retrospective chart review, we identified patients that were started on Aimovig monthly injections that had a diagnosis of trigeminal neuralgia. These patients may have had a concomitant diagnosis of chronic migraine. Response to Aimovig was measured per patient report on 5 point grading scales in respect to frequency of trigeminal neuralgia pain (Always – Never) and patient belief that medication was effective (Definitely Yes – Definitely Not).

Results: Of the 10 patients that were identified as having a diagnosis of trigeminal neuralgia and were taking Aimovig monthly injections, 8 had been contacted via phone by time of study to provide report of response to Aimovig. Data collected on both 5 point grading scales were transitioned to numerical values for data management. In respect to subjective feeling of efficacy of medication, “Definitely Not” was scored as a 1 and “Definitely Yes” was scored as a 5. In respect to frequency, “Never” was scored a 1 and “Always” was scored a 5. Six patients (75%) scored the medication a 4 or 5 in regards to feeling that Aimovig was effective in alleviating trigeminal neuralgia pain, while two patients (25%) scored it a 1. In regards to frequency of trigeminal neuralgia pain after starting Aimovig, one patient (12.5%) had complete resolution rating it a 1, three patients (37.5%) rated it a 3, and four patients (50%) rated it a 4. The mean score for subjective efficacy was 3.75, and the mean score for pain frequency was 3.25.

Conclusion: For patients with trigeminal neuralgia, Aimovig is an option that can potentially be used to reduce trigeminal neuralgia pain, while maintaining mild side effect profile. Further study must be done to assess

the efficacy of anti-CGRP monoclonal antibodies on the treatment of trigeminal neuralgia.

Disclosure of Interest: None Declared.

IHC-PO-416**Physiotherapy and aerobic exercise have similar effects for the reduction of migraine headache but patients prefer physiotherapy**

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Objective: To compare the effectiveness of an aerobic exercise with a physiotherapy intervention. A second objective was to evaluate whether patients with cervical musculoskeletal dysfunction, especially with pain referred to the head during manual palpation will benefit more from a physiotherapy intervention than patients with local pain or nor pain during palpation. Patients were allowed to choose their preferred treatment option.

Methods: After a 4-week run-in period, 103 patients with migraine received physiotherapy (n=79) or supervised aerobic exercise (n=24) according to their preference as an add-on treatment to the medical management of a specialized headache clinic. Both treatment groups had the same amount of contact time with a physiotherapist (4 weeks, 1 hour each week). The primary outcome was the number of headache days during the 4 weeks after the final intervention day. 87 patients were analysed at the primary endpoint (n=69 in the physiotherapy group; n=18 in the aerobic exercise group) and 16 patients dropped out of the intervention groups. 3 months after the final intervention, a final follow-up assessment was conducted.

Results: During the initial manual assessment of the upper cervical spine, 17 of the patients reported no pain, 45 local pain and 25 referred pain to the head. Patients in the physiotherapy group had a mean reduction of 1.55 days (SD 6.07) while patients in the aerobic exercise group had a mean reduction of 0.88 days (SD 4.27). This difference was not statistically significant. The largest improvement was noted in the patient group that showed referred pain to the head during the initial manual assessment of the upper cervical spine and received physiotherapy (2.13 days (SD 7.82)). Patients in the physiotherapy group but not in the aerobic exercise group reported clinically relevant global perceived change.

Conclusion: Patients with migraine had a strong preference for physiotherapy although effects were not statistically different to results from aerobic exercise. Patients

with pain referred to the head during manual palpation responded best to a physiotherapy intervention. Stratifying patients to find subgroups seems the key to optimizing treatment outcome.

Disclosure of Interests: This study was supported by a scientific grant from the Migraine Foundation (<https://migraineresearchfoundation.org/>).

IHC-PO-417

The SQUARE study design: A multi-centric, non-interventional study to evaluate the impact of erenumab on quality of life in a real-world population with migraine

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Objective: Real-world evidence has become an important cornerstone for evaluating newly registered pharmaceuticals. Erenumab (Aimovig), an antagonist of the calcitonin gene-related peptide (CGRP) receptor, received Swiss marketing authorization as a migraine prophylaxis in July 2018. Here, we present the design of the non-interventional SQUARE study (Swiss QUality of life and health-care impact Assessment in a Real-world Erenumab treated migraine population, CAMG334ACH01) evaluating erenumab in clinical practice.

Methods: A total of 193 adult patients with migraine will be enrolled in approx. 20 sites across Switzerland. Patients are included upon informed consent if they are willing and able to complete questionnaires and diaries. Patients with prior use of CGRP (receptor)-based therapies or recent use of investigational drugs are excluded.

Visits at 0, 3, 6, 12, 15, 18, and 24 months (± 1 month) were chosen to match those required for reimbursement in Switzerland, to monitor the treatment interruption mandatory for reimbursement after 12 months, and to capture long-term effects. Patients who discontinue or switch therapy are also followed.

Headache Impact Test (HIT-6) after 6 months compared to baseline was chosen as primary endpoint. Other endpoints include modified (monthly) migraine disability assessment test (mMIDAS) and impact of migraine on partners and adolescent children (IMPAC). Integration of the "Migraine Buddy" mobile application allows collection of migraine days and acute migraine medication days at high resolution without imposing additional burden to study sites.

Results: SQUARE was approved by the competent ethics committee on Feb 13th, 2019, and the first patient was

recruited on Feb 18th, 2019. Primary results are expected in 2021.

Conclusion: This study is among the first to describe the impact of erenumab in a real-world setting. Similar studies will be conducted in other countries, allowing pooling and cross-comparison. Results from this endeavor will corroborate the body of evidence available for erenumab in medical practice.

Acknowledgements: We thank all participating patients and study sites, as well as individuals who gave input to this study design.

Disclosure of Interests: A.R.G. has received honoraria for consulting or speaking fees from Allergan, Curatis, Eli Lilly, Novartis, Pfizer, and TEVA. I.M., M.E.A., and S.R. are employees of Novartis.

IHC-PO-418

Long term outcome for OnabotulinumtoxinA therapy in Chronic Migraine; a two year follow up of 655 patients from Hull Headache Clinic

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Objective: The long-term outcome for patients with CM treated with and responsive to OnabotulinumtoxinA remains unclear. The National Institute for Health and Care Excellence (NICE) recommends discontinuing treatment if there is no response to two consecutive cycles (negative stopping rule) or when the migraine becomes episodic (positive stopping rule). However, this is based on consensus only as the practice varies based on health-care system and individual clinicians.

To determine the outcome at two years for patients with CM treated with OnabotulinumtoxinA.

Methods: All patients treated with OnabotulinumtoxinA at the Hull Migraine Clinic were prospectively followed. Treatment was delivered as per the PREEMPT paradigm. Responders were defined as per NICE or Hull criteria. Treatment was stopped if there was no response to two consecutive cycles or until the headache days were less than 10 for three consecutive months (modified positive stopping rule).

Results: Of a series of 972 patients treated between July 2010 and September 2018 and received 5745 cycles, full data was available on 851 patients. Treatment data for at least two years was available on 655 (July 2010 – October 2016). 380 (58%) patients fulfilled either NICE (47.8%) or Hull criteria for responder at cycle 2 and continued treatment. 275 patients (42%) stopped treatment at cycle two. Of the 380 patients 152 (40%) patients were still on treatment at the end of year two while 228 (60%) had stopped

treatment for various reasons; 61/228 (26.7%) relapsed after stopping, 28/228 (12.3%) got resistant after initial response and 112/228 (49.1%) or 112 of the original responders (N = 380–29.4%) remained episodic.

Conclusion: At two years, 42% of initial cohort of responders will still require therapy with OnabotulinumtoxinA.

Disclosure of Interests: Fayyaz Ahmed served as an advisory board member for Allergan, Electrocore, Eneura, Novartis and TEVA and receive honorarium donated to charitable organisations e.g., Migraine Trust, ADMA and BASH.

Taukir Tanvir – None.

Alina Buture – None.

Modar Khalil – None.

IHC-PO-419

Five year outcome on 310 patients receiving OnabotulinumtoxinA for Chronic Migraine; data from Hull Migraine Clinic

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Objective: The long term outcome for patients with Chronic Migraine (CM) responsive to OnabotulinumtoxinA remains unclear. There is lack of consensus on the positive stopping rule that differ based on healthcare system and choice of individual clinicians. National Institute for Health and Care Excellence (NICE) recommends stopping treatment once migraine becomes episodic although this is not evidence based. Two year data has been reported. We report a 5 year outcome on a large cohort of patients from Hull Migraine Clinic.

To determine what happens to patients 5 year on from receiving their first treatment with OnabotulinumtoxinA for CM.

Methods: All patients treated with OnabotulinumtoxinA at the Hull Migraine Clinic were prospectively followed. Treatment was delivered as per PREEMPT paradigm. Responders were defined as per NICE or Hull criteria. Treatment was stopped if there was no response in two cycle or if the patient achieved less than 10 headache days per month for at least three consecutive months (modified positive stopping rule).

Results: Of a series of 972 patients treated between July 2010 and September 2018 and received 5745 cycle, full data was available on 851 patients. Treatment data for five years was available on 310 patients (July 2010 – October 2013). 186 patients (60%) fulfilled Hull Criteria for responder; (40%) stopped treatment as per negative rule. Of the 186 responders, 37 patients stopped

treatment either because of resistance (N = 22) or pregnancy (N = 8) and 7 were lost to follow up. 44 of remaining 149 patients were still on treatment at 5 years (Cycle 20) of which 18 had stopped treatment earlier but relapsed. 105 patients (57.9%) from the original cohort of responders remained episodic. Patients received treatment cycle ranging from 5- 20 before stopping treatment.

Conclusion: At five years, 30% of initial cohort of responders will still require treatment with OnabotulinumtoxinA.

Disclosure of Interests: Fayyaz Ahmed served on the advisory board of Allergan, Novartis, Electrocore, Eneura and TEVA for which he received honorarium donated to the charitable organisations e.g., Migraine Trust, BASH and ADMA.

Taukir Tanvir – None.

Modar Khalil – None.

Alina Buture – None.

IHC-PO-420

OnabotulinumtoxinA for Chronic Migraine during pregnancy; experience from Hull Migraine Clinic, United Kingdom

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Objective: The use of OnabotulinumtoxinA during pregnancy is restricted due to the lack of adequate and well-controlled studies. While women who are pregnant, nursing or planning a pregnancy are excluded from clinical trials, many women treated with OnabotulinumtoxinA for axillary hyperhidrosis, chronic migraine and cosmetic indications are of reproductive age. A 24-year retrospective review of the Allergan safety database on 574 pregnancies demonstrated that the prevalence of fetal defects in OnabotulinumtoxinA-exposed mothers to be comparable to background rates in the general population. Most of these patients were treated for cosmetic reasons or movement disorders. There are no reports regarding patients with Chronic Migraine exposed to OnabotulinumtoxinA therapy during pregnancy.

We report pregnancy outcomes on 42 patients with Chronic Migraine exposed to OnabotulinumtoxinA.

Methods: Adult patients treated with OnabotulinumtoxinA for prophylaxis of Chronic Migraine at the Hull Headache Clinic received prospective follow-up. Female patients of reproductive age were asked to report on pregnancy before each treatment. Pregnant patients were advised against further treatment unless they chose to continue following an informed discussion about the uncertain impact of treatment on the fetus.

Results: Of the 42 patients who reported pregnancy (8–16 weeks), 29 wished to continue with further treatment at three-monthly intervals. 13 patients did not continue further treatment. Of the 29 patients that continued treatment there was 1 miscarriage. Remaining 28 were full term deliveries of which there were 2 forceps and 3 caesareans. No fetal malformation was reported. The remaining 13 had full term deliveries of which there was 1 forceps and two caesareans and no fetal malformation.

Conclusion: We report the outcome in 42 pregnant patients with CM exposed to OnabotulinumtoxinA. There is need to collect further data before establishing its safety.

Disclosure of Interests: Fayyaz Ahmed serves on the advisory board of Allergan, TEVA, Novartis, Electrocore and Eneura for which he receives honorarium donated to charitable organisations e.g., Migraine Trust, BASH, ADMA. Howard Wong – None.

Taukir Tanvir – None.

Alina Buture – None.

Modar Khalil – None.

IHC-PO-421

HeMiLa – Prophylactic treatment of hemiplegic migraine with Lamotrigine (EudraCT-Nr. 2016-003223-30)

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Objective: Hemiplegic Migraine (HM) is a rare and severe subtype of migraine with aura characterized by transient unilateral motor weakness in addition to other (i.e. visual, sensory, dysphasic) aura symptoms. Mutations in three genes involved in cerebral ion translocation (*CACNA1A*, *ATP1A2*, *SCN1A*) have been found in families and some sporadic cases, characterizing HM as a channelopathy. At present, evidence-based treatment options for HM are missing. Based on limited data on a possible beneficial effect of lamotrigine (LTG) in non-hemiplegic migraine aura, LTG might be a promising therapeutic option in HM.

Methods: In this single center, prospective, open explorative study, 28 HM patients (ICHD-III^B diagnostic criteria) with a baseline attack frequency of ≥ 3 during 1 year observational phase are treated with LTG during an intervention phase of 1 year. The dose of LTG is first escalated to 200 mg daily and can optionally be raised up to 600 mg.

Frequency of attacks is monitored by a patient's diary, monthly telephone interviews and study visits every 6 months. A concomitant medication with other anticonvulsants or first line prophylactic medication for migraine is not allowed. Primary endpoint is the absolute difference of attacks between baseline and intervention phase. Secondary endpoints are the amount of attack free patients under treatment as well as the absolute difference of attacks with non-hemiplegic aura (baseline vs. intervention phase).

Results: Since October 2017, 80 patients have been pre-screened. 6 patients were included in the study, 3 of which have reached the intervention phase. First interim results of the study will be presented at the international headache congress.

Conclusion: HM is a severely compromising disease with serious impact on patients' well-being. Reliable data on effective treatment options are missing. This explorative trial evaluates a biologically plausible pharmacological treatment, which may guide future treatment in clinical routine and set the scene for follow-up interventional studies.

Disclosure of Interest: None Declared.

IHC-PO-422

The multicenter, randomised, double-blind, sham-controlled PREMIUM 2 trial: study design for evaluating non-invasive vagus nerve stimulation (nVNS) as a preventive treatment of migraines

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Objective: Non-invasive vagus nerve stimulation (nVNS; gammaCore[®]) is FDA approved for the acute treatment of pain associated with migraine and episodic cluster headache and for adjunctive use to prevent cluster headache. Efficacy for migraine prevention was observed in a post hoc analysis of patients who were >67% compliant with treatment (n=278) in the large European PREMIUM 1 study of episodic migraine (n=332). The randomised, double-blind, sham-controlled PREMIUM 2 trial underway in the United States aims to establish the efficacy of nVNS in migraine prevention through an updated protocol based on findings in PREMIUM 1.

Methods: Following a 4-week observational run-in period, patients will be randomly assigned (1:1) to nVNS or sham for a 12-week double-blind period. The preventive treatment regimen consists of 2 unilateral stimulations administered to the neck 3 times daily. Acute migraine medication and no more than 1 adjunctive preventive migraine medication will be allowed. The PREMIUM 2 trial was initiated in November 2018. Up to 500 patients will be enrolled across 35 sites. Expected study duration is 18 months—14 months for enrolment and 4 months for active study participation. Use of an inactive sham will avoid the active vagal stimulation seen with the sham in some previous studies.

Results: A *modified intent-to-treat population* (ie, patients with $\geq 66\%$ weekly treatment compliance) will be the primary efficacy analysis set. The primary efficacy endpoint is change in migraine days from the run-in period to the last 4 weeks of the double-blind period; secondary efficacy endpoints are changes in headache and acute medication days and $\geq 50\%$ responder rates. The primary safety endpoint is the incidence of device-related serious adverse events.

Conclusion: This trial is intended to establish nVNS as an effective treatment option for migraine prevention.

Disclosure of Interests: S. Silberstein has received honoraria from Abide Therapeutics, Alder Biopharmaceuticals, Allergan, Inc., Amgen, Avanir Pharmaceuticals, Inc., Biohaven Pharmaceuticals, Cefaly, Curelator, Inc., Dr. Reddy's Laboratories, Egalet Corporation, GlaxoSmithKline Consumer Health Holdings, LLC, eNeura, Inc., electroCore Medical LLC, Lilly USA LLC, Medscape LLC, NINDS, Satsuma Pharmaceuticals, Supernus Pharmaceuticals, Inc., Teva Pharmaceuticals, Theranica, and Trigemina, Inc.

J.R. Saper has received consultancy fees from Alder Biopharmaceuticals Inc., Allergan, Inc., Johnson & Johnson (Ethicon, Inc.), Migraine Research Foundation, NuPathe Inc., Purdue Pharma L.P., Supernus Pharmaceuticals, Inc., Teva Pharmaceutical Industries Ltd., and Tian Pharmaceutical Co. Ltd. Dr. Saper has also received research grants from Achelios Therapeutics, Inc., Alder Biopharmaceuticals Inc., Allergan, Inc., Amgen, Inc., Astellas Pharma Inc., Autonomic Technologies, Inc., Cerephex Corporation, Daiichi-Sankyo Co. Ltd., Dr. Reddy's Laboratories Ltd., Eli Lilly and Company, GlaxoSmithKline, Labrys Biologics, Inc., Merck & Co., Inc., Pfizer, Inc., Scion NeuroStim, LLC, Vanda Pharmaceuticals, and Winston Laboratories, Inc.

L.L. Mechtler has received speaker fees from Allergan, Inc., Depomed, Inc., and Supernus Pharmaceuticals, Inc., and research support from Celldex Therapeutics, Cincinnati Children's Hospital Medical Center, GlaxoSmithKline, PharmaNet Group Ltd., and Questcor Pharmaceuticals, Inc.

E. Liebler is an employee of electroCore, Inc., and receives stock ownership.

T. Smith has received speaker fees from Amgen, Novartis, Lilly, and Promius and advisory board or consultancy fees from Biohaven, Amgen, Lilly, Alder, Promius, and Zosano. He has also received research support from Amgen, Alder, Lilly, Teva, Allergan, Biohaven, Dr. Reddy's Laboratories, Zosano, electroCore, Scion Neurostim, Novartis, Novo Nordisk, Ionis, and Impel.

IHC-PO-423

Hull Prospective Analysis of OnabotulinumtoxinA (Botox) in the treatment of Chronic Migraine; a real-life data in 972 patients; updated results on over 8 years of experience

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Objective: To evaluate the efficacy and safety of OnabotulinumtoxinA in adult patients with Chronic Migraine (CM) in real-life settings.

Methods: Adult patients with CM attending the Hull Migraine Clinic were treated with OnabotulinumtoxinA based on clinical needs. Patients were treated as per PREEMPT protocol. Patients were asked to maintain a headache diary for at least 30 days prior to and continuously after treatment. Patients with medication overuse were included based on the expert opinion. Data were extracted for headache days, migraine days, crystal clear days (headache-free) as primary outcome; also analgesic consumption, adverse events and quality of life using HIT-6. Responder was defined as per Hull criteria (50% reduction in either headache or migraine days or increment on headache free days twice the baseline) for treatment in the first cycle.

Results: Of a series of 972 patients (July 2010 – September 2018) full data were available on 851 patients (158 male, median age 45 years; range 14–79 years, 693 female, median age 45 years; range 17–96 years). A total of 5745 cycles were given. 836 (98.2%) had failed three preventive treatments. 448 (52.6%) patients were overusing analgesics. Patients had CM for a median of 4 years (Range 0.5–67 years). 448 (52.6%) responded based on Hull Criteria and reported improved health related quality of life outcome. 88 (12.6%) reported adverse events mainly stiffness in the neck with 58 (6.8%) reporting mild ptosis.

Conclusion: To our knowledge we have the largest post-PREEMPT real world data on the use of OnabotulinumtoxinA for chronic migraine. Our results

will be compared with various outcomes from the PREEMPT study.

Disclosure of Interests: Fayyaz Ahmed has served on the advisory board of Allergan, Electrocore, Eneura, TEVA and Novartis for which he is paid honorarium donated to charitable organisations i.e. Migraine Trust, BASH and ADMa.

Modar Khalil – None.

Taukir Tanvir – None.

Alina Buture – None.

IHC-PO-424

Prophylactic effect of ultramicrozoned N-Palmitoyl Ethanol Amide (PEA) on pediatric migraine

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Objective: The aim of this open-label study was to evaluate the efficacy of ultramicrozoned PEA (um-PEA) in the prophylactic treatment of migraine.

Methods: We prospectively evaluated patients attending the Headache Center of Bambino Gesù Children Hospital, with diagnosis of migraine without aura (ICHD 3 criteria) receiving umPEA (600 mg/day orally) for minimum three months. We compared the attack frequency (AF) and attack intensity at baseline and after three months. Patients were asked to classify the intensity of the attack with a value ranging from 1 to 3 where 1 means mild attack, 2 moderate and 3 severe attack.

Results: The study included 53 patients with mean age of 10.67 ± 3.1 (24.5% Male and 75.5% Female). After 3 months of treatment with um-PEA, the headache frequency was reduced by >50% per month in 56.6% patients. Three patients discontinued treatment too early (less than a month) and were not considered in the results. After three months of treatment the number of monthly attacks decreased significantly compared to the start of therapy (from 13.89 ± 7.6 SD to 6.43 ± 5.1 SD; $p < 0.05$) The intensity of the attacks went from 1.70 ± 0.6 (pre-PEA) to 1.19 ± 0.5 (post-PEA).

Conclusion: PEA is an amide of endogenous fatty acids widely distributed in different tissues, including nervous tissues. PEA is emerging as a new therapeutic approach in pain and inflammatory conditions and it has been evaluated in studies on various painful diseases. However, to

date no studies have been conducted to evaluate the role of PEA in the management of migraine in pediatric patients. Our preliminary data show that um-PEA administered for three month reduces pain intensity and the number of attacks per month in in pediatric patients with migraine. Although the small number of patients and the lack of control group do not allow us to consider these initial results as definitely reliable, they encourage us to expand the sample.

Disclosure of Interest: None Declared.

IHC-PO-425

Saline nasal irrigation (Jaaneti) reduces headache days in chronic migraine: a randomized, waitlist -controlled study

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Objective: The aim of this study was to evaluate the efficacy of Yogic saline nasal irrigation for the prevention of chronic migraine in a randomized, wait-list-controlled trial.

Methods: Patients (18–65 years) who experienced chronic migraine, with > or =15 monthly days with headache out of which at least > or = 12 with migraine, for > or =3 months were randomized to jala neti group or waitlist control group for a 12-week trial. Jala neti was practiced under the therapist supervision thrice a week for 4-weeks. After 4-week of intervention, each participant continued following give intervention for 8-weeks. Existing migraine acute treatments were continued throughout the trial. The primary efficacy measure was the change in number of migraine days from the 28-day baseline phase to the 12-week follow up. Health-related quality of life was evaluated with the Migraine Specific Quality of Life Questionnaire and the Headache Impact Test (HIT-6).

Results: Eighty-six patients diagnosed and referred by neurologist were included in the study. Forty-two patient's complete intervention period and forty-one in wait list control. No significant between group differences were found for at baseline. After four weeks of intervention, days with headache reduced significantly in Jalaneti group ($P < 0.0001$) along with quality of life and disability. After 12-week of follow-up assessment showed consistent program impact with 85% of adherence.

Conclusion: This randomized, waitlist-controlled trial demonstrates that Yogis Saline nasal Irrigation (jalaneti) is effective in treatment of chronic migraine.

Disclosure of Interest: None Declared.

IHC-PO-426**IV Valproate Sodium as a Preventive Treatment for Chronic Migraine**

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Objective: This is a small pilot study to evaluate the effectiveness of an intravenous valproate sodium therapy protocol for migraine prevention in a population of patients with chronic migraine refractory to multiple preventive medications.

Methods: 13 adult patients with chronic migraine were admitted for a 4-day course of IV valproate sodium. Patients received 250 mg of valproate sodium over a standard infusion time of 60 minutes every 8 hours. Most patients received 9 doses over the 4-day course of treatment. 1 patient had to discontinue after one dose of 250 mg valproate sodium, as he developed increased nausea, vomiting and vertigo with his first dose.

To avoid positive selection bias, we evaluated the most recent admission for analysis for patients with multiple admission (there was 1 patient with two admissions and 1 with three admissions for IV valproate sodium).

Headache diaries were reviewed from one month before, during, and two months after their admission.

Results: 8 out of 12 (67%) patients had an improvement in their headache status post-admission and reported a reduction in headache frequency, intensity and/or use of acute medications four to six weeks following their admissions. 5 out of 12 (42%) patients also reported an improvement in headache severity during the 4 day period of inpatient admission. The other 7 of 12 patients reported stable headache status.

1 patient had feelings of restlessness, which improved with prolongation of infusion time to 120 minutes.

Conclusion: These results indicate that this repetitive dosing valproate sodium protocol is a safe and well-tolerated intervention for the treatment of chronic migraine resistant to oral medications. Given the promising outcomes on patient headache status with this small pilot study, studies to confirm this benefit in a larger cohort of chronic migraine patients are warranted, preferable with the addition of a blinded control group for comparison.

Disclosure of Interest: None Declared.

Neuromodulation for Headaches**IHC-PO-186****Effects of prolonged treatment of single pulse Transcranial Magnetic Stimulation (sTMS) in animal models of migraine**

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Objective: Single-pulse transcranial magnetic stimulation (sTMS) is a non-invasive neuromodulation technique shown to be successful for migraine treatment. Previous research has shown that acute sTMS treatment increases the threshold of cortical spreading depression (CSD) induction, but it does not influence trigeminal nociception. Its long-term effects have not been previously investigated.

Methods: Daily treatments of either 1.1 T or 0 T sTMS were applied to awake male adult Sprague-Dawley rats for a period of 30 days using a custom made sTMS coil with a diameter of 11 mm and stimulating parameters similar to the migraine treatment. Behavioural testing of paraorbital von Frey thresholds was performed every other day for the first two weeks followed by every 5th day until day 30. At the conclusion of daily-treatments, CSD induction thresholds by electrical stimulation of the occipital cortex were determined in anaesthetised animals. All procedures were performed under a UK Home Office Licence in accordance to the 1986 Animal (Scientific Procedures) Act.

Results: Thirty days of daily treatment with 1.1 T sTMS induced no significant changes in the paraorbital von Frey threshold compared to the control group (0 T sTMS) ($P = ?$). CSD induction thresholds were found to be significantly increased in the 1.1 T sTMS treatment group compared to the 0 T controls ($F_{1, 14} = 7.53, p < .016$).

Conclusion: Daily sTMS treatment did not alter mechanical von Frey thresholds suggesting it does not sensitize the trigeminal system. The increase in the CSD threshold in the active treatment group does suggest that sTMS has a long-term cumulative effect in inhibiting cortical excitation.

Disclosure of Interest: None Declared.

IHC-PO-187**Rationale and design of the REAL study, a randomised, open-label, multicentre trial of preventive and acute migraine treatment with non-invasive vagus nerve stimulation versus standard of care**

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Objective: Randomised controlled trials (RCTs) usually focus on safety and efficacy in narrowly defined homogeneous populations and are not designed to evaluate the practical utility of novel therapies such as non-invasive vagus nerve stimulation (nVNS) in practice. We initiated the REAL study to collect real-world data on nVNS to complement findings from RCTs.

Methods: The study is enrolling adults who have migraine with or without aura and suffer 6–24 headache days per month. After a 4-week run-in period, subjects are randomly assigned (1:1) to 12 weeks of open-label therapy with their standard of care (SoC) alone or nVNS plus their SoC. Those in the nVNS group deliver 2 consecutive 120-s stimulations twice daily as preventive therapy, as well as acute therapy consisting of 2 consecutive stimulations at migraine pain onset and 15 minutes after the first stimulation for each attack. Stimulations are given on the neck, ipsilateral to pain. For bilateral pain, 1 side is chosen for each set of stimulations. Approximately 300 subjects will be enrolled and ~232 randomised at ≤20 European sites.

Results: The primary effectiveness endpoint is the mean reduction in number of migraine days during the last 4 weeks of the randomised period (vs the run-in period). Secondary endpoints include reduction in number of headache days (randomised vs run-in) and rates of acute treatment response (defined as no/mild pain and no rescue medication use) at 30, 60, and 120 minutes post-treatment.

Conclusion: This study will provide data on the practicality, efficacy, and safety of nVNS for the treatment of migraine. This trial should provide a broader view of the efficacy of nVNS in a real-world setting and supply insights for further integration of nVNS into clinical practice.

Disclosure of Interests: M. Láinez has received consultancy fees and research support from Allergan, Amgen, ATI Pharma, Bayer, Boehringer Ingelheim, electroCore, Inc., Eli

Lilly, Lupin Pharmaceuticals, Medtronic, Novartis, Otsuka, Roche, and Teva.

C. Gaul has received honoraria from Allergan, Bayer, Boehringer Ingelheim, Desitin Arzneimittel, electroCore, Inc., Eli Lilly, Grünenthal, Hormosan Pharma, Novartis, Ratiopharm, Reckitt Benckiser Group, and Teva. He has no ownership interests and does not own stock in any pharmaceutical company.

C. Tassorelli has received consultancy fees from Allergan S.p.A., electroCore, Inc., Eli Lilly, and Novartis AG and research grants from the European Commission and the Italian Ministry of Health. She is also a principal investigator or collaborator for RCTs sponsored by Alder BioPharmaceuticals Inc., Eli Lilly, and Teva Pharmaceutical Industries Ltd.

E. Liebler is an employee of electroCore, Inc., and receives stock ownership.

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IHC-PO-427**Non-invasive Peripheral Vagal Nerve Stimulation prevents migraine aura: a case report**

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⁴electroCore LLC, Basking Ridge, United States

Objective: Non-invasive neuromodulation techniques have shown efficacy in the acute treatment of migraine. Cortical spreading depression, the electrophysiological event underlying migraine aura, is significantly suppressed by non-invasive vagal nerve stimulation (nVNS).

Methods: We describe a patient affected by migraine with visual and somatosensory aura, whose symptoms were consistently attenuated by nVNS in multiple prospectively recorded attacks. The patient (female, 38-year-old) is affected by migraine with aura (5–6 episodes per year) and without aura (7–8 days per month).

Results: During the observation period, the patient reported nine migraine with aura attacks; five were treated with nVNS, while the other four were managed with SoC. When compared with current standard of care, nVNS significantly reduced the duration of visual aura in all the attacks and prevented the somatosensory aura in 3 out

of 5 attacks. The duration of the visual symptoms was significantly shortened by nVNS when compared to SoC (17.0 ± 4.5 vs. 53.5 ± 4.8 minutes, respectively). The overall duration of nVNS treated auras was 19.0 ± 4.2 minutes, significantly shorter than the duration of aura in attacks treated with standard of care (103.8 ± 10.3 minutes).

Conclusion: This single case study requires confirmation in a larger sample size, but we believe that this first report is suggestive of likely efficacy given the relatively high number of treated attacks and the consistent effect of nVNS.

This observation could be of interest considering that nVNS is already FDA approved and CE marked, portable, easy to use and with a favorable benefit/risk ratio.

Disclosure of Interests: CT received fees for the participation in advisory board for Allergan S.p.A., electroCore, Inc, Teva, Eli Lilly and Novartis.

IHC-PO-428

Application of micro-cauterization (on cervical, occipital and temporal areas) for patients with chronic migraine and/or Medication Overuse Headache (MOH). Report of 25 cases

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Objective: The aim of this study is to evaluate the efficacy of micro-cauterization on cervical, occipital and temporal areas for patients with chronic migraine -with and without aura- and Headache due to Medication Overuse (MOH). The method used is inspired by Agnikarma, an old Indian treatment for pain with therapeutic microcautery and is based on the theory of the distorted communication within trigeminocervical complex.

Methods: A total of 25 patients with migraine were selected. All of them were chronic migraneurs with poor response to medication – failure of at least one prophylactic treatment was prerequisite. The cauterisation was performed on the cervical, occipital and temporal areas (also on some patients on supraorbital & scapular areas) depending on what patients referred to as the most painful points during the attack of migraine or the inter-ictal period. A total of 4 sessions were held, every 7–10 days.

Results: Evaluation scales were completed before, throughout and at the end of all 4 sessions. The majority reported a significant improvement (reduction in frequency, intensity or duration of episodes). For 3 patients there was a complete remission of migraine attacks, whereas for 2 there was no change and left the study. A reduction in symptomatic (No of tabs/week) and prophylactic treatment was also reported. To be noted that 17

patients continue the sessions of cauterization and report even greater improvement.

Conclusion: Alternative methods can be supportive to drugs on altering the features of migraine or even play a leading role in treatment. Possible mechanisms underlying the effectiveness of the method are discussed.

Disclosure of Interest: None Declared.

Other

IHC-PO-188

Physician-Assistance Algorithm for Migraine Medications

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Objective: For patients with multiple medical problems, choosing potential migraine medications can be a challenge. We construct an algorithm to systematically identify all contraindicated migraine medications based on the input of medical comorbidities. Our goal is to build a computer program that assists physicians in finding safe migraine medications for patients.

Methods: Our study uses two data sets containing lists of abortive medications (set A) and preventive medications (set B). A separate file lists known contraindications to the above medications as a pairing (2-tuple). For example, "(ergotamine, coronary artery disease)" denotes that ergotamine is contraindicated in coronary artery disease. All data files can be generated by the development team or user-defined.

Graph theory conventions denote that a graph is composed of object called "nodes"; two connected nodes establish an "edge" between them. All nodes connected by an edge to a specific node are called "first-degree neighbors." For example, if nodes C and D form an edge, and nodes D and E form an edge, then C and E are first-degree neighbors.

The algorithm generates two models for contra-indications of abortive and preventive medications from the above data sets as follows: the nodes of each graph consist of individual medication or co-morbidity; an edge exists between a comorbidity and a medication if both are in the same 2-tuple.

To use the algorithm, a user inputs a defined list of medical comorbidities. Both the abortive and the preventive models identify the first degree neighbors of each comorbid condition. These first-degree neighbors describe the list of all contraindicated medications. We outputs them as set X. The algorithm calculates set differences between A

and X as well as B and X, generating lists of “allowed” medications.

We implement the above in C# and Python, programming languages, using NetworkX, a graph theory toolkit.

Results: Given a list of medical problems, our algorithm generates a list of contra-indicated and non-contraindicated migraine medications. This software is pending distribution without a cost to general public through Rutgers University website.

Conclusion: A graph theoretical algorithm can be implemented to help headache physicians pick migraine medication. With further clinical validation, our algorithm may allow for safer prescription practices in clinical headache medicine.

Disclosure of Interests: Pengfei Zhang: Consultant for BoardVitals Inc., Consultant for Fieve Clinical Research.

IHC-PO-189

A comparison of pain control between Occipital nerve block and Occipital nerve radiofrequency; A retrospective cohort study

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Objective: Objectives: The primary objective was to evaluate the comparative effect of occipital nerve block

(ONB), occipital nerve pulsed radiofrequency (P-RF) ablation and ONB+ P-RF ablation on patient with occipital neuralgia.

Methods: This was a single center, retrospective cohort study with inclusion of all consecutive patients who were admitted to Allevio pain management clinic during the period January 01, 2014 to December 31, 2017 and underwent one of three types of pain management interventions: occipital nerve block, occipital nerve P-RF or occipital nerve block followed by P-RF.

Patient were included in this cohort who fit the ICHD-3b definition of occipital neuralgia as defined above. Patients who only received occipital nerve blocks were given the option for radiofrequency ablation but declined. Patient who only received radiofrequency ablation had occipital nerve blocks performed at an outside clinic by landmark guidance.

Results: From 2014–2017 in Allevio Pain Management clinic, 25 patients had Occipital nerve blocks, 10 patients had Occipital nerve RF ablations, and 31 patients had Occipital nerve blocks followed by RF. All the 66 charts had been reviewed and 60 patients had replied to the questionnaires. The longest recorded follow-up time of 40 months. The median age of study participants was 54. 73% of the sample was not retired: 83% in the nerve block group, 61% in nerve block followed by RF group and 89% in the RF group. Of non-retired patients, 55% returned to work after the intervention. More patients returned to work after nerve block followed by RF compared with group of patients who had nerve block only (94.1% vs. 57.9%, non-adjusted $p = 0.019$). Near half of the sample indicated reduction in narcotic use after the intervention, with no difference between groups The median pain-free period was 3 months.

Abstract number: IHC-PO-189

Table. Patients' outcome at follow-up

	Total n = 66	Nerve blocks n = 25	Nerve block followed by RF n = 31	Nerve RF n = 10	p-value
Work Status					
Retired, n (%)	16 (26.7)	4 (17.4)	11 (39.3)	1 (11.1)	0.178
Non-retired, n (%)	44 (73.3)	19 (82.6)	17 (60.7)	8 (88.9)	
Returned to work, n (%)	33 (55.0)	11 (57.9)	16 (94.1)	6 (75.0)	0.040
Pain medication					
Reduction in narcotic use, n (%)	28 (46.5)	8 (34.8)	15 (53.6)	5 (55.5)	0.364
No reduction in narcotic use, n (%)	32 (53.5)	15 (65.2)	13 (46.4)	4 (44.4)	
Pain relief duration, months (median, IQR)	3.0 (1.0–6.0)	3.0 (1.0–5.5)	2.0 (1.0–6.5)	2.0 (1.0–6.0)	0.939

IQR: interquartile range; RF: radiofrequency.

Note: Missing data is reported for the following variables: retirement status (n = 6); changes in medication (n = 6), pain relief duration (n = 6).

Conclusion: In summary, our study shows a combined greater and lesser pulsed radiofrequency ablation technique provides substantial benefit in return to work and reduction in narcotic consumption. A further study to evaluate the potential anastomosis between these nerves may provide further insight into mechanism of modulation.

Disclosure of Interest: None Declared.

IHC-PO-190

Endothelial dysfunction in migraine patients

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Objective: Endothelial dysfunction is a diminished production or availability of nitric oxide metabolites. The aim of the study was to evaluate the endothelial dysfunction in migraine population analyzing nitric oxide metabolites.

Methods: The study sample consist of 75 migraine patients with and without ischemic events (cardiac and cerebral) collected from the stroke unit, cardiology department and headache center, divided in three groups: Gr. I (migraine with stroke) – 30 pts., Gr. II (migraine with myocardial infarction) – 30 pts. and Gr. III (migraine without ischemic event) – 15 pts. All patients have their diagnosis established by a specialist after the proper investigation and blood samples for nitric oxide metabolites. The data was analyzed using SPSS, v 23.

Results: S-nitrosothiols levels was $2.28 \pm 1.23 \mu\text{M/L}$ in migraine with stroke group, $2.64 \pm 1.03 \mu\text{M/L}$ and $3.08 \pm 1.35 \mu\text{M/L}$ in migraine without ischemic event group ($p=0.000$ I/II, II/III). Nitrate levels was $80.15 \pm 5.21 \mu\text{M/L}$ in migraine with stroke, $79.5 \pm 6.11 \mu\text{M/L}$ in migraine with myocardial infarction and $77.46 \pm 6.40 \mu\text{M/L}$ in migraine without ischemic event ($p > 0.005$). Nitrite levels was $22.45 \pm 10.64 \mu\text{M/L}$ in migraine with stroke group, $22.37 \pm 10.25 \mu\text{M/L}$ in migraine with myocardial infarction group and $26.02 \pm 17.20 \mu\text{M/L}$ in migraine without ischemic event group ($p > 0.005$). When patients stratified by the presence of aura the level of S-nitrosothiols was $2.83 \pm 1.54 \mu\text{M/L}$ with aura and $3.60 \pm 1.64 \mu\text{M/L}$ without aura ($p=0.005$), nitrate – $77.63 \pm 8.81 \mu\text{M/L}$ with aura vs. 80.18 ± 5.75 without aura ($p=0.026$), nitrite – $21.79 \pm 10.81 \mu\text{M/L}$ in migraine with aura vs. $22.97 \pm 13.91 \mu\text{M/L}$ in migraine without aura ($p > 0.005$).

Conclusion: The nitric oxide metabolites level was diminished in the migraine with stroke group, especially in

migraine with aura which could indicate the indirect sign of endothelial dysfunction in this subgroup of patients.

Disclosure of Interest: None Declared.

IHC-PO-191

Comparing postdromal and premonitory symptoms to self-reported triggers in spontaneous and nitroglycerin (NTG)-triggered migraine attacks

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Objective: The postdrome of migraine is generally under-researched. We aimed to study the effectiveness of NTG in triggering non-headache migraine symptoms. Spontaneous premonitory symptomatology was compared to self-reported triggers to determine if early premonitory symptoms may be misidentified as triggers.

Methods: Subjects ($n=53$) were screened, consented and recruited. Following a history of spontaneous attacks, including triggers, premonitory symptoms, headache characteristics, abortive medications and postdrome symptoms, each subject was exposed to either a 0.5 mcg/kg/min NTG infusion over 20 minutes or to placebo. Following the infusion, the timeline and phenotype to development of symptoms were documented. The migraine headache was treated with either 6 mg subcutaneous sumatriptan or 1 g intravenous aspirin, depending on usual response. The phenotype of any residual symptoms following effective headache resolution was documented. Agreement analysis (percentage agreement and Cohen's kappa) was performed between spontaneously reported and triggered postdrome symptoms, triggered premonitory and postdrome symptoms and between commonly reported triggers and corresponding premonitory symptoms. A percentage agreement of $\geq 60\%$, or Cohen's kappa ≥ 0.4 , or both, was considered positive.

Results: There was generally good agreement between the phenotype of the postdrome between spontaneous and triggered attacks (51–100%) and between the triggered premonitory and postdrome symptoms (49–94%). The following trigger-premonitory symptom associations showed good agreement; physical exertion and movement sensitivity; relaxation from stress and premonitory elation;

skipping meals and hunger; nausea and GI discomfort; bright light and photophobia; and loud sounds and phonophobia.

Conclusion: The agreement between the phenotype of the premonitory phase and the postdrome suggest that some of these symptoms may represent a continuum during the attack, and that these phases may be biologically linked. Consistent with evolving literature, at least some of what patients perceive as migraine triggers are likely to be early manifestations of the premonitory phase.

Disclosure of Interests: Dr Karsan was funded by an Association of British Neurologists and Guarantors of Brain Clinical Research Training Fellowship for the duration of this research. The remaining authors have no conflicts of interest related to this work.

IHC-PO-192

Evaluation of the 6-Item Identify Chronic Migraine (ID-CM) Screener in a Large Medical Group

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Objective: To assess the sensitivity and specificity of the 6-item Identify Chronic Migraine (ID-CM) screener.

Methods: Patients from a large medical group with at least 1 medical claim with an International Classification of Diseases 9th/10th revision (ICD-9/10) code for migraine in the 12-month prescreening period were enrolled. Those with an ICD-9/10 code for CM or a migraine-related onabotulinumtoxinA claim in the 12-month prescreening period were excluded. The 12-item ID-CM screener was administered by e-mail, in person, or over the telephone to all enrolled. The 12-item ID-CM screener is based primarily on 30-day patient recall and comprises questions assessing headache (HA) frequency, HA symptoms, medication use for HA, interference with activities due to HA, and planning disruption due to HA. The 6-item ID-CM screener, a subset of the 12-item version, includes only questions that assess HA frequency and

HA symptoms. Additionally, a Semi-Structured Diagnostic Interview (SSDI) was administered by telephone to a subset of eligible patients by a trained physician. The SSDI assesses HA symptoms, frequency, disability, and medication use based on 30- and 90-day patient recall and served as the study gold standard for determining CM status. The analysis excluded patients to whom the SSDI was not administered.

Results: The analysis included 109 patients with a migraine diagnosis who completed the ID-CM screener and the SSDI. The mean (SD) age of the patient sample was 48.7 (14.5) years; 91.7% were female. Using the SSDI as the diagnostic gold standard for CM, the 6-item ID-CM screener had a sensitivity of 70.8% (46/65) and a specificity of 93.2% (41/44).

Conclusion: Optimal treatment of CM requires accurate diagnosis. Based on the SSDI as the gold standard for CM diagnosis, the 6-item ID-CM screener demonstrated acceptable sensitivity and good specificity in determining CM status, supporting its real-world validity as a simple yet accurate tool to identify CM patients.

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Steve H. Kawahara, PharmD, in the past 12 months is a full-time employee of the DaVita Medical Group.

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Karen L. Campbell, PharmD, is a former employee of Allergan.

Riya Pulicharam, MD, in the past 12 months is a full-time employee of DaVita Medical Group.

Hema N. Viswanathan, BPharm, PhD, is an employee of Allergan and holds stock, stock options, and patent or other intellectual property in Allergan.

Richard B. Lipton, MD, serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to

Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS, serves as consultant, serves as advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Teva, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford Press University) and Informa. He holds stock options in eNeura Therapeutics and Biohaven.

IHC-PO-193

Forecasting Headache Using Bayesian Models

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Objective: Recently, a statistical forecasting model based on current stress was developed to forecast future headache attacks. Such a model could be used in a preemptive treatment paradigm where individuals could treat high-risk periods rather than waiting to abort an attack after pain is experienced. However, achieving successful preemptive treatment requires a forecasting model to accommodate a diverse range of individual differences in headache triggering processes. The objective of this study is to illustrate the value of Bayesian methods in creating forecasting models for individuals with headache.

Methods: Several philosophies of science can be employed to guide the nature of forecasting models. Summarized as *Frequentist* and *Bayesian*, these models espouse different approaches to forecasting based on their implications for what evidence should be used to generate a forecast, how probability should be interpreted, and how estimates for each model should be crafted. The Bayesian approach appears to have distinct advantages over the Frequentist approach when creating prospective predictions for individuals who have not previously been studied. Each approach was illustrated using the recently published HAPRED model where $N = 95$ participants contributed 4195 diary days. A model was created for each individual as though they were initiating a prospective diary study, and the discrimination, calibration, and resolution of forecasts were compared.

Results: Participants experienced a headache attack on 1613/4195 days (38.5%). The Bayesian approach, which estimated prior probabilities of the model parameters using data from the other individuals in the sample, exhibited superior discrimination ($AUC_{\text{Bayesian}} > AUC_{\text{Frequentist}}$) and calibration of predictions compared to the Frequentist

approach. The Bayesian approach allowed better than chance prediction (e.g., $AUCs > 0.60$) during the first week of diaries and exhibited evidence of statistical learning (i.e., each model adapted to the individual under study). As data accumulated, the group-level performance of both models approached equivalent discrimination and calibration.

Conclusion: The use of Bayesian forecasting methods increases the potential of headache forecasting models to allow preemptive treatment through adaptive learning capabilities and allows the models to be used without substantial "warm-up" periods.

Disclosure of Interest: None Declared.

IHC-PO-429

Long lasting persistent visual aura without infarction: an uncommon complication of migraine with aura

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Objective: About 30% of Migraine have Migraine with aura (MA), characterized by migraine attacks preceded by transient focal neurological symptoms, mostly visual, lasting between 5–60 minutes. 17% of these patients can have prolonged aura (PA), with aura lasting more than 60 min and less than a week. Neurological symptoms related to aura lasting more than a week are scarce with normal neuroimaging findings.

Methods: Clinical case report.

Results: A 32-year-old healthy woman, without personal or family history of migraine, started three months ago with a history of episodic throbbing orbital left headache of high intensity with continuous visual symptoms characterized by variable degree of blurring central vision, sometimes scintillating, associated with superior left quadrantanopsia. There were no abnormal findings on neurological and ophthalmological examination, including visual acuity, color vision, field of vision and ophthalmoscopy.

We performed as complementary studies: blood test (including autoimmunity, coagulation and serologies), cerebrospinal fluid analysis, visual cortical evoked potentials, optical coherence tomography (OCT), doppler ultrasonography of intracranial and extracranial arteries, brain computed tomography and conventional brain MRI, that were all normal.

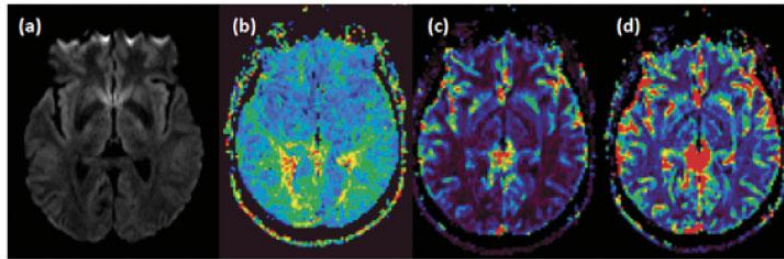


Figure 1: MRI study of the patient with persistent aura without infarction. (a) Diffusion Weighted Imaging (DWI) without acute brain ischemia (b) MTT: increase of occipital mean transit time (MTT) in occipital lobes, more in right lobe. (c) CBF (cerebral blood flow): hypoperfusion in right occipital lobe. (d) CBV (cerebral blood volume): without abnormalities.

Abstract number: IHC-PO-429

Twelve weeks after the symptoms started, we performed a brain perfusion study including DWI and perfusion sequences T2 using a 3T MRI, which showed a decreased perfusion in right occipital lobe without evidence of infarction (figure 1).

The patient was initially treated with valproic acid and prednisone in descending doses, without improvement. After that, we started lamotrigine 25 mg/day in ascending dose, with good response.

Conclusion: Persistent aura without infarction is very rare condition coded I.4.2 in the IHC III and described as aura symptoms persisting for one week or more without evidence of infarction on neuroimaging. They are often bilateral and may last for months or years. Pathophysiology is not yet well established but seems related to spreading cortical depression. There is so much to learn yet about this astonishing disease that could give us some new keys to unmask the pathophysiology of auras.

Disclosure of Interest: None Declared.

IHC-PO-430

Anti-GQ1b antibody syndrome with a 4-month history of ocular pain: a case report

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Objective: Anti-GQ1b antibody syndrome constitutes Miller Fisher syndrome, Bickerstaff's brain stem encephalitis and acute ophthalmoparesis. We here report a patient with acute ophthalmoparesis presenting with a 4-month history of intermittent ocular pain which preceded the onset of diplopia and photophobia.

Methods: Case report.

Results: A 50-year-old man noticed intermittent ocular pain, when the patient pressed on the eyeballs with the fingers through the closed eyelids. Four months later, he developed photophobia, diplopia and ocular pain when he moved his eyes. No antecedent infection was reported. He had normal visual acuity, but showed bilateral midriasis. Extraocular movement examination revealed bilateral limitation of abduction. There was no motor weakness, sensory impairment or cerebellar ataxia. Tendon reflex was preserved. Brain magnetic resonance imaging was unremarkable. Cerebrospinal fluid testing showed albuminocytologic dissociation. Anti-acetylcholine receptor antibody, anti-thyroid peroxidase antibody and anti-nuclear antibody were all negative. Intravenous methylprednisolone 1000 mg/day for 3 days, followed by oral prednisolone taper, led significant improvement of his eye symptoms. The patient was diagnosed with acute ophthalmoparesis variant of anti-GQ1b antibody syndrome, according to the results of anti-ganglioside antibody testing.

Conclusion: We should be aware that mild ocular pain can be preceding symptoms for anti-GQ1b antibody syndrome.

Disclosure of Interest: None Declared.

IHC-PO-431

Danish Knowledge Center for Headache – getting headache right

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Objective: Migraine is a major public health problem. In Denmark more than 700.000 people suffer from migraine or frequent headaches. Headache is primarily diagnosed and treated in primary care, and the accessibility to

specialized treatment is limited. To overcome this, the Danish Knowledge Center for Headache was established in 2018.

Methods: The Danish Knowledge Center for Headache collects and shares evidence-based knowledge to health-care professionals, people suffering from headache, their relatives and the public.

Surveys among health professionals will gauge knowledge levels and gaps in headache care. This will contribute to the continuous development and planning of country-wide courses. Enabling primary and secondary healthcare providers will lead to faster and more accurate diagnoses and treatment for headache disorders. The center collaborates with different stakeholders e.g. patient organizations, Danish health authorities, research units and others. The center also works actively to get headache in the media and on the political agenda.

Results: The website of the Danish Knowledge Center for Headache functions as a knowledge bank with evidence-based and updated information on headache, diagnoses, treatment, fact sheets for printing, ongoing research and more. Several projects have been initiated: 1) Treatment of medication overuse headache in primary and secondary care – implementation of an effective, systematic and validated approach for treatment. 2) Headache ABC – development of a simple tool to support diagnostics and treatment. 3) Headache and health economics – estimation of the health economic impact of headaches. 4) Workplace environment and headache – investigation of workplace and the employee challenges. 5) Headache panel – involvement of patients and relatives. The Center works actively to establish a headache treatment database to monitor and improve quality of headache diagnoses and care.

Conclusion: The knowledge center is an addition to the headache field and works to disseminate evidence-based knowledge on headache diagnoses and care to health care providers and the public.

Disclosure of Interest: None Declared.

IHC-PO-432

Intravenous Fosphenytoin as rescue treatment in Trigeminal Neuralgia crisis

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Objective: Trigeminal Neuralgia (TN) is a common cause of facial pain. Its treatment relies on preventive therapy with either carbamazepine or oxcarbazepine. During a severe pain episode patients are unable to eat, drink or continue with oral medication, requiring in-hospital treatment. There is scarce evidence based support for

intravenous (iv) medications for TN, hindering the management of these situations.

The aim of this study is to analyze the response to iv fosphenytoin in TN crisis in order to gather evidence for its use in daily neurological practice.

Methods: A retrospective review was carried out from clinical records of patients with TN crisis, who attended the emergency department in a referral tertiary neurological center in Buenos Aires, Argentina, and received iv fosphenytoin as analgesic strategy; having being followed-up for at least one month afterwards. Patients were diagnosed of TN and classified according to ICHD-3 diagnostic criteria. Response to treatment was considered when a 50% or more decrease of pain was achieved, considering failure when this goal was not achieved or required another analgesic to do so. Demographic features, magnetic resonance imaging (MRI) and emergency room pharmacological management were analyzed.

Results: Thirty-nine patients with TN crisis were included. Eighteen of the subjects received i.v. fosphenytoin applications more than once (separated by at least 24 hs), reaching a total of 65 infusions.

Of the 65 infusions, 58 (89.07%) achieved control of the pain, while 7 (10.93%) failed to i.v. phenytoin requiring in most cases opium derivative or non steroidal anti-inflammatory drugs as rescue treatment. Furthermore, alongside with preventive therapy adjustments, individualized attendance to the emergency service decreased after each infusion in 63% episodes.

Adverse effects were seen in 10 (15%) of the 65 infusions. Nystagmus, dizziness, ataxia, dysarthria, hypotension and sleepiness were among the most frequent side effects.

Conclusion: According to our results, iv fosphenytoin may be a safe and useful strategy for TN crisis, considering the lack of treatment choices for these situations. Nonetheless a prospective placebo controlled study is needed to make a valid statement.

Disclosure of Interest: None Declared.

IHC-PO-433

Chocolate as a Risk Factor for Migraine Attacks

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Objective: Chocolate is considered as a trigger of migraine attack in migraine headache patients. The aim

of our study was to reveal if chocolate can trigger migraine.

Methods: Totally 80 non-chronic migraine patients, 32 male, 48 female, aged 18 to 55 have been investigated. The patients confirmed to take 50 mg. chocolate daily during 3 months and not to take any mg. of chocolate following 3 months. All patients completed headache diary during overall 6 months.

Results: In the first 3 months patients showed migraine attacks on average 6,4 days per months with mean duration of 9,2 hours. The mean intensity of pain on scale (from 0 to 10 – maximal intensity of pain) was 4,1.

During the next 3 months there were migraine attacks on average 5,8 days per months, mean duration was 7,8 hours. The mean intensity of pain on scale (from 0 to 10 – maximal intensity of pain) was 4,3.

Conclusion: In our study we found migraine attacks average frequency was more and mean duration was increased in the first 3 months when patients received chocolate compared to the next 3 months without chocolate. Chocolate is generally considered to be a trigger of migraine attacks. Our study confirms the general view.

Disclosure of Interest: None Declared.

IHC-PO-434

Migraine Headache: Network Analysis Overview of Publications Study

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Objective: Researchers from different fields and various communities performed a lot of studies related to Migraine headache. Considering a large number of works, some approaches are needed for scientists who try to find out how significant a particular article is.

We apply recently developed models of network analysis for publications in the fields of Migraine headache to reveal the links between research clusters, rank their importance and track changes of scientific groups attention to, for instance, previously unknown studies and developments.

Methods: One of the applied approaches is citation analysis which is the study of the impact and assumed quality of an article, an author, or an institution based on the number of times works and/or authors have been cited by others.

The presented models of network analysis of publications on various aspects of Migraine headache allow to reveal the links between research clusters, rank its importance and track changes.

WOS Key Categories of Migraine headache related articles	Number (in thousand)
Clinical Neurology	23.9
Neurosciences	13.4
Medicine General Internal	3.7
Pharmacology & Pharmacy	2.7
Psychiatry	2.0
Pediatrics	1.2
Anesthesiology	0.87
Surgery	0.81
Medicine Research Experimental	0.68

Abstract number: IHC-PO-434

Recently developed network analysis algorithms including new centrality indices have been applied for publications databases on different aspects of Migraine. Articles with keywords “Migraine” were analyzed. Data were taken from Web of Science (WOS) publications database and consist of more than 40,000 articles dated from 1980 to 2017.

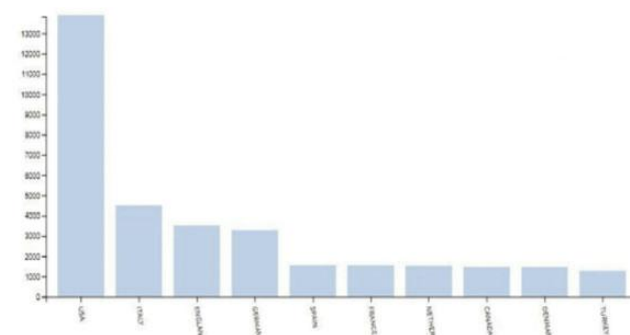


Figure 1: Number of Migraine headache related articles by Region/Country

Abstract number: IHC-PO-434

Results: Networks of publications are modeled as graphs, where the nodes are identification numbers and the edges of the graph carry the information about the citations between them.

Table I shows Categories of Migraine headache related articles.

Figure I is a Bar Chart showing Top TEN countries in Migraine headache related articles.

1. 135 × –2017 publication dates of analyzed articles.
2. Average citation per item: 18.83, while Sum of times cited: >50,000.

3. ~43 thousand articles in WOS related to Migraine headache²15.

4. 2499 articles in 2017.

5. Document types related to Migraine headache:

- 24530 articles.

- 3783 reviews.

- 7695 Meeting Abstracts.

TOP-3 most cited papers:

1. MOSKOWITZ, 1992: Neurogenic Versus Vascular Mechanisms of Sumatriptan And Ergot Alkaloids in Migraine.

2. Tfelt-Hansen et al., 2000: Triptans in migraine – A comparative review of pharmacology, pharmacokinetics and efficacy.

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Conclusion: This overview analysis showed the significance, impact and quality of migraine headache articles, authors, or institutions based on the number of citations.

Disclosure of Interests: No funding was received by the author to carry out the present study.

The Author have no conflict of interest to declare.

Other Primary Headache Disorders

IHC-PO-194

Favourable prognosis of trigeminal neuralgia when enrolled in a multidisciplinary management program – a two-year prospective real-life study

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Objective: Prognosis of medically treated trigeminal neuralgia patients is assumed to be poor, but the evidence is lacking. The objective was to provide evidence concerning the real-life efficacy of medical management of TN when directed by specialists. Additionally, to inspire other TN treatment centres to develop specific TN management programs to ensure best possible care for this patient group.

Methods: This was an observational study. Patients were consecutively enrolled in a structured management program at a specialist centre for facial pain. Optimisation of medical treatment, physiotherapy, psychotherapy, and advice from trained nurses, were parts of the program. Medically intractable patients were referred for

neurosurgery. Data-collection was prospective using standardised schemes and patient surveys. The aim was to describe the two-year outcome of medical treatment at the specialist centre. The primary outcome was a 50% reduction in the overall burden of pain according to a Numerical Rating Scale (NRS) after two years.

Results: A total of 186 primary TN patients were enrolled in the program of which 103 patients remained medically managed and completed the two-year follow-up. Fifty patients were treated surgically within the first two years of follow-up. Half of the medically managed patients (53 (51%)), had more than a 50% reduction in the overall burden of pain over the two-year period. The overall burden of pain on NRS decreased from mean 5.34 to 3.00, $p < 0.01$. There was no significant association between primary outcome and sex, depression and/or anxiety, concomitant persistent pain, or neurovascular contact with morphological changes of the trigeminal nerve.

Conclusion: Patients with trigeminal neuralgia improve over a two-year period when enrolled in a structured medical management program. Optimisation of drug treatment, continuous advice and education and support by the multidisciplinary team, referral of the medically intractable patients for surgery or the natural history of the disease, can be some of the reasons for the improvement. The favourable prognosis provides hope and optimism for medically managed TN patients.

Disclosure of Interest: None Declared.

IHC-PO-195

Headache in the past history in patients with cervical artery dissection (Pathogenetic mechanisms)

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Objective: Background. Spontaneous cervical artery dissection (CeAD) is the most frequent cause of ischemic stroke (IS) in young adults. According to morphological data arterial wall dysplasia is the main factor predisposing to dissection. 30–60% CeAD patients have headache in the past history (HPH), which is usually classified as migraine. It occurs more frequently in CeAD patients than in patients with IS of other causes that suggests non-accidental association between dissection and HPH.

The aim of the study is to evaluate electrophysiological characteristics of HPH in CeAD patients and compare them with migraine.

Methods: We studied 35 CeAD patients (mean age $36,8 \pm 6,5$; 30 females, 86%) and 35 patients with migraine (mean age $32,3 \pm 8,9$; 26 females, 74%). In 15 CeAD patients (43%) HPH met the International Criteria for

migraine (with aura – 2 (6%), without aura – 13 (37%)), in 20 patients (57%) HPH did not meet them (non-migraine headache). All patients underwent EEG and visual evoked potentials (VEP).

Results: The visual EEG analysis less often found rhythmic disorganization in CeAD patients with HPH than in migraine. The hyperventilation caused a slight increase in the spectral power of Teta, Delta waves in CeAD patients and significant enhancement in the occipital and frontal parts of the brain in migraine ($p < 0.05$). Pattern reversal VEP had a greater latency and smaller amplitude of cortical responses in CeAD patients in comparison with migraine patients ($p = 0.028$ and $=0.037$, respectively). The flash VEP amplitude was lower in CeAD patients than in migraine ($p = 0.01$).

Conclusion: Central mechanisms, namely, the hypersensitivity of the cerebral cortex playing the main role in migraine pathogenesis, are not significant in genesis of HPH in many CeAD patients. The main role appears to have peripheral mechanisms – dysplastic changes in the wall of extra-intracranial arteries that predispose both to headache and dissection.

Disclosure of Interest: None Declared.

IHC-PO-196

Pilot study of injection of onabotulinumtoxinA towards the sphenopalatine ganglion for the treatment of classical trigeminal neuralgia

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Objective: To investigate the safety of injecting onabotulinumtoxinA (BTA) towards the SPG using the MultiGuide[®] in 10 patients with refractory classical TN, and collect preliminary efficacy data. The SPG has previously been targeted in trigeminal neuralgia (TN), but its role in this condition has not been established.

Methods: 25 international units (IU) of BTA were injected towards the SPG in a prospective, open-label study in 10 patients with refractory classical TN. Primary outcome: adverse events (AEs). Primary efficacy outcome: number of TN attacks at weeks 5–8 after injection compared to baseline. A treatment responder was predefined as at least 50% reduction in the median number of attacks per day between baseline and weeks 5–8. Other efficacy outcomes were intensity of attacks (numeric rating scale, 0 to 10) and functional level (1 to 4; 1 best and 4 worst) at weeks 5–8 after injection compared to baseline. Percentage of the

day with concomitant persistent pain was registered at baseline and at weeks 1–4, 6, 8 and 12 after injection.

Results: For the primary endpoint we analyzed data for all 10 patients. For efficacy outcomes we analyzed data for 9 patients (one patient violated protocol). We registered 13 AEs, none of which were serious. The median number of TN attacks during the 4-week baseline and weeks 5–8 after injection was 5.5 (range: 1.0–51.5) and 5 (range: 0–225.0) respectively ($p = 0.401$). Four patients were treatment responders. The median intensity of attacks at baseline and weeks 5–8 after injection was 6 (range: 3.0–8.5) and 3 (range: 0.0–9.0) respectively ($p = 0.024$). The median functional level at baseline was 2 (range: 1.0–3.3) and at month two, 1 (range 1.0–4.0; $p = 0.750$). Median percentage of the day with concomitant persistent pain was 75% (minimum 37.5%, maximum 100%) at baseline and 18.75% (minimum 0%, maximum 100%) at week 8 ($p = 0.023$).

Conclusion: Injection of BTA towards the SPG using the MultiGuide[®] in patients with TN appears to be safe and well tolerated. This study was negative for the main efficacy endpoint (reduction in the number of attacks from baseline to weeks 5–8). Further studies examining the role of the SPG in TN are necessary.

Disclosure of Interest: None Declared.

IHC-PO-197

DESCRIPTIVE ANALYSIS OF A SERIES OF 19 PATIENTS WITH HYPNIC HEADACHE (HC) IN A THIRD LEVEL HOSPITAL

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Objective: To describe the clinical characteristics, the adaptation to the diagnostic criteria and the response to treatments of patients diagnosed with hypnic headache.

Methods: A review of cases of hypnic headaches selected retrospectively between 2010 and 2017 in a tertiary hospital is presented.

Results: We included 19 patients diagnosed with CH from a total of 1600 patients reviewed in said period. 16 (84%) were women. The mean age at onset of the disease was 62 years (SD: 11.23, range 31–78 years). 6 (31%) patients described pain as oppressive, 7 (37%) stabbing and 6 (31%) pulsating. In 37%, headache was bilateral, 42% unilateral and 21% frontal. 100% of patients had headache during sleep. The average onset after sleep was 166 minutes (range: 15–360). The average number of days per month was 19 (range: 3–30). 42% presented headache less than 15 days a month. A single patient presented autonomic symptoms. 4 (21%) patients presented phonophobia, 1 (5%) photophobia and phonophobia. 55% had a good

response to indomethacin. 58% had tried 3 or more drugs, the most effective being amitriptyline, flunarizine and indomethacin. 9 (47%) patients also had another primary headache. 5 (26%) patients did not fully meet the diagnostic criteria of ICHD-3.

Conclusion: Hypnic headache is a rare primary headache, characterized by presenting during sleep and waking the patient. Its diagnosis is clinical. The characteristics of our series overlap with others published in the literature. A greater knowledge about the pathophysiology of this type of headache is necessary to find effective treatments.

Disclosure of Interest: None Declared.

IHC-PO-198

Carcinomatous Meningitis: Chameleon of the Meninges

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Objective: Carcinomatous meningitis (CM) is a rare but devastating complication of malignancies. Circulating tumour cells (CTCs) enter the cerebral spinal fluid (CSF) and deposit in the leptomeninges. Presentation is varied with a constellation of cerebral dysfunction, cranial and/or spinal neuropathies. Headache is the most common symptom (up to 75% of cases), followed by mental status changes, nausea, diplopia and paraesthesias. CM occurs in 5% of solid tumours, rising to 20% on autopsy. Breast (12–35%), lung (10–26%) and melanoma (5–25%) are frequently implicated malignancies. We will discuss two cases of CM and a review of the topic.

Methods: Two cases of CM presented to the Mercy University Hospital in 2018. We conducted chart reviews as well as a review of the topic.

Results: Mrs ES was a 75 year old lady with a previous history of breast carcinoma. She presented with a month of blurred vision, gait disturbance and severe headaches. She then developed dysarthria and ataxia. MRI brain with Gadolinium did not demonstrate leptomeningeal involvement. Her CSF was lymphocytic, had low glucose, high protein and CTCs. Symptom palliation was the main focus of her management and she died within 3 weeks.

Our second case is that of Mrs MD, a 51 year old lady who presented with severe headaches, multiple cranial neuropathies and a previous ENT malignancy. MRI with Gadolinium did not show leptomeningeal changes. Her first CSF was positive for Human Herpes Virus 6. A

second CSF was lymphocytic, had low glucose, high protein and contained CTCs. She did not respond to antiviral therapy. Mrs MD had an Ommaya shunt inserted and underwent intrathecal chemotherapy but died 6 weeks later.

Conclusion: CM should be suspected in patients with an oncology history demonstrating multifocal neurological signs and symptoms. Headache is the most common symptom and is often severe. The road to securing a diagnosis is challenging. Radiology and CSF can be negative initially. Treatment is directed at raised intracranial pressures, radiation therapy, intrathecal/ systemic chemotherapy and symptom palliation. Prognosis is guarded with an overall survival of 12–16 weeks.

Disclosure of Interest: None Declared.

IHC-PO-435

Reversible Cerebral Vasoconstriction Syndrome (RCVS) presenting with Cluster-like headaches triggered by sexual intercourse

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Objective: 32 year old male presented to emergency department with post intercourse headaches. He reported three stereotypical episodes over the last week immediately after sexual intercourse. The onset was hyper-acute (thunderclap) reaching its peak in less than 5 minutes. The pain started in the left occipital region and moved over to the left orbit, was excruciating in intensity (10/10) and accompanied by a full spectrum of autonomic symptoms i.e. conjunctival tearing, lacrimation, rhinorrhea and ptosis. Each episode lasted 30 minutes during which patients was extremely restless and experienced nausea, photo and phonophobia. Examination was normal. He was given simple analgesics and oral sumatriptan with no improvement in the first two episodes. A diagnosis of cluster headache was made and was given high flow oxygen and subcutaneous sumatriptan to which he responded well.

Methods: N/A.

Results: Routine bloods including inflammatory markers were normal. CT scan was normal. MRI /MRA brain showed variable caliber of both posterior cerebral arteries, irregular narrower segment of right vertebral artery intracranially. Appearances were in keeping with arterial spasm or vasculitis within the posterior circulation. No aneurysms were identified. CSF examination was refused by patient. A diagnosis of RCVS was made that presented with cluster-like episodes triggered by sexual intercourse. The patient was discharged with sumatriptan injections for subsequent attacks. A repeat MRI/MRA in three months shows complete resolution of radiological findings.

Conclusion: We report a case of RCVS presenting as cluster-like episodes triggered by sexual intercourse. Cluster-like headaches have been previously reported but to our knowledge sexual intercourse has not been previously reported as a trigger. The absence of systemic symptoms, normal inflammatory markers and absence of T2/Flair lesions on MR brain imaging was against the diagnosis of primary or secondary angiitis of the CNS and a complete resolution of MRA abnormalities on repeat scanning without immunosuppression supported the clinical diagnosis of RCVS.

Disclosure of Interest: None Declared.

IHC-PO-436

Body temperature fluctuation in intraoral cold stimulation

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Objective: Headaches caused by cold stimulation, previously known as “ice cream headaches,” are classified into those attributed to the external application of a cold stimulus and those attributed to ingestion or inhalation of a cold stimulus. Although empirical data is available regarding the symptoms of ice cream headaches, there is a scarcity of research.

Methods: We administered a several-item questionnaire to 127 people (68 men and 59 women, aged 19–22 years), including migraine and non-migraine sufferers, to assess the characteristics of ice cream headaches and review the participants’ headache history. After obtaining informed consent from the participants, cold stimulation was applied to their oral cavity using ice scrapings, and temperature fluctuation in the oral cavity and neck skin surface was monitored using a digital thermometer (thermophrases[®]). During cold stimulation, the participants were asked to raise their hands at the onset of headache began and to lower them when the headache disappeared and were asked to measure the duration of ice cream headaches.

Results: Of the study participants, 11% suffered from migraines (2% men; 9% women) and 51% had experienced ice cream headaches in the past. Furthermore, 64% participants experienced ice cream headaches and were migraine sufferers as well, and the remaining experienced ice cream headaches but were not migraine sufferers. A decrease of approximately 2.59°C in the intraoral temperature and an average increase of 0.31°C in the neck

skin surface temperature was observed in seven of the eight subjects who received the intraoral cold stimulus.

Conclusion: Our results suggest that participants with a history of migraine are more likely to develop headaches due to cold stimulation. Furthermore, we observed an increase in the temperature of the neck skin surface at the onset of the ice cream headaches. We intend to build on these findings by performing a literature review and investigating a larger study population in the future.

Disclosure of Interest: None Declared.

IHC-PO-437

Chronic Headache Pain related to Spontaneous Internal Carotid Dissection in Adult Patients

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Objective: Aim To describe signs and features of chronic headache after spontaneous internal carotid artery dissection (SICAD).

Methods: Defining a new chronic headache by using current criteria.

Results: 8 patients (4 males, 4 females; mean age 33.14 ± 3.2SD gave their informed consent.

Right Side SICAD n = 2 2 males, Left Side n = 4 2 males, 2 females, Bilateral n = 2 1 male, 1 female.

Computed Tomography Angiography n = 8 Intramural hematoma partial thrombosis MRI, Magnetic Resonance Angiography: 2, 30, 90 days and yearly after SICAD n = 8 Intramural hematoma and thrombosis resolution in 3 months, Ischemic areas n = 6, small ischemic areas: n = 4 1 year after, n = 2 2 years after SICAD;.

MRI diffusion 3 months and 1 year after SICAD n = 8 abnormal metabolism in infarct areas.

Subjective noise/bruit ears n = 7 onset of SICAD.

Subjective noise/bruit whole head n = 2 onset of SICAD, n = 6 episodic month 3.

Pain head n = 8 onset of SICAD till last observation. (0–10)8.9 ± 4.1SD, constrictive, throbbing; Pain neck n = 4 onset of SICAD resolution in 2.5 months ± 1.2SD, 0–10 2.3 ± 1.9SD.

Headache Disability Inventory -range 90–100 n = 8.

Horner’s Syndrome-Assessment of Pupillary Asymmetry, Response to Bright Reflex n = 2, moderate.

Asthenia n = 8 from month 7 Pichot Brown test range 20–24, 6 chronic 2 episodic.

Altered Equilibrium n = 8 from month 3 Romberger’s test positive.

Nitroglycerin 0,3 mg/sublingual n=8 (VAS 0–10) $3.9 \pm 4.3SD$ vs $3.8 \pm 6.2SD$ NS.

Allodynia Checklist n=8 (ASC12) $2.3 \pm 0.9SD$ NS; Hyperalgesia by stretching vein wall as elsewhere described n=8 VAS 0–10 $0.1 \pm 2.2 SD$ NS.

Tiggers in neck /neck movents triggering n=8 None.

Dysethasia–head & widespread in the body n=8 episodic.

Paresthesia limbs n=8, subchronic.

Inefficacy of FANs and Corticosteroids n=8.

Topiramate 0% Amytriptilyne 10,5% relief vs baseline n=8.

Free Testosterone reduction in males from month 6 $14.11 \text{ pg/mL} \pm 3.1SD$ NS lower cortisol level ($95.6 \pm 7.8SD \text{ microg/L}$) from month 6 n=8 Family history primary pain n=0 Family history cerebrovascular problems n=8 Personal history headache n=8 less then 1 migraine attack/month.

Perceived stress month before SICAD n=8 (range 18–19).

Conclusion: It is not possible to roule out a pivotal role of stress in chronification of SICAD-related headache. The headache is disablinhg ad seemigly has no features of either migraine or tension-type headache.

Disclosure of Interest: None Declared.

IHC-PO-438

Refractory Headache Diagnosis and Management

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Objective: The definition of refractory headache(RH), is still not clearly described.

Methods: I searched MEDLINE,ScienceDirect and used the latest IHS guideline and reported my personal experiences with more than 30,000headache patients.

Results: There are different causes that make a headache refractory.

I. First, misdiagnosed cases due to of different reasons:.

A-When a physician cannot get an accurate history. One of the causes of misdiagnosis is medication overuse headache (MOH) which is sometimes ignored by physicians.

B-When a physician ignores the previous history of headache in the patient. For example in chronic migraine headache the history of episodic migraine with gradual accentuation is necessary but sometimes the patients give the history of their recent chronic headache and taking the history of their previous episodic headaches is very difficult and needs more attention.

C-When a physician does not consider the probability of secondary headaches including cervicogenic headaches,SIH,IIH without papilledema, oral, nasal or temporomandibular joint disorders.

2. Improper treatment: It is very important to titrate prescribed medications to the maximum tolerable dosage and wait for at least two months for propper response. Concurrent analgesic overuse is also common among RH subjects and might cause prophylactic treatment ineffective,.

3. Presence of comorbidities: Psychiatric disorders, particularly in adolescent patients should be treated with high accuracy.

4. Drugs that a patient consumes for the other diseases could also be a reason for susceptibility to RH.

5. Ignoring other modalities of treatment: Nerve or ganglion blocks, neurostimulations and surgeries could be promising in the management of difficult to treat patients.

6. Real refractory cases are present but are not as numerous as physicians think. Chronic migraines, chronic clusters, other TACs, and different types of neuralgias might be refractory.

Conclusion: In RH cases with poor response to outpatient therapy, or unsuccessful outpatient detoxification for overuse of specific medications, or those with severe psychiatric comorbidities, inpatient management should be considered and should include controlling patient's pain, discontinuing offending drugs in the case of MOH, medical or psychiatric consults and initiating the suitable prophylactic therapy.

Disclosure of Interest: None Declared.

Other Secondary Headache Disorders

IHC-PO-199

Grey and White Matter Changes in Spontaneous Intracranial Hypotension

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Objective: This study aimed to map the regional brain volume changes in spontaneous intracranial hypotension (SIH) and to propose underlying mechanisms behind the changes.

Methods: We retrospectively reviewed the brain MRI findings as well as demographics and clinical profiles of consecutive patients with SIH in Taipei Veterans General Hospital. The follow-up neuroimaging studies were performed within three years after recovery. Voxel-based morphometry were used to examine the brain volume changes during and after resolution of SIH. The brain structure volume was analyzed using Statistical Parametric Mapping v12.0 and FMRIB Software Library v6.0. The brain MRI signs used to correlate the brain volume changes were transverse sinus angle and mid-brain-pons angle.

Results: Between January 2007 and July 2015, 188 consecutive patients with SIH were recruited. Of them, 61 had qualified initial and follow-up neuroimaging studies. Compared to follow-up neuroimages, patients during SIH showed decreased grey matter (GM) volume (766.7 vs. 798.2 mL, $p < 0.001$), increased white matter (WM) volume (419.1 vs. 399.6 mL, $p = 0.013$), decreased ventricular cerebrospinal fluid (CSF) volume (16.3 vs. 21.5 mL, $p < 0.001$), decreased midbrain-pons angle (38.0° vs. 56.3° , $p < 0.001$), and dilated transverse sinus (71.6° vs. 54.6° , $p < 0.001$). The reduction of GM volume was widely distributed, especially in bilateral inferior frontal gyrus and interhemispheric cortices. Conversely, the GM volume in cerebellum was increased. The change of ventricular CSF volume correlated with change of the midbrain-pons angle ($r = 0.30$, $p = 0.018$), but not that of the transverse sinus angle ($r = 0.01$, $p = 0.946$).

Conclusion: This study suggests that the GM and WM volumes may change in patients with SIH, which is contrary to the Monro-Kellie doctrine, i.e. brain parenchyma volume remains constant in spite of CSF volume change. We hypothesize that CSF volume depletion in SIH may result in disturbance of water content within brain parenchyma; however, further investigation of the underlying mechanisms is needed.

Disclosure of Interest: None Declared.

IHC-PO-200

Spontaneous Intracranial Hypotension (SIH) Secondary to CSF Venous Fistula: Case Series

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Objective: CSF venous fistulas have only recently been described as a distinct cause of SIH. We aim to describe the clinical presentation, imaging, treatment, and outcome of 47 cases of SIH secondary to CSF venous fistula.

Methods: Case series report. Retrospective review of charts from 1994–2019 with SIH secondary to CSF

venous fistula confirmed by neuroimaging or intraoperatively. Cases with an undetermined etiology of SIH, an alternative etiology, or a possible but unconfirmed fistula were excluded.

Results: Of 156 patients reviewed, 47 met criteria (14 men, 33 women). Mean age of symptom onset was 49 years (range 33–71 years). Fifty-one percent of patients had no prior headache history. All but 2 patients had an associated headache. Headaches were daily (71%), and most commonly occipital and suboccipital. The most common characterization of headache was pressure. Thirty-one patients (69%) had an orthostatic component to their pain. Interestingly, 80% reported Valsalva-induced exacerbation of their pain, 11% of these patients experienced pain isolated to Valsalva behaviors. Eighty-five percent of patients reported associated symptoms, the most common being cognitive changes and tinnitus. Out of 37 patients with documented opening pressure, 13% had pressure < 6 cm H₂O. Eight patients had a normal MRI scan at some point during the course of their illness. Diagnosis was most commonly made by digital subtraction or positive pressure myelogram. fistulas were almost exclusively thoracic (96%). None of our patients responded definitively to epidural blood patch (EBP). Average time to surgery was 2.8 years, 45 patients underwent surgery. The majority of patients improved following surgery, 47% were completely headache free and 28% had at least 50% improvement.

Conclusion: This is the largest case series to date of SIH secondary to CSF venous fistula. Our results provide a better understanding of the typical presenting features in this condition, including frequent occurrence of Valsalva-induced pain and almost exclusive thoracic location of fistulas. In our experience, CSF venous fistulas appear largely unresponsive to EBP and surgical treatment may provide the best clinical outcome. More study is needed, but it may be reasonable to consider CSF venous fistula early in the differential diagnosis of Valsalva-induced headache.

Disclosure of Interest: None Declared.

IHC-PO-201

Detailed Intra-cranial Pressure Monitoring in Idiopathic Intracranial Hypertension probes Diurnal and Postural Variability

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Objective: The objectives of this study were to assess changes in Idiopathic Intracranial Hypertension (IIH) Intracranial Pressure (ICP) diurnally and with positioning.

Methods: Female participants were recruited with active IIH (>25 cmCSF lumbar puncture opening pressure and papilloedema) age between 18–60. Participants underwent implantation of a telemetric, intraparenchymal ICP monitor (Raumedic p-Tel, Helmbrechts, Germany) and ICP was recorded during a 24 hour visit and evaluated with changing position. 1 mmHg = 1.36 cm H₂O.

Results: 16 participants, mean age 29.5 ± 9.5 and BMI $38.1 \pm 6.2 \text{ kg/m}^2$, were recruited. During the 24-hour monitoring period there was no significant change during waking hours. During nocturnal recording (prolonged, continuous supine posture) ICP rose significantly (15.4–20.6 mmHg, 33.8% $p = 0.02$). During the day there was a significant rise in ICP if the patient had a prolonged supine recording: after 30 minutes (21.3–24.8 mmHg, 16.4%, $p = 0.0002$), and after 3 hrs (23.8–25.9 mmHg, 8.8%, $p = 0.04$).

Mean ICP was 21.2 mmHg (4.8) supine, 24.0 mmHg (3.8) left lateral (lumbar puncture position), 10.1 mmHg (5.1) sitting and 10.3 mmHg (3.7) standing. ICP was higher in the lumbar puncture position compared to supine (13% difference, $p = 0.028$), significantly higher supine compared to standing (51.3% difference, $p = 0.0001$), but no difference standing to sitting ($p = 0.82$).

Conclusion: Detailed ICP characterization in IIH has not been previously reported. We demonstrate that ICP does not vary diurnally but rises with time in the supine position. We confirm that ICP is higher in a lumbar puncture position compared to supine. The implications for clinical practice and research are that lumbar puncture diurnal timing is not relevant. It is only prolonged supine posture that causes ICP to rise and thus variability. Time in a supine position needs to be taken into account when interpreting ICP measures.

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IHC-PO-202

Evaluation of characteristics and associated features of Headache attributed to ischemic stroke

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Objective: To assess the frequency of headache attributed to ischemic stroke, the clinical characteristics of the headache attributed to ischemic stroke and the clinical characteristics of the patient or of the ischemic stroke which are associated with the occurrence of headache attributed to ischemic stroke.

Methods: Consecutive patients admitted within 72 hours of the onset of ischemic stroke symptoms were included. All of them underwent a diffusion-weighted magnetic resonance of the brain. All participants provided written informed consent, and the study protocol was approved by ethics committee of Universidade Federal de Pernambuco. The diagnosis of ischemic stroke was determined by the presence of restricted-diffusion patterns in a compatible clinical context. Patients were evaluated through a semi-structured questionnaire, the National Institutes of Health Stroke Scale and neuroimaging analysis.

Results: 154 patients were included, 41.6% were female and the mean age was 68.6 ± 13.3 years; 25.3% had previous migraine and 9.3%, tension-type headache. The median of the National Institutes of Health Stroke Scale at admission was 2. The most frequent determined etiologies were small vessel disease (27.3%) and cardioembolic stroke (26%). Headache attributed to ischemic stroke had a frequency of 20.1%. The most common characteristics of this headache were: onset of headache at the same time of focal neurologic deficit (45.2%), gradual development (77.4%), moderate intensity, a pulsating quality (41.9%) and with a unilateral location (58.1%), and a right side location (88.9%). The mean duration of pain was 39 ± 44 hours. The majority of patients presented with a “tension-type headache pattern” (58.1%). There was an association between the previous diagnosis of migraine and the occurrence of a “migrainous headache” during the acute ischemic stroke. The occurrence of headache attributed to ischemic stroke was significantly more frequent in patients aged less than 65 years (OR: 3.40; 1.31–8.79) and in those with previous tension-type headache (OR: 4.37; 1.14–16.7) (logistic regression).

Conclusion: Headache attributed to ischemic stroke is frequent, with a more habitual pattern similar to tension-type headache and is associated with age and a previous history of tension-type headache.

Disclosure of Interest: None Declared.

IHC-PO-203**A unique androgen excess signature in idiopathic intracranial hypertension is linked to cerebrospinal fluid dynamics**

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Objective: Idiopathic intracranial hypertension (IIH) is a chronic and disabling condition characterized by elevated intracranial pressure (ICP). IIH is overwhelmingly a disease of obese women of reproductive age, and endocrine disturbances have been hypothesized to play a pathogenic role. We aimed to delineate the androgen phenotype of women with active IIH and explore the potential role of androgens in disease pathogenesis.

Methods: In this study, we comprehensively examined the systemic and cerebrospinal fluid (CSF) androgen metabolome in women with IIH in comparison to sex-, body mass index- and age-matched control groups with either simple obesity and PCOS, i.e. obesity and androgen excess.

Results: IIH women showed a pattern of androgen excess distinct to that observed in PCOS and simple obesity, with increased serum testosterone, and increased CSF testosterone and androstenedione. Human choroid plexus expressed the androgen receptor, alongside the androgen-activating enzyme aldoketoreductase type 1C3. We show that in a rat choroid plexus cell line testosterone significantly enhanced the activity of Na⁺/K⁺ ATPase, a surrogate of CSF secretion.

Conclusion: We demonstrate that IIH patients have a unique signature of androgen excess and provide evidence that androgens can modulate CSF secretion via the

choroid plexus. These findings implicate androgen excess as a potential causal driver and therapeutic target in IIH.

Disclosure of Interest: None Declared.

IHC-PO-204**Temporal profile of blood-brain barrier breakdown in reversible cerebral vasoconstriction syndrome: a cross-sectional bi-center study**

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Objective: Reversible cerebral vasoconstriction syndrome (RCVS) is an important cause of thunderclap headache, which can lead to severe neurological complications. Recently, we documented a high prevalence and diagnostic role of blood-brain barrier (BBB) breakdown in patients with RCVS. In the present study, we aimed to evaluate the temporal profile of BBB breakdown and factors affecting the extent of BBB breakdown using a quantitative imaging analysis method.

Methods: We collected MRI data of patients with RCVS from Samsung Medical Center and Taipei Veterans General Hospital. Patients who underwent contrast-enhanced FLAIR MR imaging within two months from onset were included for this study. BBB breakdown was defined as CSF hyperintense signal in the contrast-enhanced FLAIR MRI. The presence and extent of BBB breakdown was evaluated according to time from onset. The univariable and multivariable linear regressions were performed to find independent effect of time from onset with adjustment for covariates with univariable $p < 0.2$.

Results: Of 251 patients with RCVS, the prevalence of BBB breakdown was about 50% in the first two weeks, then decreased but remained above 20% after 3rd week. The mean extent of BBB breakdown was greater at the 1st and 2nd week ($p=0.018$ and 0.003 , respectively) compared to ≥ 5 th week. Time from onset ($p=0.019$, for 2nd week compared with ≥ 5 th week) was independently associated with a greater extent of BBB breakdown. A synergistic effect of time from onset and BP surge was found ($p=0.017$).

Conclusion: The prevalence and extent of BBB breakdown are greater in the first two weeks in the disease course, with a peak in the 2nd week after onset.

However, BBB breakdown is still evident in 3–7th week in at least one fifth of patients. Our data suggest that BBB breakdown occurs early, providing a pathophysiologic background of earlier incidence of hemorrhagic stroke and PRES than ischemic stroke in patients with RCVS. Our data shows BBB breakdown may remit spontaneously with time, but a proportion of patients with prolonged untreated RCVS are still at risk of neurological complications.

Disclosure of Interests: This study was supported by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (Nos. 2017R1A2B2009086 and 2017R1A2B4007254).

IHC-PO-205

A novel CACNA1A gene mutation in a patient with episodic ataxia type 2, initially misdiagnosed as migraine aura without headache

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Objective: To report a case of episodic ataxia type 2 misdiagnosed and mistreated as migraine aura without headache.

Methods: We report the case of a 23-year old female presenting with episodes of balance dysfunction, associated with blurred vision, nausea and occasional vomiting. The episodes started at the age of six, having a duration between 1 hour and 24 hours and occurring three times a week. The patient denied the presence of headaches, vertigo or any other neurological disturbance. She is asymptomatic outside the episodes. The patient received a previous diagnosis of migraine aura without headache and was treated with Sumatriptan, Amitriptyline, Topiramate, Propranolol, Venlafaxine without benefit. The clinical examination revealed gaze evoked nystagmus but no other neurological signs. The family history was negative.

Results: The patient had two MRIs of the brain in the course of the disease that were reported as normal. The routine blood tests (full blood count, biochemical profile, autoimmune profile) were unrevealing. Analysis of a sample of genomic DNA has shown that she is heterozygous for the c.2411G>A (Trp804*) likely pathogenic mutation in the exon 19 of the CACNA1A gene. This mutation has not been previously described in the literature nor present in normal control populations. The result is consistent with autosomal dominant episodic ataxia type 2. Acetazolamide was initiated following the diagnosis.

Conclusion: A patient previously misdiagnosed and mistreated as migraine aura without headache was identified

to have a novel mutation of the CACNA1A gene causing episodic ataxia type 2.

Disclosure of Interest: None Declared.

IHC-PO-206

Obstructive sleep apnea (OSA) in headache sufferers with Idiopathic intracranial Hypertension (IIH): a prospective study

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Objective: It has been recognized that Obstructive sleep apnea (OSA) may be a risk factor for chronic daily headache (CDH). However, the relationship between OSA and CDH with idiopathic intracranial hypertension (IIH) remains uncertain. The aim of this study was to evaluate the frequency of OSA in patients with CDH and IIH.

Methods: In this prospective study patients with CDH and suspected of having high cerebrospinal fluid (CSF) pressure underwent a careful neurological evaluation, recording the frequency of headache through a monthly headache diary, the effects of postural changes and associated symptoms; we also evaluated pain intensity, disability related to headache, cutaneous allodynia, depression and anxiety, and medical overuse. Brain MRI and cerebral MR-venography were also performed. The patients underwent 1-hour lumbar CSF pressure monitoring via a spinal puncture needle and a polysomnographic evaluation with apnea-hypopnea index (AHI) and Snoring index for diagnosing OSA.

Results: We enrolled in this study 56 patients. Forty-three patients (76,8%) were diagnosed with IIH. Fifteen patients presented both IIH and OSA (6 M, 9 F). Among them, 8 subjects presented a mild OSA (AHI $9,1 \pm 3,7$, CSF mean pressure $255,4 \pm 32,4$ mmHg), 3 presented a moderate OSA (AHI $18,8 \pm 6,2$, CSF mean pressure $264,0 \pm 35,0$ mmHg) and 4 presented a severe OSA (AHI $62,1 \pm 26,6$, CSF mean pressure $277,5 \pm 32,0$ mmHg).

Conclusion: Our data showed that the frequency of OSA in patients with IIH was of 32,6% (15/43), a rate higher than prevalence of OSA in the general population, and with a similar representation of male and female patients (6 M, 9 F). Moreover we found that there is a positive relationship between increase of CSF pressure and severity of OSA. These results indicate that OSA is more common in IIH patients than in the general population. Cerebral vasodilatation related to hypoxia and hypercapnia, increase of systemic blood pressure and reduction of

cerebral venous return are considered possible causes of the increase of the intracranial pressure. We conclude that OSA may have a causative role in the pathogenesis of IIH. Thus, OSA should be investigated in patients with CDH associated with IIH.

Disclosure of Interest: None Declared.

IHC-PO-207

Dilation of superficial temporal artery and postoperative headache with moyamoya disease in adult patients

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Objective: To clarify the factors that are associated with headache in adult moyamoya disease (MMD) patients after revascularization with superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis.

Methods: We retrospectively analyzed the cases of 68 adult MMD patients: 30 with surgery and 38 without surgery. Each STA-MCA anastomosis was performed by the standard technique. MRA and SPECT with normalization were performed pre- and postoperatively. We stratified the intensity and the frequency of the patients' headaches into four ranks, respectively, and the sum of the two was used as the severity score. Pre- and postoperative STA diameters were retrospectively measured on DSA and/or MRA.

Results: In the surgery group, a univariate analysis showed that both the number of cases showing preoperative rCBF laterality indicated by an rCBF decrease <80% of the corresponding contralateral region, and the number of cases showing a postoperative rCBF increase >20% compared to the preoperative rCBF value in the corresponding area showed no significant difference between the patients with and without headache. The postoperative STA diameters of the distal branch (DSA) and main trunk (DSA and MRA) in the patients with headache were significantly larger compared to those of the patients without headache. The rate of postoperative increase of the STA diameters of the distal branch and main trunk were also significantly higher in the patients with headache than those without headache. We conducted a multivariate analysis with four models by forced entry methods, and it showed that the standard regression coefficient β for gender, a >20% increase of postoperative rCBF, and the increase rate of the STA diameter of the distal branch shown by DSA was 0.37, 0.54, and 0.56, respectively. In the

no-surgery group, the mean STA diameters of the main trunk shown by DSA and MRA were not significantly different between the headache and non-headache patients.

Conclusion: The results of our analyses revealed that aside from ischemia, the postoperative increase rate of the STA may be a candidate reason for headache, especially in adult MMD patients.

Disclosure of Interest: None Declared.

IHC-PO-208

Psychosocial predictors for pain outcomes in patients with temporomandibular disorders and headaches

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Objective: To establish the influence of psychosocial variables on pain outcomes (intensity and disability) in patients with temporomandibular disorders and headaches.

Methods: A retrospective, cross-sectional study was conducted at a specialized clinic for orofacial pain and dysfunction in Amsterdam (ACTA). The medical records of 2493 adult patients were screened. Inclusion for the study was a diagnosis of temporomandibular disorder (TMD) and one of three headache types: headache attributed to TMD (HA-TMD), migraine or tension-type headache (TTH). Measurement instruments were: Numeric Pain Rating Scale for pain intensity, Graded Chronic Pain Scale for pain-related disability, General Anxiety Disorder Screener (GAD-7), Patient Health Questionnaire for somatization and depression (PHQ-15 & PHQ-9) and Life Orientation Test-Revised for optimism (LOT-R). Linear multiple regressions were performed to assess the influence of psychosocial variables on both pain outcomes. In case of a significant interaction with headache type, analyses were stratified for the headache types. P-values <.05 were considered significant.

Results: A total of 948 patients were included in this study. For pain intensity, somatization was significant in the multiple regression analysis ($R^2 = 10.2\%$) and there was a significant interaction with headache type. Stratified analyses for headache type showed depression as a predictor for pain intensity in patients with HA-TMD ($R^2 = 15.2\%$) and somatization for patients with TTH ($R^2 = 7.2\%$). For migraine, none of the predictors were significant. For pain-related disability, both somatization

and depression were predictors in the multiple regression model ($R^2=16.5\%$). Stratified analyses were not performed as the interaction with headache type was not significant.

Conclusion: Depression was a predictor for pain intensity in patients with TMD and HA-TMD, whereas somatization was for patients with TMD and TTH. There were no psychosocial predictors for pain intensity for patients with TMD and migraine found. Depression and somatization were both predictors for pain-related disability, regardless of experienced headache type by patients with TMD.

Disclosure of Interests: This study was funded by the Dutch Organization for Scientific Research (NWO) and approved with a non-medical research law form by the ethics committee of ACTA (2018038).

IHC-PO-209

Taurine prevents recurrence of headache and stroke-like episodes in MELAS, the first-ever tRNA modification disorder

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Objective: Migraine-like headache is common in patients with mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS), a major clinical entity encompassing mitochondrial diseases. Most patients have the A3243G mutation in the mitochondrial DNA encoding tRNA^{Leu(UUR)}. We found that post-transcriptional taurine modification at the antisense wobble nucleotide is deficient in the mutant tRNA which causes a defect in deciphering codons and results in disturbances in mitochondrial protein translation. Thus, we proposed that MELAS is regarded as a tRNA-modification disorder. The aim of this study is to investigate the therapeutic effects of high-dose taurine supplementation in cultured MELAS-model cells as well as patients with MELAS.

Methods: We measured the oxygen consumption, the mitochondrial membrane potentials, and the oxidative stress in cultured MELAS cybrids with or without taurine in the culture media. We conducted a multicentre, open-label, phase III trial in which ten patients were received high-dose taurine (9 g or 12 g per day) for 52 weeks.

Results: Addition of taurine to culture media ameliorated reduced oxygen consumption, decreased mitochondrial membrane potential, and increased oxidative stress in

MELAS patient-derived cells. In the clinical trial taurine reduced the annual relapse rate of headache from 1.58 to 0.47 ($p < 0.05$), as well as stroke-like episodes from 2.22 to 0.72 ($p = 0.001$). In six patients stroke-like episodes were completely prevented, and thus 100% responder rate was 60% [95% confidence interval (CI), 26.2%–87.8%]. The 50% responder rate, i.e., the number of patients achieving a 50% or greater reduction in frequency of stroke-like episodes, was 80% [95% CI, 44.4%–97.5%]. Five patients showed a significant increase in the taurine modification of mt tRNA^{Leu(UUR)} from peripheral blood leukocytes ($p < 0.05$). No severe adverse events were associated with high-dose taurine supplementation.

Conclusion: The current study demonstrates that oral taurine supplementation can effectively reduce the recurrence of headache as well as stroke-like episodes in MELAS.

Disclosure of Interest: None Declared.

IHC-PO-210

Pseudotumour cerebri Syndrome (PTCS) in childhood: one-year follow-up of a national prospective population-based cohort study

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Objective: To ascertain current management of children and young people aged 1–16 years with pseudotumour cerebri (PTCS) in the United Kingdom and Republic of Ireland, and their outcomes one year after diagnosis.

Methods: A national prospective population-based cohort study was conducted over 25 months. Newly diagnosed PTCS cases, ascertained using classical diagnostic

criteria, were notified to the British Paediatric Surveillance Unit.

Data on incidence, investigations, and risk factors has been published: Matthews *et al.* Arch Dis Child 2016 doi: 10.1136/archdischild-2016-312238.

Data was also collected on treatments used, and outcomes at 1 year.

Results: We identified 185 PTCS cases. At one year data was available for analysis on 163/185 (88%).

10/163 (5%) had only one diagnostic lumbar puncture (LP). 150/163 (81%) had 1 or 2 further LPs, and 35/163 (19%) had more than 3 LPs in the year.

9/166 (5%) self-resolved, and in 4/166 (2%) causative medication was stopped (minocycline, prednisolone, growth hormone). Medication was prescribed: acetazolamide in 151/166 (82%), frusemide in 30/166 (16%), corticosteroid in 13/166 (7%), topiramate in 10 (5%).

Invasive interventions were: lumboperitoneal shunt in 16, ventriculoperitoneal shunt in 8, ventriculatrial shunt in 2, optic nerve fenestration in 1, decompressive skull surgery in 3, venous sinus stenting in 1.

From diagnosis to one year later: troublesome headache reduced from 161/185 (87%) to 44/158 (28%); papilloedema reduced from 165/185 (89%) to 37/158 (23%). Visual impairments reduced from 61/185 (33%) to 17/158 (11%) at 1 year: in 4/17(24%), 4/58(7%) and 9/110(8%) of those diagnosed at 1–6, 7–11 and 12–16 years, respectively.

Conclusion: Significant variation in management was identified reflecting the lack of high quality clinical trials in PTCS.

A significant minority had continuing symptoms and visual impairment one year after diagnosis.

Clinical trials are urgently needed to inform the best treatment approaches in PTCS.

Disclosure of Interest: None Declared.

IHC-PO-211

Swedish register study confirms association with idiopathic intracranial hypertension and some previously described risk factor drugs

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Objective: The etiology of idiopathic intracranial hypertension (IIH) is not fully understood. Several drugs have been described as proposed risk factors associated with IIH and its development. The aim was to investigate if we can confirm this association when comparing IIH patients to matched comparators.

Methods: Using data from the Swedish health registers and predefined algorithms, we identified incident IIH patients between July 2006–Dec 2016 and compared them with comparators (five healthy + five obese randomly selected individuals matched for age, sex, region and vital status). The Prescribed Drug register provided information on treatment. Logistic regression with robust standard errors was used to estimate odds ratios (OR) and 95% confidence intervals (CI).

Results: We included 654 IIH patients. IIH patients showed an increased risk for exposure to several drugs previously described as associated with IIH; tetracyclines (OR = 3.6, CI 2.7–4.8), sulpha-antibiotics (OR = 15.2, CI 4.1–56.5), corticosteroidal use (OR = 5.4, CI 4.0–7.1), and lithium (OR = 8.4, CI 3.0–23.4). This difference was also significant compared to obese comparators. However use of contraceptives (OR = 0.7, CI 0.6–0.9) were less common among IIH patients compared to healthy comparators and treatment with retinoidal drugs were in general uncommon and did not reach significance (OR = 1.25, CI 0.1–11.2). Iron anemia treatments were more common in IIH versus healthy comparators (OR = 2.8, CI 1.8–4.3) but obese comparators had a much higher exposure (OR = 4.1, CI 3.0–5.6).

Conclusion: This study confirms an association to several previously described risk factor drugs that might be involved in IIH development; such as treatments with tetracyclines, sulpha-antibiotics, corticosteroidal use and lithium. Contraceptives and iron anemia have been debated as being possibly associated with IIH; this study did not show such an association.

Disclosure of Interest: None Declared.

IHC-PO-212

Change in headache phenotype after withdrawal of medication overuse

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Objective: Long-term overuse of analgesics or acute migraine medication may mask symptoms important for the correct primary headache diagnosis. Headache often transforms from episodic to chronic with increased intensity and duration. Withdrawal of the overused medication may reveal the nature of the primary headache, helping the clinicians provide more precise diagnoses, crucial for correct treatment. In a multicenter study, we aimed to evaluate the consistency of headache diagnoses from baseline to after medication-overuse withdrawal.

Methods: Patients with confirmed medication overuse headache (MOH) according to ICHD-2 were included from 6 centres in Europe and Latin America and followed for 6 months. Patients underwent 2-month withdrawal: reduced acute medication intake maximum 2 days/week and preventive medication per need. Baseline primary headache was diagnosed using headache history and calendar. Headache phenotype after withdrawal was decided using detailed headache diaries. Primary outcome was change in headache phenotype from baseline to after 2-month withdrawal.

Results: Complete dataset was available on 489 patients. On top of the MOH, the initial, primary headache diagnosis was migraine in 327 patients (66.9%), migraine and tension-type headache (TTH) in 123 (25.2%), and TTH in 39 (8.8%). At month 2, 13 patients (2.7%) were headache free, 343 (70.1%) had episodic headache, 51 (10.4%) chronic headache without medication overuse, and 80 (16.4%) still had MOH. The headache diagnosis at month 2 had changed in 231 patients (47.2%). Of the patients initially with only migraine, 49 (15.0%) now had TTH and 166 (50.8%) both migraine and TTH. Of the patients with only TTH at baseline, 3 (7.7%) presented only migraine and 13 (33.3%) with migraine and TTH.

Conclusion: Proper MOH management with withdrawal and preventives is very important as the most remit to episodic form or become headache free. Further, almost half the patients presented with changed headache phenotype after withdrawal, so re-evaluation of the diagnosis after withdrawal is essential for selecting the proper future treatment.

Disclosure of Interest: None Declared.

IHC-PO-213

How do females with episodic cervicogenic headache cope with an acute stress provocation?

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Objective: Physiotherapists are regularly consulted by patients suffering from episodic cervicogenic headache. Since such headaches easily become chronic, recognizing factors that contribute to the chronification process is essential. No study analysed the role of the autonomic system in the pathophysiology of episodic cervicogenic headache, although abnormal activity of the autonomic nervous system is associated with its chronification. The goal of the current study was therefore to analyse autonomic nervous system responses before, during and after cognitive stress provocation.

Methods: Autonomic nervous activity was compared between 17 females with episodic cervicogenic headache (26.6 ± 11.6 years) and 17 age- and gender-matched asymptomatic controls (26.8 ± 11.9 years) via repeated measures of the peripheral circulation (blood volume pulse), activity of the dermal sweat glands (skin conductance (μmho)) and electrical activity of the bilateral m. trapezii descendens (surface electromyography (μV)) before (relaxation), during and after (recuperation) a cognitive stress provocation. The study was approved by the Medical Ethical Committee of the Ziekenhuis Oost-Limburg (B37120142305) and registered at ClinicalTrials (NCT02887638).

Results: Compared to the control-group, participants with episodic cervicogenic headache showed: significant ($P < .05$) lower responses of skin conductance (3.03 (0.44) vs. 4.19 (0.91)) and blood volume pulse (-5.56 (1.45) vs. (-5.61 (1.85)) on stress provocation, significant ($P < .05$) less (-2.57 (0.4) vs. -3.29 (0.84)) recuperation of the skin conductance after stress provocation and a significant ($P.03$) negative correlation (Spearman's rho -0.51) between dermal sweat gland activity and muscular activity of the right m. trapezius descendens during recuperation.

Conclusion: In general, females with episodic cervicogenic headache showed an abated response to stress and a more problematic recuperation. The maladaptive, dissociated stress response observed in these participants could be a threat to allostasis and might, in time, facilitate headache chronicity. Physiotherapists should be aware that autonomic nervous system activity can be disturbed in patients with episodic cervicogenic headache during and after acute stress. Examining such activity seems advised.

Disclosure of Interest: None Declared.

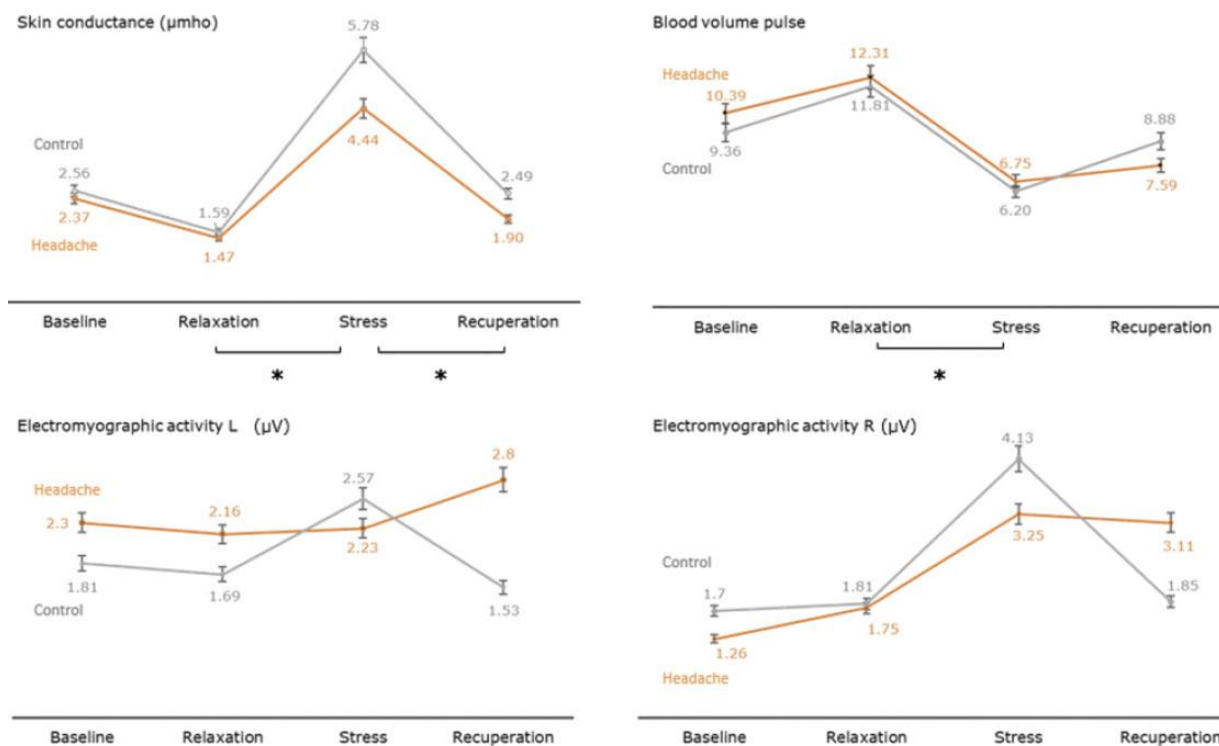


Figure 1. Visualization of the autonomic responses (*, $p < .05$ between groups; L, left; R, right; electromyographic activity of the m. trapezius descendens)

Abstract number: IHC-PO-213

IHC-PO-214

Headache as a presenting symptom in nervous system infections: a retrospective study in tertiary center from 2007–2018

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Objective: to analyze the occurrence of acute headache at the admission in patients presented with neuroinfections in the emergency department of the tertiary neurology clinic.

Methods: The medical records of all patients admitted to the emergency department between 2007–2018 was reviewed. Patients with central nervous system infections was selected for the study. Using a structured questionnaire was analyzed the presence of headache at the admission. All the data collected was analyzed with SPSS software for Windows.

Results: The study sample included 201 patients, 110 (54.7%) males and 91 (45.3%) females. In the study group – 121 patients (60.2%) presented with acute headache at the admission. According to topic diagnosis, complains

about headache presented 72.3% patients with meningitis, 50% patients with meningoencephalitis, 21.7% pts. with myelitis, 52.6% pts with encephalitis and all patients with brain abscess. Headache was in 63.7% of the patients with septic forms of neuroinfections and 54.4% of the patients with aseptic forms. Headache was presented in 48.2% of the patients considered immunocompromised and in 75.3% of the patient without immunocompromised status. The patients with headache at the presentation were younger than the patients without headache at the admission (39.57 ± 15.07 years vs. 51.26 ± 14.40 years, $p = 0.000$), Glasgow coma scale (13.91 vs. 12.61 , $p = 0.001$) and Glasgow outcome scale (3.98 vs. 3.11 , $p = 0.000$) were better. The presence of the acute headache at the admission positively correlate with the age ($r = 0.280$, $p = 0.000$), presentation type ($r = 0.263$, $p = 0.000$), septic form ($r = 0.246$, $p = 0.001$) and time spent to ICU ($r = 0.466$, $p = 0.000$) and negatively correlated with GOS (Glasgow outcome scale) ($r = -0.205$, $p = 0.006$) and alcoholism ($r = -0.217$, $p = 0.004$).

Conclusion: Headache is a frequent presenting symptom in patients with central system infections and depends on many factors (age, presentation type, septic form, immunocompromised factor) and correlate with the time spent in the intensive care and outcome.

Disclosure of Interest: None Declared.

IHC-PO-215**Follow-up of 22 patients with spontaneous intracranial hypotension**Vlasta Vukovic Cvetkovic^{1,*} and Henrik W. Schytz²¹Neurology, The Rigs Hospital-Glostrup²Neurology, Danish Headache Center, The Rigs Hospital-Glostrup, Copenhagen, Denmark

Objective: spontaneous intracranial hypotension (SIH) is a neurological condition characterized by symptoms as postural headache, neck stiffness, nausea, vomiting, tinnitus, and vertigo. Brain magnetic resonance imaging (MRI) findings in most patients is characterized by diffuse pachymeningeal gadolinium enhancement (PGE). Epidural blood patch (EBP) is considered as the treatment of choice in patients with severe symptoms nonresponsive to pharmacological treatments. The objective of our study was to investigate clinical and imaging features of 22 patients with SIH.

Methods: we retrospectively reviewed the medical records of 22 patients with SIH in our hospital: demographic variables, clinical symptoms, pain score, brain MRI findings, the response to EBP and pharmacological treatment. All EBPs are performed lumbar at a single-level by injecting autologous venous blood.

Results: 8 male and 14 female patients were analysed. The average age of symptom onset was 42 years (19–75). The mean follow-up time was 62 months (6–96). All patients presented with postural headache; additional clinical symptoms included nausea, stabbing headache (2), tinnitus (9), neck pain (9), dizziness (2). Brain MRI showed signs of intracranial hypotension in 17/22 patients: diffuse PGE (13), hygroma (5), downward displacement of the brain (4).

Follow up of patients after EBP showed that 6 patients had good response and full remission of all symptoms after the 1. EBP; a 2. was required by 5, a 3. by 5, a 4. by 3 and a 6. EBP by 2 patients, respectively. Eventually 12 patients had full remission (7 female, 3 male), 1 had daily headache but responded well to indomethacin (1 male), and 9 had moderate to severe daily non-postural headache with no significant response to medication. Medication with no effect on headache: indomethacin (4), amitriptylin (4), analgesics (4), gabapentin (2), metoprolol (1). No difference to EBP response was observed between males/females, in relation to age or the presence of MRI findings. In three cases the onset of SIH could be related to airplane travelling.

Conclusion: more than half of the patients required repeated EBP. A significant number of patients with SIH remain symptomatic even after repeated EBPs. The majority of patients do not respond to the pharmacological medications in the treatment of SIH.

Disclosure of Interest: None Declared.

IHC-PO-216**Headache after Ischemic Stroke: A Systematic Review and Meta-Analysis**Andrea Harriott^{1,*}, Fahri Karakaya² and Cenk Ayata¹¹Neurology, Massachusetts General Hospital, Boston, MA²University of Massachusetts, Dartmouth, Dartmouth, MA, United States

Objective: Headache associated with ischemic stroke is poorly understood and understudied. To gain further insight, we systematically reviewed studies examining the prevalence and characteristics of new onset post-stroke headache.

Methods: Medline and PubMed databases were queried. 1812 articles were identified. Of these, 50 were included in this systematic review. Twenty were subsequently included in a meta-analysis and meta-regression.

Results: Headache occurred in 6–44% of the ischemic stroke population. Most headaches had tension type features, were moderate to severe and became chronic in nature. Meta-analysis using an inverse-variance heterogeneity model revealed a pooled prevalence estimate of 0.14 (95% CI 0.07–0.23) with heterogeneity among studies. Meta-regression revealed a significant association between prevalence and study location, the source population's national human development index (HDI), and study quality. We found higher prevalence in European (0.22, 95% CI 0.14–0.30) and North American (0.15, 95% CI 0.05–0.26) studies compared with Middle eastern and Asian studies (0.08, 95% CI 0.01–0.18). After accounting for regional differences, populations from countries with higher HDI ($p=0.03$) and studies with higher quality scores ($p=0.001$) had lower prevalence. Calculated crude odds ratios showed that posterior circulation stroke (pooled OR 1.92, 95% CI 1.4–2.64; $n=7$ studies) and female sex (pooled OR 1.25, 95% CI 1.07–1.46; $n=11$ studies) had greater odds of headache associated with ischemic stroke.

Conclusion: Taken together, these data suggest that headache is common at the onset of or shortly following ischemic stroke and may contribute to post-stroke morbidity. Better understanding of headache associated with ischemic stroke is needed to establish treatment guidelines and inform patient management.

Disclosure of Interest: None Declared.

IHC-PO-217**A survey of clinical symptoms with RCVS in a Japanese regional headache center**

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Objective: Reversible cerebral vasoconstriction syndrome (RCVS) constitutes various clinical and radiologic features, which mainly involve sudden onset of severe headache and segmental vasoconstriction of cerebral arteries that resolves in 3 months. Several studies have reported meaningful findings for RCVS; however, characteristics of RCVS in Japan remain inconclusive. Thus, we have characterized the clinical profile of RCVS in Japan by surveying RCVS patients.

Methods: The clinical features of 32 consecutive patients with RCVS (5 males, 27 females; mean age, 44.9 ± 15.5 years) who visited Tominaga hospital from February 2011 to January 2019 were analyzed. RCVS was diagnosed if patients met the following three criteria: 1) Invasive or noninvasive angiographic evidence of multifocal segmental vasoconstriction in multiple intracranial arteries; 2) no evidence of aneurysmal subarachnoid hemorrhage; and 3) reversibility of angiographic abnormalities within 3 months. The diagnosis of headache attributed to RCVS was based on ICHD-3.

Results: In total, there were 27 idiopathic cases (84.3%), and 5 secondary cases (15.6%), which included 4 drug-induced cases and 1 case of Cushing's syndrome. Seventeen cases (53.1%) had migraine without aura. Triggers were bathing in 4 cases, defecation in 5 cases, exercise in 4 cases, sexual activity in 3 cases, and cough in 4 cases, with no clear triggers in 12 cases. Twenty-five cases (78.1%) were hospitalized for symptomatic treatment, with 2 cases of convulsion and 1 case of transient global amnesia, which spontaneously improved. Posterior reversible encephalopathy syndrome was noted in 1 case, but there was no case of stroke or neurological deficit. Recurrence of RCVS was not noted, and thunderclap headaches disappeared in 1 month in all cases. In 2 cases, headache with different characteristics remained even after 3 months, which may be persistent headache attributed to past RCVS.

Conclusion: RCVS cases in Japan mainly included middle-aged women with a history of migraine like those in Caucasian

populations. There was no concurrent stroke or poor prognosis, which can be linked to the fact that the study included the patients visiting the headache center and most cases were hospitalized. Moreover, ethnic differences could exist.

Disclosure of Interest: None Declared.

IHC-PO-218**Bilateral superior labial neuralgia secondary to midface hyaluronic acid injectable fillers for facial rejuvenation**

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Objective: Injectable fillers have recently increased in popularity for minimally invasive cosmetic improvement of facial aging and volume loss. Of reported complications, facial pain represents about a quarter, most often involving cheek injections. However, details of facial pain characteristics are largely unknown. We report a case of bilateral superior labial neuralgia following midface hyaluronic acid injectable fillers for cosmetic facial rejuvenation. The superior labial nerves are branches of the infraorbital nerves arising from the maxillary divisions (V2) of the trigeminal nerves.

Methods: Case report.

Results: A 53-year-old woman presented with left anterolateral upper lip pain which started 3 months after getting bilateral maxillary injections of hyaluronic acid fillers. Three months after the left sided face pain onset, she developed an identical type of pain on the right side. The pain occurred on one side or the other and never simultaneously. For the most part pain started spontaneously, but sometimes drinking hot soup or breathing cold air could trigger it. Symptoms would start with a brief tingling in the affected area for three to five seconds, followed by severe, sudden-onset, sharp, stabbing pain, lasting 3–5 seconds shooting towards the nasolabial fold, just lateral to the nasal ala. The pain occurred anywhere from 2 to 25 times daily. There were no associated migrainous or autonomic features. The pain never woke her from sleep, and she denied sensory loss in the face or mouth. MRIs with and without gadolinium of the head and face were normal. Her neurologic exam was normal. Gabapentin 3600 mg daily in 3 divided doses has controlled her pain in the last 2 years, but a lower dose has not.

Conclusion: Bilateral superior labial neuralgia has not been previously reported and may be a relatively unique complication of injectable fillers. The mechanisms for this occurrence are unclear. Based on recently reported variant anatomy of the labial branches of the infraorbital nerve in cadavers, some patients may be at a greater risk for this phenomenon than others. Patients and providers should be aware of this risk.

Disclosure of Interest: None Declared.

IHC-PO-219**Effect of nimodipine treatment on the clinical course of reversible cerebral vasoconstriction syndrome**Soohyun Cho^{1,*}, Mi Ji Lee¹ and Chin-Sang Chung¹¹Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic Of

Objective: In reversible cerebral vasoconstriction syndrome (RCVS), nimodipine is currently used for the treatment, although no evidence is available to support its disease-modifying effect. In this prospective observational study, we investigated whether earlier nimodipine treatment can modify the clinical course of reversible cerebral vasoconstriction syndrome.

Methods: We prospectively observed patients with angiogram-proven RCVS within 1 month after onset in the Samsung Medical Center between October 2015 and January 2018. Nimodipine was started in all patients immediately after diagnosis. Time from onset to the first nimodipine treatment was categorized as tertiles. We analyzed Kaplan-Meier curve and Cox proportional hazard model to test if the timing of nimodipine treatment can affect the clinical course of thunderclap headaches (TCHs) defined as the duration from onset to remission of thunderclap headaches.

Results: Eighty-two patients were included in the analysis. In 71 (85.5%) patients, TCHs entered remission immediately after the start of nimodipine treatment. When categorized into earliest (<6 days), early (6–13 days), and late (≥ 14 days) treatment groups, earlier treatment was significantly associated with shorter clinical courses (median, 2 days [interquartile range 1–3] vs. 7 days [4–10] vs. 10 days [5–15]; log-rank, $p < 0.001$). Univariable and multivariable Cox regression analyses also demonstrated an independent effect of earlier nimodipine treatment on earlier remission of TCHs (adjusted hazard ratio, 0.75 per 1-day delay in treatment; 95% CI, 0.693–0.802, $p < 0.001$).

Conclusion: We provide the first evidence of the role of nimodipine in the treatment of RCVS. The clinical course of RCVS may be modulated by earlier nimodipine treatment. Additional beneficial effects of earlier nimodipine treatment on the progression of vasoconstriction and development of neurological complications should be investigated in future studies.

Disclosure of Interest: None Declared.

IHC-PO-220**Secondary occipital neuralgias. Report of four cases**Maria V. Nagel¹, Lucas Bonamico¹ and María T. Goicochea^{1,*}¹Neurología, Fleni, CABA, Argentina

Objective: Occipital nerve irritation may be related to different causes. We report four cases of secondary occipital neuralgia.

Methods: We reviewed electronic medical records of patients diagnosed with secondary occipital neuralgia evaluated in the headache clinic of Fleni.

Results: Case 1.

A 64-year-old female with history of rheumatoid arthritis, developed constant pain with paroxysmal exacerbations in the right occipital region and transient episodes of dysarthria. Examination demonstrated right deviation of the tongue and pain in the right greater and lesser occipital nerves territories. Magnetic Resonance Imaging (MRI) revealed a heterogeneous mass involving the clivus suggestive of chordoma. Occipital nerve block improved the symptomatology.

Case 2.

A 73-year-old female developed a 3-month history of paroxysmal, severe burning pain in the right occipital region. The palate elevated asymmetrically and dysaesthesia and pain of greater and lesser occipital nerves territories were present. Skull base and neck MRI showed an expansive para-pharyngeal lesion that infiltrated boulder and clivus. Biopsy showed a paving carcinoma. Pain improved after occipital nerve block.

Case 3.

A 48-year-old female presented with a 3-week history of paroxysmal burning pain in the right occipital region. Physical examination demonstrated hyperesthesia in right occipital area. Angio MRI demonstrated hematoma in the arterial wall and narrowing of the lumen of the right vertebral artery, suggestive of dissection.

Case 4.

A 75-year-old female complained of a 6-day history of severe sharp, stabbing headache in the left occipital region. Brain with angio MRI were normal. Occipital nerve block was performed with partial relief. After 5 days she developed blistering rash over the distribution of the fifth cervical nerve. 5 days later she experienced proximal weakness of her left arm. A brachial plexus MRI revealed enhancement of the right C5 nerve root and the upper trunk of the brachial plexus.

Conclusion: We recommend that patients who refer pain in the occipital region should have a detailed clinical evaluation, head and neck gadolinium enhanced MRI and complete blood test. These patients should be controlled in the following days to check for any atypical feature of pain

and/or physical abnormalities that should raise the suspicion of an underlying etiology.

Disclosure of Interest: None Declared.

IHC-PO-221

Red Ear Syndrome Case Report: a Rational Use of Erenumab

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Objective: Red Ear Syndrome (RES) presents as ear redness and pain. It can be idiopathic, related to a primary headache disorder such as migraine, or due to a secondary cause such as cervical spondylosis.¹⁻³ Angry Back-firing C-nociceptor (ABC) syndrome has been described as a potential underlying mechanism in which non-noxious stimuli lead to antidromic discharges and release of peptides including calcitonin-gene related peptide (CGRP). These peptides lead to vasodilation, erythema, and pain.⁴⁻⁷ This case report describes a case of RES with response to Erenumab, a CGRP receptor monoclonal antibody.

Methods: Case report.

Results: The patient is a 24 year-old man with a 10 year history of chronic migraine (daily headache with an average of 12 migraine days per month) who experienced the sequential onset of bilateral external ear pain involving the helix, antihelix, and auricular tubercle. The symptom complex evolved to include persistent burning and redness with 1-3 painful exacerbations per day each lasting 1-2 h. Secondary causes were excluded. He failed multiple oral preventive medications. Erenumab led to complete resolution of migraine attacks and headache days, and significant (>75%) improvement of RES symptoms.

Conclusion: Erenumab may be effective for the treatment of RES, especially in those with a history of migraine. CGRP may be an important mediator of the erythema and pain in patients with RES. The effectiveness of anti-CGRP monoclonal antibodies in idiopathic and secondary RES awaits further support from other case reports. Whether ligand or receptor targeted anti-CGRP mAbs have differential efficacy is unknown at this time.

Disclosure of Interest: None Declared.

IHC-PO-440

Correlation between the total number of features of paediatric pseudotumor cerebri syndrome and cerebrospinal fluid pressure

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Objective: Accurate diagnosis of Pseudotumor Cerebri Syndrome (PTCS) in children is essential. We aimed to see if the clinical and radiological assessment that is carried out before lumbar puncture could predict subsequently recorded CSF pressures, and thus whether it could be used to increase diagnostic accuracy of paediatric PTCS.

Methods: We performed a retrospective cohort study of children referred to our centre with suspected PTCS. We created a 15-point score that summed 11 Clinical features and 4 Brain neuroimaging features (the PTCS-CB score), and a 16-point score that included one further Venography feature (the PTCS-CBV score). The clinical features were: headache, nausea, vomiting, transient visual obscurations, optic disc oedema, pulsatile tinnitus, neck or back pain, diplopia, cranial nerve palsies, reduced visual acuity and abnormal visual fields. The neuroimaging features were: (partially) empty sella, flattening of the posterior aspect of the globe, distension of the perioptic subarachnoid space (with or without a tortuous optic nerve), transverse venous sinus stenosis and protrusion of the optic nerve into the vitreous. The venography feature was transverse venous sinus stenosis. All features were included or mentioned in internationally recognised diagnostic criteria. We looked for correlation between the scores and recorded CSF pressures.

Results: PTCS-CB and PTCS-CBV scores were both significantly positively correlated with recorded CSF pressures and were 'good' predictors of raised CSF pressures.

Conclusion: PTCS-CB and PTCS-CBV scores can help in the management of paediatric PTCS. Children with high scores are more likely to have severely raised CSF pressures and thus may warrant more urgent LP investigations. In children with subtle abnormalities in optic disc appearance where disc oedema cannot be ruled out, a low score may add further reassurance, and a high score would support a decision to progress to lumbar puncture investigation.

Disclosure of Interest: None Declared.

Abstract number: IHC-PO-441**Table 1.** Retrosplinal C1-2 fluid collection

Case	Cervical MRI	CTM	CSF leakage site
1	Positive	Positive	C6-7
2	Negative	Negative	T8-9
3	Equivocal*	Positive	C5-6
4	Positive	Positive	C7-T1
5	Positive	Positive	T10-11
6	Positive	Negative**	C6-7
7***	Positive	Equivocal	Undetermined (lower cervical-upper thoracic)
8***	Negative	Negative	Undetermined (lower cervical-upper thoracic)
9***	Positive	Negative	Undetermined (lower cervical-upper thoracic)

*Probably due to metallic artifact.

**CTM performed 17 days after cervical MRI.

***Large amount of CSF leakage.

IHC-PO-441**Evaluation of retrosplinal C1–2 fluid collection in spontaneous intracranial hypotension**

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Objective: Retrosplinal C1-2 fluid collection has been reported to be a false localizing sign of C1-2 CSF leakage in patients with spontaneous intracranial hypotension (SIH). We present here detailed retrosplinal C1-2 fluid collection findings obtained in SIH cases.

Methods: Nine patients with SIH were included. All underwent cervical magnetic resonance imaging (MRI) with a fat-saturation technique, as well as computerized tomography myelography (CTM) and radioisotope cisternography examinations. Each radiological finding was evaluated to determine the exact site and distribution of CSF leakage.

Results: Retrosplinal C1-2 fluid collection was detected by MRI in 6 and CTM in 4 cases (Table 1), which our findings indicated to be derived from extradural CSF, with the origin a remote region of CSF leakage ranging from the lower cervical to thoracic levels. The exact site of leakage could not be determined in 3 cases with large amounts of fluid, while no leakage was detected at the C1-2 level in any of our cases.

Conclusion: Retrosplinal C1-2 fluid collection may be commonly observed as a false localizing sign of C1-2 CSF leakage in patients with SIH, thus a multimodal evaluation

strategy is required to determine the exact site of leakage. Considering the dynamic nature of CTM examinations as well as the possibility of technical failure, MRI with a fat-saturation technique is considered to be superior for depicting retrosplinal C1-2 fluid collection.

Disclosure of Interest: None Declared.

IHC-PO-442**What makes a difference between with and without ischemia of cerebral arterial dissection**

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Objective: Advances in imaging and changes in knowledge of cerebral artery dissection (CAD) have increased the chance to find CAD as a cause of headache. The purpose of our study is to evaluate clinical characteristics of CAD with headache alone compare with CAD with both headache and ischemic stroke.

Methods: In serial 37 patients (27men, 10women, 48.6 years) who admitted Kyorin University Stroke Center between April 2013 and March 2018 because of CAD were evaluated.

Information about clinical characteristics, history about headache, imaging study and clinical course were obtained from medical records retrospectively. We assessed the difference between Group H (with headache alone) and Group I (with both headache and ischemic lesion).

Results: Group H were 19 cases (17men, 5women, 47.1 years), and group I were 18 cases (13men, 5women, 50.2 years). There were no differences between the two groups in age, gender and the frequency of hypertension, dyslipidemia, diabetes, and smoking.

Sudden onset and pulsating pain were more frequent in group H (47.4 vs 72.2%, 52.6 vs 5.6%).

Dissection of posterior circulation is more frequent in group H (89.5 vs 61.1%). The time from onset of headache to the first MR examination was significantly longer in group H (8 vs 2 days). MR findings suggesting dissection directly (double lumen, intimal flap, intramural hematoma), aneurysm formation (fusiform aneurysm, pearl sign, dilatation), and stenosis/occlusion (string sign, stenosis, tapered occlusion) were observed in 85.2%, 66.7%, and 85.2% respectively. The morphological changes in MRA during hospitalization were more frequent in group H (60.0 vs 33.3%).

The frequency of antithrombotic therapy during hospitalization was significantly higher in group I (88.9 vs 6.7%).

The number of hospitalization days was significantly longer in group I (25.6 vs 11.8 days).

After discharge, an aneurysmal enlargement had observed in some cases more than a year after.

Conclusion: Compared to CAD with both headache and ischemic lesions, CAD with headache alone took more days from onset of headache to visit, had more throbbing quality of pain, and less objective neurological findings. The factors to be related to develop ischemia in patients with CAD remain unclear. It's necessary to accumulate more knowledge of CAD to resolve clinical questions.

Disclosure of Interest: None Declared.

IHC-PO-443

Brief Intervention – treatment of medication overuse headache in primary and secondary care, a study protocol

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Objective: Medication-overuse headache (MOH) is chronic headache caused by overuse of analgesics or acute migraine-medication. In Denmark, 100.000 people suffer from MOH resulting in high disability and low quality of life.

MOH can be treated by a complete stop of medication for two months (withdrawal). *MOH Brief Intervention* is an effective and systematic approach to withdrawal developed and validated for use in primary and secondary care.

The objective of the study is to implement the Brief Intervention approach in Denmark to ensure a standardized, feasible, and effective MOH-treatment in primary and secondary care.

Methods: The study design is a prospective study with 6 months follow-up.

· **Step 1** (pilot testing the concept): All private practicing neurologists in Denmark are invited to participate and BI for treatment of patients with MOH.

· **Step 2:** Invitation of all GPs in Denmark to participate and use the approach for treatment of patients with MOH.

Results: The endpoints will be change in headache days, medication use and sick leave. Additionally, feasibility will be evaluated in collaboration with neurologists before implementation in primary care.

Conclusion: The vision is to improve and standardize the MOH-treatment in primary and secondary care. Implementing the Brief Intervention for Medication-overuse headache will potentially benefit thousands of patients in Denmark.

Disclosure of Interest: None Declared.

IHC-PO-444

Headache disorders in the clinical psychiatric population

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Objective: Contrary to numerous studies showing a high degree of comorbidity between psychiatric disorders and primary headache disorders, pointing to psychiatric disorder as a risk factor for headache progression and chronification, the number of studies that put in the spotlight headache occurring only during the psychiatric disturbance, e.g. "headache attributed to psychiatric disorder" [1,2], is significantly smaller.

Methods: Hereby, we present the clinical sample of psychiatric patients, treated for a period of one year, during the 2016, at the Clinical Department for Psychotic Disorders of the Institute of Mental Health, who complained of headache. The psychiatric disorder has been diagnosed according to diagnostic criteria given in the ICD 10[4], while the headache has been diagnosed according to diagnostic criteria given in the ICHD-3 [2].

Results: Only 25 patients, out of 427 patients that had been treated in this period complained of headache. Majority of patients with headache (19) had major depressive disorder, recurrent in 15 patients. One patient had bipolar affective disorder. Five patients had psychotic disorder, four of them schizophrenia, and one patient presented with acute polymorphic psychotic disorder with symptoms of schizophrenia. Primary headache was present in 19 patients. One patient had medication overuse headache. The diagnosis of headache attributed to depressive disorder was established in three patients. One patient had headache attributed to somatization disorder, and one patient had headache attributed to psychotic disorder.

Conclusion: The distribution of headache types among patients with headache supports the current headache classification in which the headache attributed to somatization disorder and headache attributed to psychotic disorder had been recognized. Also, this report supports the opinion that the headache attributed to depressive disorder, as the most common type of headache attributed to psychiatric disorders, corresponding to the additional codes in the appendix of the classification (code 12.3) could be added to the classification itself.

Disclosure of Interest: None Declared.

IHC-PO-445

Analysis of cervical spine dysfunctions affecting quality of life in Cervicogenic headache

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Objective: To assess in patients with Cervicogenic headache, the extent to which muscle tenderness, sagittal cervical alignment, Cervical angle may relate to their impaired quality of life.

Methods: In this descriptive study 23 (12 males and 11 females) patients aged 19 to 65 years were enrolled. Subjects were recruited as a part of an intervention trial thus form a consecutive sample of patients.

For each patient, a muscle tenderness score by muscle palpation were carried out. A Pericranial Muscle Tenderness Score (PTS) and a Cervical Muscle Tenderness Score (CTS) were calculated (range 0–3). For cervical curve analysis the four-line Cobb method at C2–C7 and the Harrison posterior tangent method (PTM Harrison) was used in this study. Also Roussouly sagittal analysis method was used to classify cervical curves as lordosis, straight, sigmoid and kyphosis. Neck disability index(NDI) and Headache impact test –6 (HIT-6) score

was also calculated to assess the quality of life in these patients. A thorough assessment through structured interview regarding the type of headache pain was also made.

Results: In this sample NDI for all the subjects was $64.09\% \pm 12.41\%$ in which females had higher disability score as compared to males ($p = 0.00$). Overall score for HIT-6 score was 64 ± 5.69 in which females scored higher than the males ($p = 0.03$). However pericranial tenderness was comparable in males and females ($p = 0.16$). Similar trend was observed in cranial tenderness score where males and females scored ($p = 0.43$) respectively. In patients with CeH, the pain lasted minutes to days, and was pressing/tightening in quality, of mild or moderate intensity, bilateral or variable in location and worsened with physical activity. Nausea was absent, but phono or photophobia was occasionally present. Cervical pain was concomitantly present with headache. Of 23 patients all except 1 had a straight cervical spine according to Roussouly classification and the cervical angle varied from -14° to $+6^\circ$.

Conclusion: Straightened cervical spine and Pericranial and Cranial muscle tenderness may play an important role in the pathogenesis of cervicogenic headache and its accessory symptoms. Both these factors can significantly affect the QOL of the patients as measured by NDI and HIT-6.

Disclosure of Interest: None Declared.

IHC-PO-446

Tuberculous meningitis in the form of epicrania fugax: a case report

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Objective: Headache is a prominent feature of inflammation of the meningitis. But the headache rarely presents in the form of epicrania fugax especially for tuberculous meningitis. This article aims to describe clinical and imaging approaches to the diagnosis and management of one tuberculous meningitis patient in the form of epicrania fugax encountered in clinical practice.

Methods: We report one case of tuberculous meningitis with an unusual onset. We analyzed the clinical manifestation, neurological evaluation, brain magnetic resonance imaging (MRI), therapeutic and prognostic characteristics.

Results: A 43-year-old male was admitted to our department who experienced with brief paroxysms of pain that is felt to move across the head surface from left occipital area toward left eye for three days. The headache was stabbing in character and along a linear trajectory across the surface. Pain intensity was moderate and VAS was 5. The frequency of pain was about 10 attacks per day and

most attacks were spontaneous, but some of them could be triggered by touch. He was combined with fever and the temperature was 38°C. He denied of tuberculous in the past. Neurological examination showed meningeal signs were positive including neck stiffness and Brudzinski sign. Brain MRI was normal. CSF examination showed that the pressure was 210 mm water. The CSF protein concentration was 300 mg/dL. The CSF Glucose level was 20 mg/dL. The acid-fast stain was positive. He was diagnosed with tuberculous meningitis and then transferred to infectious disease hospital. The patient was given carbamazepine for 1 weeks and antituberculosis drugs including isoniazid, rifampicin, pyrazinamide and ethambutol for 9 months. Headache was disappeared and temperature was normal after treated for two weeks. He was interviewed in the next 12 follow-up months and never recurred.

Conclusion: Epicrania fugax is a primary headache consisting of brief paroxysms of pain that are felt to move across the head surface through the territories of different nerves. But there was not always present with epicrania fugax onset for the tuberculous meningitis in clinical practice. Here we highlight the importance of special headache style and differentiation diagnosis can be challenging, especially early in the course.

Disclosure of Interest: None Declared.

IHC-PO-447

Morning headache in patients with obstructive sleep apnea syndrome: a case series of three patients

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Objective: Morning headache is common in patients with obstructive sleep apnea syndrome (OSAS). However, diagnosis and management of morning headache in patients with OSAS are sometimes difficult.

Methods: We here report 3 patients with obstructive sleep apnea syndrome (OSAS), presenting with morning headache.

Results: Case 1. A 38-year-old man presented with morning headache, excessive daytime sleepiness and witnessed sleep apnea. Those symptoms started when he was 30 years of age. He showed microgenia and obesity. His headache occurred three times a week, which was throbbing parietal pain, lasting for 60–90 minutes. No phonophobia or photophobia was reported. Epworth sleepiness scale (ESS) score was 17. Polysomnography revealed severe OSAS (Apnea-hypopnea index (AHI) was 126.7/h). After treatment with continuous positive airway pressure (CPAP), his headache and sleepiness improved dramatically.

Case 2. A 77-year-old woman presented with morning headache, which started from 2 months ago and lasted 3 hours every morning. She did not have nausea nor photophobia. No neurological deficits were detected. She had been treated with CPAP for OSAS. Brain magnetic imaging showed no abnormality. Careful history taking revealed that she stopped using CPAP because of nasal obstruction. Morning headache resolved rapidly after she re-started to use CPAP treatment.

Case 3. A 43-year-old man had habitual snoring since the age of 30 years. Since the age of 40 years, he had morning headache and daytime sleepiness. His morning headache was throbbing in quality with predominantly generalized localization, and occurred twice a week and lasted for 8 hours after awakening. He had a past medical history of depression at the age of 35 years. Polysomnography revealed moderate OSAS (AHI was 22.3/h). After CPAP treatment, his sleepiness improved, but his headache worsened in intensity and frequency. Three months later, he was diagnosed with a recurrence of depression at another hospital. After treatment for depression with selective serotonin reuptake inhibitor, his headache significantly improved within 1 month.

Conclusion: Sleep apnea headache can be treated with adequate treatment for OSAS. When patients with OSAS complain of morning headache, CPAP adherence should be monitored and other factors including depression should also be screened.

Disclosure of Interest: None Declared.

IHC-PO-448

Susac's syndrome presenting with clinical features suggestive of Multiple Sclerosis; a case report and literature review on MR findings

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Objective: To explore the clinical features and MRI findings in Susac's syndrome.

Methods: A case report based on a patient our neurology team was taking care of on the neurology ward with relevant literature review of the topic.

Results: 35 year old gentleman presented to outpatients with a 4 month history of headaches and intermittent vertical diplopia. The headache was continuous and global. Diplopia was often accompanied by vertigo and left upper limb weakness. The examination showed nystagmus and positive head impulse test to the left and there was no other focal findings. A diagnosis of brainstem demyelination was suspected and an MRI brain was arranged as an out-patient. The MRI revealed very extensive, multifocal almost confluent, brain, parenchymal and leptomeningeal enhancement following which he was urgently admitted

for further investigations. He then revealed he had right sided hearing loss for a few months; this immediately led us toward a diagnosis of susac's syndrome. CT angiogram, VEPs and LP were all normal; retinal fluorescein angiography revealed a vasculitic process. Prednisolone and mycophenolate was started to which he responded well.

Susac syndrome is a rare condition characterized by a clinical triad of encephalopathy, sensorineural hearing loss, and visual disturbance resulting from branch retinal artery occlusion (BRAO). The classical MRI findings are multiple small hyperintense foci "snowball images" and contrast enhancement in the white matter as well as DWI showing hyperintense lesions, "string of pearls", in the internal capsule and multiple lesions in the genu and splenium of corpus callosum. Our patient's imaging, in addition, showed leptomeningeal enhancement, reported only in less than a third of cases and may help differentiate from multiple sclerosis.

Conclusion: We present a rare case of headache syndrome that can easily be missed particularly if the diagnosis is not considered and if the patient does not present with a full triad. MRI findings as described above are clear features to distinguish from other common causes of headache. A full literature review and differentiating features of imaging will be discussed with the case report.

Disclosure of Interest: None Declared.

IHC-PO-449

Correlation of Secondary Headache with Stroke Clinical Outcome

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Objective: Stroke is a major cause of disability in the world and the leading cause of death in Indonesia. Stroke patients came with neurological deficits and were accompanied by headache. Secondary headache can be caused by cerebral edema and increased intracranial pressure. National Institutes of Health Stroke Scale (NIHSS) is used to evaluate stroke clinical outcome which includes many aspects, including motoric, sensory and others. The higher NIHSS score shows the more severity. This study aims to determine correlation between secondary headache with outcome in the acute stroke patients in Dr. Soetomo general hospital, Surabaya Indonesia.

Methods: This is a descriptive, retrospective study of stroke patients in neurology ward Dr. Soetomo general hospital, Surabaya Indonesia in 2013. NIHSS data were

obtained from stroke registry and calculated for correlation analysis.

Results: There were 298 patients with male 154 (51.7%) and female 144 (48.3%). Age ranging from 13 until 92 years old. There were 69 (23.3%) stroke patients accompanied by secondary headache.

Conclusion: There was no significant correlation between secondary headache and clinical outcome measured with NIHSS in acute stroke patients ($r = -0.025$; $p = 0.680$). Keywords: Secondary headache, Stroke, NIHSS.

Disclosure of Interest: None Declared.

IHC-PO-450

Unravelling Mysterious Headache

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Objective: A 76 year old gentleman with headache, droopy left eye and double vision was referred to Ophthalmology. He had partial left ptosis with possible sixth nerve palsy and mild proptosis. Investigations showed normal bloods and inflammatory markers. MR scan showed thickened left lacrimal gland which was subsequently biopsied showing idiopathic dacryoadenitis. Patient was given high dose intravenous steroids to which he responded well with complete resolution of headache and double vision. However, headaches returned within few weeks when he was referred to the headache clinic. Prior to this, he had been to the maxillofacial surgeons and rheumatologists, but no conclusion was drawn. In the headache clinic, he gave a history of recurrent excruciating left sided headaches at least once in 24 hours lasting 3 hours during which it spread globally before resolving. He had light and sound sensitivity, with exacerbation to physical activity. There were no autonomic features, focal neurological symptoms or red flags. A diagnosis of chronic migraine was made, and amitriptyline was prescribed. Indomethacin trial was considered but not given.

Methods: N/A.

Results: In the subsequent few months (before the next headache clinic r) he had rheumatological visits with normal inflammatory markers except the last visit when CRP was raised at 26 ($N < 8$). Temporal artery biopsy showed changes consistent with healed temporal arteritis. He was commenced on high dose steroids to which he responded dramatically with complete resolution of symptoms. The steroids are now being slowly tapered.

Conclusion: We report a case of biopsy proven temporal arteritis with no suspected clinical features and normal inflammatory markers (described in 4% of cases) on

many occasions. The presentation was more in line with a primary headache disorder. It is difficult to be certain whether initial presentation of ptosis and dacryoadenitis was a separate entity, although a dramatic response to steroids may indicate atypical presentation of temporal arteritis. One could argue making a case of temporal artery biopsy in every case of new onset headache over the age of 60, although presence of skip lesions may yield false negative results making this unjustifiable. Similarly, a therapeutic trial of steroids might not be appropriate given the side effect profile and therapeutic response in some primary headache disorders.

Disclosure of Interest: None Declared.

IHC-PO-451

Alphaherpesviruses reactivation and headache disorders: a retrospective case-control study

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Objective: To explore the relationship between headache disorders and reactivation of alphaherpesviruses (varicella-zoster virus, VZV; herpes simplex virus type 1 and 2, HSV-1 and -2) in patients of a tertiary headache clinic. Alphaherpesviruses are latent in trigeminal ganglia in >90% of people, can reactivate with or without rash and have been anecdotally associated with headaches (HAs), including migraine. The frequency of HAs associated with alphaherpesvirus infection is unknown yet important to determine since these HAs may be treatable with antiviral medications.

Methods: With IRB approval, a retrospective study was conducted on adult patients of the University of Colorado Health (UCH) headache clinic, who had their serum tested for IgG and/or IgM antibodies against at least one of the alphaherpesviruses. Their headache disorders were diagnosed according to the International Classification of Headache Disorders (ICHD-3 β) between July 2013 and June 2016, and results of antibody testing analyzed along with multiple clinical data. The prevalence of positive anti VZV and anti-HSV antibodies in patients of the headache clinic were compared to the prevalence of the same antibodies in patients without headache who were seen in other UCH clinics during the same time interval.

Results: In this study, 260 patients with headache were identified (mean age 45, 83% women), in which HSV or VZV serum antibodies were determined. The vast majority had head/face pain for over one year. The most common diagnosis was chronic migraine (142/260 patients, 55%) followed by painful cranial neuropathies (31/260, 12%) and trigeminal autonomic cephalalgias (20/260, 8%). The prevalence of positive IgG antibodies to VZV, HSV-1 and

HSV-2, indicative of past exposure, was 90%, 63% and 24%, respectively. The prevalence of positive IgM antibodies against HSV-1/2 (non-discriminative), indicative of reactivation or primary infection, was 35% in headache patients vs 21% in controls, while prevalence of IgM anti VZV was 5% and 3% respectively in the 2 groups.

Conclusion: Alphaherpesviruses reactivation, especially of herpes simplex, as assessed by positive serum antiviral IgM antibodies, is common in patients with headache disorders. The significance and reciprocal causality alphaherpesviruses reactivation-headache, is uncertain but worth exploring further.

Disclosure of Interest: None Declared.

IHC-PO-452

Bilateral internal carotid artery dissection in a patient suspected of fibromuscular dysplasia

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Objective: Bilateral internal carotid artery dissection has been rarely reported. We report a patient who developed bilateral internal carotid artery dissection and was diagnosed with suspected fibromuscular dysplasia (FMD) by detailed examination.

Methods: Case report.

Results: A 43-year-old man with hypertension noticed pain in the left lower jaw and temporal region of the head. Three days later, he developed vertigo followed by the right upper limb paralysis and dysarthria while using mobile phone (day X). The patient had family history of ruptured cerebral aneurysm. At arrival of the hospital, the paralysis of the upper limb and dysarthria disappeared, and the National Institutes of Health Stroke Scale score was 0. Diffusion-weighted magnetic resonance imaging (MRI) revealed diffuse high signal areas at the border of left middle cerebral artery and anterior cerebral artery territories. The left internal carotid artery was poorly visible by magnetic resonance angiography (MRA). After hospitalization, dysarthria and right hemiparesis recurred and worsened. Cerebral angiography showed severe stenosis in the left internal carotid artery and dissection, and catheter treatment was performed on X+4. On day X+14, brain MRI was re-examined because he developed disturbance of consciousness and left hemiparesis. Diffusion weighted MRI showed high signal intensities in the border of right middle cerebral artery and anterior cerebral artery territories. MRA showed findings suggestive of stenosis and dissection in the right internal carotid artery. Therefore, stent placement was performed on the right internal carotid artery. The patient was diagnosed with

suspected FMD based on the findings of bilateral internal carotid artery dissection[SKI] (and stenosis) and distal stenosis in the right renal artery.

The differential diagnosis include Marfan syndrome, Ehlers-Danlos syndrome, Eagle syndrome, Osteogenesis imperfecta, and pseudoxanthoma elasticum. However, there was no finding suggesting these diseases.

Conclusion: In a patient with young onset bilateral internal carotid artery dissection, it is important to include FMD as a different diagnosis.

Disclosure of Interest: None Declared.

IHC-PO-453

Role of Physical Therapy in the Diagnosis and Management of Trigeminal Neuralgia

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Objective: There have been limited case reports of clinically diagnosed trigeminal neuralgia (TN) caused by tooth infection with resolution of symptoms following oral surgical procedures. In these cases, symptoms were in the *mandibular* division of the trigeminal nerve and its associated branches. We present a case of a 44-year-old male referred to physical therapy with classic features of TN in the *maxillary* division secondary to an upper first molar infection.

Methods: The patient was referred to PT with a diagnosis of right sided TN. His current medical history included right sided temporomandibular dysfunction (TMD) and chronic migraine headaches (CMH). His migraines are well controlled with Botox and right sided TMD was treated successfully in the past with PT. The neurologists' aim was to determine if PT treatment directed to TMD could help with his TN-related pain.

Physical therapy treatment was multimodal and consisted of manual therapy, neuromuscular re-education, and transcutaneous electrical nerve stimulation. After one month of PT, the patient reported "gum irritation" along the right upper gum line persisting for over a week. The patient was subsequently referred by the physical therapist for a dental consultation.

Results: The dental consultation resulted in the discovery of an upper right molar infection. After appropriate oral surgical treatment of this tooth, the pain in the region of V2 was completely abolished. The patient was able to return to eating and subsequently able to return to his ideal body weight and prior level of activity.

Conclusion: Idiopathic TN should be periodically re-evaluated for secondary causes. This case provides an example where a PT evaluation of TN may be a useful diagnostic tool for the effective management of these patients alongside the neurologist.

Disclosure of Interest: None Declared.

IHC-PO-454

A Headache Patient with Spontaneous Basilar Artery Dissection Confirmed by Vessel Wall Imaging

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Objective: Background.

Cerebral arterial dissection, especially basilar artery dissection is an uncommon etiology in ischemic stroke. However, arterial dissection should be considered one cause of stroke in young adults. We report a headache patient with spontaneous basilar artery dissection with typical radiological findings confirmed by vessel wall imaging.

Methods: Case.

A 45-year-old man admitted with a sudden onset of headache in both temporal areas. The patient also complained a tingling sensation of left face, upper and lower extremities. He had history of smoking, but denied histories of other cardiovascular risk factors, and recent history of trauma and medication were absent. On initial neurologic examination, he demonstrated alert mentality, normal motor strength. And other neurologic signs were absent including dysarthria, nystagmus and visual defect.

Results: Diffusion-weighted imaging showed focal diffusion restriction in the right occipital lobe and thalamus. The complete blood count, serum electrolyte, renal and hepatic function test, coagulation profile and autoimmune study were unremarkable within normal ranges. The transthoracic echocardiogram was also unremarkable. Magnetic resonance angiography revealed smooth contoured narrowing of mid to distal basilar artery and *gradient echo* images demonstrated 'double-lumen' sign of basilar artery. The patient's final diagnosis was basilar artery dissection resulting in acute ischemic stroke. He was treated by a dual antiplatelet (aspirin 100 mg, clopidogrel 75 mg) and conservative management. He discharged without any symptoms and signs. Follow up Brain magnetic resonance imaging with vessel wall imaging was done on 42 days from the onset. The 'double-lumen' sign is still observed, and

pseudo-lumen with intramural hematoma in mid to distal basilar artery is confirmed.

Conclusion: We confirmed our patient's condition occurred spontaneously without any other causes. Therefore, basilar artery dissection should be considered as a different diagnosis if the young-age patient presents with brainstem or cerebellar signs even without trauma or other medical history. Though transfemoral cerebral angiography is gold standard for diagnostic evaluation, we performed vessel wall imaging as non-invasive imaging tools. That was useful for diagnosis and follow-up of basilar artery dissection.

Disclosure of Interest: None Declared.

IHC-PO-455

Therapeutic efficacy of pregabalin and greater occipital block on cervicogenic headache -a case series-

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Objective: To compare the therapeutic efficacy of pregabalin alone and in combination with greater occipital nerve (GON) block on cervicogenic headache (CH), which is caused by cervical spinal diseases.

Although CH is reported to be resistant to pharmacological treatments with NSAIDs, a recent small sized (N=34) randomized controlled trial reported that large amounts of pregabalin (341 mg/day) could be effective in patients with CH and post-traumatic headache. To reduce the dose of pregabalin, therapeutic efficacy of multimodal approaches needs to be evaluated.

Methods: We retrospectively analyzed 8 patients with CH, who were diagnosed according to the ICHD-3. Pregabalin was started at 50 mg/day and the dose was increased gradually. The GON block was performed using a mixture of 1% mepivacaine 2 ml and dexamethasone 1.65 mg in patients who were allowed to receive the block, were not undergoing anti-coagulation therapy. The headache intensity was assessed pre-treatment and 2 weeks post-treatment using visual analogue scale (VAS :0–100 mm). Therapeutic response was rated depending on headache intensity reduction under 4 grades: (i) complete headache relief, (ii) excellent (>50% reduction), (iii) good (21–50%), and (iv) poor (<20%).

Results: The study enrolled 8 patients (5 female, 67.6 ± 11.8 years), and all had neck pain and ipsilateral occipital pain with no relief with NSAIDs. The mean disease duration was 2.6 ± 3.2 years (2 months-10 years). Efficacy grades for pregabalin therapy (n=3) were complete=2, excellent=1, and in combination therapy (n=4) were complete=1, excellent=3. The mean dose of pregabalin in the pregabalin alone group and combination therapy group was 58.3 ± 14.4 mg/day and 50 ± 0 mg/day, respectively (p=0.29). Only one patient was treated with GON block alone because dizziness was reported with pregabalin before, but the therapeutic response was excellent.

Conclusion: The present study demonstrated that therapeutic efficacy of combination therapy was not superior to the pregabalin monotherapy. Although there was no significant difference between combination therapy and pregabalin monotherapy for the pregabalin dose, it could be reduced. Further accumulation of patients for a prospective multi-institutional study may be required.

Disclosure of Interest: None Declared.

IHC-PO-456

Intractable temporal headache in a patient with amyotrophic lateral sclerosis under mechanical ventilation

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Objective: To report an unnoticed but serious headache in patients with amyotrophic lateral sclerosis (ALS) under long-term mechanical ventilation.

Methods: Case report.

Results: A 57-year-old bed-ridden woman with ALS receiving mechanical ventilation developed intractable right temporal pain. She had been suffered from the right otalgia and treated with oral antibiotics and analgesics for 3 years. The pain gradually got worse during 2 weeks before the hospitalization. On admission, the right tympanic membrane was erythematous and accompanied with purulent drainage. Contrast-enhanced computed tomography of the brain revealed a ring-enhanced lesion of 3 cm in diameter in the right temporal lobe. There were also soft tissue density and thinning of the tegmen tympani

in the right middle ear cavity. Intravenous antibiotic therapy with meropenem was started immediately, and tympanoplasty and brain abscess drainage were performed simultaneously 12 days after admission. After 8 weeks of antibiotic treatment, the size of brain abscess reduced, and her temporal pain improved. To the best of our knowledge, this is the first case report that a patient with ALS developed brain abscess which spread from chronic suppurative otitis media.

Conclusion: An intractable headache associated with brain abscess secondary to chronic suppurative otitis media should be recognized as one of the serious complications in patients with ALS under long-term mechanical ventilation.

Disclosure of Interest: None Declared.

IHC-PO-457

Bullet train headache—A variant of airplane headache?

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Objective: Headaches caused by riding mass transportation are known to occur. Airplane headache (AH) is a typical example. However, there are almost no reports on headaches occurring from other means of transportation. We report an unique headache induced by getting on the bullet train.

Methods: *Case description:* A 33-year-old male company employee presented with a complaint of headache when riding the Shinkansen, Japan's high-speed train. He had no history of primary headache such as migraine or tension headache, but he did have a history of airplane headache.

Results: Pounding headache from the frontal region to the entire head sometimes occur about 30 minutes to one hour after he boards a high-speed train. He experiences no vomiting, scintillating scotoma, lacrimation, or nasal obstruction. He endures the headache on the train until arriving at his destination, and then when he rests for about 10 minutes in the station the headache dissipates naturally. No abnormalities were identified in his general physical findings, neurological findings, or head MRI or other diagnostic imaging.

Conclusion: Bullet train headache (BH) may be a new type of headache that occurs on mass transportation. The cause is unknown. However, there is a possibility that these headaches occur through similar mechanism

as AH. The change in pressure within the plane is thought to be the most likely cause of headache. The cabin pressure changes considerably as the airplane ascends and descends. According to Boyles law, air expands as the air pressure decreases and air contracts as the air pressure increases. The paranasal sinuses are in the anterior cranial bones. Air accumulates, and normally passes freely in and out through a hole that communicates with the nasal sinuses. However, when these holes become blocked because of inflammation or a congenital anatomical structure susceptible to obstruction, the air in the paranasal sinuses is trapped. In this closed state, the air in the paranasal sinuses expands and contracts during taking off and landing. Changes of air volume can induce inflammation

Table 1. Type of headaches of dissecting aneurysms

	Vascular headache	Muscle contraction headache	neuralgia	History of habitual headache
VA	14	1	4	7
IC	1	1	0	1
PCA	0	1	0	0

VA:vertebral artery IC:internal carotid artery PCA:posterior cerebral artery.

and called "barotrauma". Rapid air pressure changes are also reported to occur within a vehicle at high speed, particularly when going through tunnels and passing other trains. Such an air pressure change may induce BH.

Disclosure of Interest: None Declared.

IHC-PO-458

Current Status of the Headache Clinic of the Second Kawasaki Saiwai Clinic

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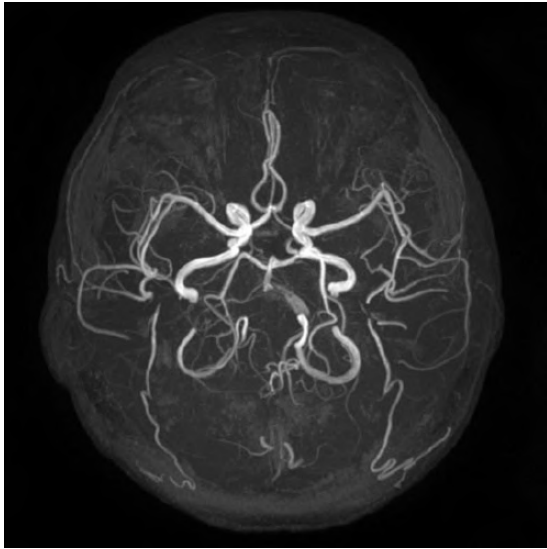
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Objective: Our headache clinic started about 4 years ago as the outpatient department of one of the major hospitals in Kawasaki city. What we wanted to do was investigating the current status of characteristics of our patients with headaches.

Methods: All-first-time patients with headaches filled out our headache questionnaire and most of them took MRI or CT scans as soon as possible if their headaches were

severe or patients had not previously taken those examinations.



Results: 1. Sex ratio and age distribution: 60% of our patients were female and 40% were male. The most common patients were in the 40 age group, followed by the 50 and 60 age groups.

2. Frequency of headache types: 59% of the patients had vascular headaches, muscle contraction headaches accounted for 29%, neuralgia for 8%, and cluster headaches for 5%. Secondary headaches were only experienced by 2% of patients.

3. Secondary headache: In this study the most frequent cause was a dissecting aneurysm (left vertebral dissecting aneurysm). So far, 22 patients with dissecting aneurysms have visited and 19 cases out of these had vertebral dissecting aneurysms. The most common type of their headache was vascular headache and 36% of them had a history of habitual headaches. (table I).

Conclusion: Compared with other headache clinics our results in terms of type of habitual headaches was quite similar. However, the high frequency of dissecting aneurysms was different from other clinics. Easy accessibility to MRI scans might be the reason for this.

Disclosure of Interests: The high frequency of dissecting aneurysms was found in this investigation.

IHC-PO-459

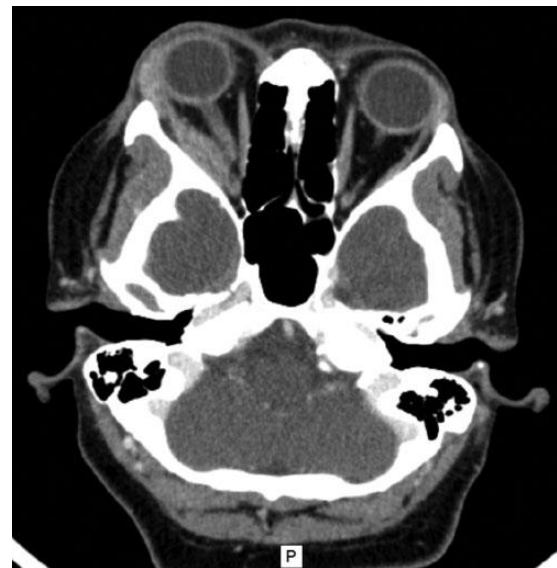
Idiopathic orbital inflammatory pseudotumor treated with low dose of methotrexate

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Objective: This case report has the objective to illustrate a female patient, 36 years old with complaints of sudden diplopia, retro-orbital and temporal headache at the right side, pressure type, no nausea or photo/phonophobia. Orbital and brain MRI and CT scan showed significant inflammation of the extraocular muscles on the right side, after exclusion of lymphoma, metastatic lesions, immunoglobulin G4 related ophthalmic disease, she was diagnosed with idiopathic orbital inflammatory pseudotumor. Treated with prednisone 1 mg/kg with rapid improvement of all symptoms, except for a mild paresis of the lateral rectus muscle. Over 4 years patient developed symptoms at each corticosteroid withdrawal attempt. In the meanwhile she gained weight, developed high blood pressure and diabetes. As a steroid-sparing agent, Azathioprine was initiated up to 2 mg/kg but symptoms returned every dose reduction of prednisone. Methotrexate was then started at 5 mg once a week and after 4 months 10 mg once a week with total remission of symptoms and prednisone could be suspended. After one year of Methotrexate the patient has no more relapses of symptoms.

Methods: This case report was elaborated with medical record and literature review.



Results: After administration of Methotrexate 5 mg once a week and 10 mg once a week after 4 months patients symptoms drastically improved and corticoid could be removed.

Conclusion: Idiopathic orbital inflammation is a rare condition with an exclusion diagnosis that affects the orbit tissue. Its treatment with corticoid and even with Azathioprine is well established, however, there is no guideline or consensus of treatment for patient that do not respond or cannot use corticosteroid for a long time, thus the importance of alternative agents. Our case

demonstrated the efficacy of treatment with Methotrexate in low dose with fewer side effects than corticoid.

Disclosure of Interest: None Declared.

IHC-PO-460

A case study of CGRP receptor blockade in New Daily Persistent Headache secondary to Zika Virus

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Objective: New Daily Persistent Headache (NDPH) is a distinct clinical syndrome which can represent a primary headache disorder or be secondary in aetiology, such as an antecedent viral trigger. NDPH can be bland or be accompanied by migrainous symptoms like photophobia; it's as yet unclear how the endophenotype influences therapeutic response. There are two published cases of a flavivirus, Dengue, causing NDPH, but not yet Zika virus (ZV). This single case report of NDPH secondary to ZV aims to track the clinical progress of multiple medical and interventional management strategies.

Methods: The clinical notes were reviewed regarding the headache semiology, other symptoms of note and comorbidities. The patient was investigated to ensure there were no persistent foci of infection utilising magnetic resonance imaging and repeated lumbar puncture. Response to treatments were measured with a headache diary and Headache Impact Test Score (HIT-6).

Results: This 63 year-old man acquired ZV infection in the Cook Islands in March 2014, confirmed with a positive ZV neutralisation test. Prior to infection there was no personal or family history of migraine. During follow-up investigations there was no demonstrable evidence of ongoing infection. His headaches with migrainous features were not responsive to the triptan class of medications. Since the acute presentation, headache persisted every hour of every day, irrespective of any of the 17 prophylactic treatments trialled. Erenumab 140 mg every 28 days was the only treatment to give a 50% reduction in the migraine days – defined as moderate to severe headache associated with sensitivity to light and noise and movement sensitivity – at both 3 and 6 month follow-up. His ability to exercise and function improved significantly. The HIT-6 score improved from a baseline of 64 to 56 at three months and 36 at six months subsequent to the initiation of erenumab treatment.

Conclusion: This is the first reported case of ZV triggering NDPH. Migrainous features may prompt consideration of utilising migraine preventives to improve symptom severity and quality of life. Further research on the

aetiology and heterogeneity of NDPH and the role therein of calcitonin gene-related peptide (CGRP) is recommended.

Disclosure of Interests: Dr Bronwyn Jenkins has received fees for lectures and advisory boards for Allergan, Eli Lilly, Novartis and Teva. Dr Michael Eller has received lecture and advisory board fees from Novartis.

IHC-PO-461

Worsening of cluster headache with intravenous dihydroergotamine? Think out of the box!

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Objective: To describe subacute angle closure glaucoma (SACG) causing unilateral orbitofrontal pain and mimicking cluster headache (CH) but with deterioration after intravenous (IV) administration of dihydroergotamine (DHE).

Methods: A 36-year-old woman underwent a neurologic and ophthalmic evaluation.

Results: The patient was referred with a diagnosis of chronic CH (International Classification of Headache Disorders Third Edition code 3.1.2.) because of a three year history of episodes with right-sided unilateral orbital pain lasting three to five and a half hours associated with scanty lacrimation and nasal congestion. Pain relief was partial to sumatriptan 6 mg injections but oxygen therapy was not helpful. Maintenance therapy with verapamil, topiramate, indomethacin and prednisolone had failed. Therefore, inpatient treatment with IV DHE was started. Despite this treatment, no relief of pain was achieved, however, she developed additional unilateral redness of the eye and visual loss. Urgent ophthalmic evaluation revealed a best corrected visual acuity of 1/10, corneal edema, narrow anterior chamber angle, ciliary injection and IOP of 38 mmHg, leading to a diagnosis of acute angle closure glaucoma. Treatment with YAG laser iridotomy, acetazolamide and topical pilocarpine and dorzolamide/timolol was initiated with rapid resolution of typical cluster-like orbital pain attacks.

Conclusion: SACG with presumed deterioration caused by IV DHE is presented. The pathophysiological mechanism is unclear, but we hypothesize a role for DHE in angle closure and/or outflow obstruction. Awareness of SACG as a mimic of CH is important in the differential diagnosis of CH to direct a patient to an adapted non-neurologic treatment plan and to prevent visual loss.

Disclosure of Interest: None Declared.

IHC-PO-462**Secondary Cluster Headache Due to Connective Tissue Disorder: A Case Report**

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Objective: Cluster headache is a primary headache characterized by unilateral excruciating pain accompanied by autonomic features. Cluster-like headache secondary to unruptured saccular aneurisms is very rare. Difficult to rupture gigantic aneurisms that reappear after being intervened can be seen in patients with connective tissue disorder.

Methods: To report a clinical case of a young patient with secondary chronic cluster headache due to huge bilateral unruptured saccular aneurisms of the internal carotid arteries, and reappearance of headache symptoms after the aneurisms were surgically intervened.



Results: We describe a case of a 28-year-old man with joint hypermobility and a secondary cluster headache history longer than three years. Patient's headache started a day after he hit his head in the upfront seat in a tram. Headache characteristics corresponded to cluster headache, although there were some red flags such as de novo chronic form, exacerbation when changing head position, partial response to oxygen. Brain MRI revealed two

gigantic unruptured saccular aneurisms of the cavernous segments of the internal carotid arteries. They were intervened endovascularly with coils and onyx. The patient entered a long remission until the cluster headache appeared again (recurrent aneurisms). Based on the clinical presentation, the performed exams, and the response to treatment, secondary cluster headache was established as diagnosis. A connective tissue disorder was suspected as an underlying cause, but the patient refused to be tested genetically.

Conclusion: Although, secondary cluster headache is more common in patients with internal carotid artery dissection, saccular aneurisms can also be the cause. When a young patient is presenting with chronic cluster-like features, MRI should be performed at the start. If the aneurisms have tendency to become huge and the headache reappears after the aneurisms are surgically treated, a connective tissue disorder may be the underlying cause.

Disclosure of Interest: None Declared.

Post-Traumatic Headache**IHC-PO-222****Longitudinal Pediatric Post-traumatic Headache Treatment Outcomes**

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Objective: This study compares the treatment of headache without medications or with simple analgesic medications (NSAID/acetaminophen), triptans, or other headache medications on 3-month headache outcomes in children and adolescents following concussion.

Methods: This study involved 528 pediatric concussion patients (239 females, 289 males), ages 6–18, who presented to any of 5 ConTex clinic sites within 30 days of concussion, completed both initial post-injury and 3-month follow-up surveys, reported no previous history of headache and no previous use of medications for headache (NSAIDs, triptans, opiates, other). Headache severity (0–6 scale, with 6 = worse and 0 = no headache) was assessed in both the initial survey and at 3-month follow-up, and medication use (NSAIDs, triptans, opiates, other) was evaluated at 3-months.

Results: A majority (67.4%) of subjects (n = 356) reported using any medication for acute treatment of PTH following concussion. Regardless of treatment option, the number of subjects reporting headache

decreased from 75.4% at initial post-injury visit to 18.6% at the 3-month follow-up surveys ($p < 0.035$). However, individuals with headache who used only NSAIDs acutely for symptom relief did not show significant resolution of headache at 3 months compared to subjects who chose to not use medications ($p = 0.165$). Significant differences in headache prevalence at 3-month follow-up were noted in those who used only triptans. Specifically, 5 out of 5 subjects who only used triptans reported persisting headache at 3-months compared to 10 out of 28 of those using triptans in combination with NSAIDs or 23 out of 172 using only NSAIDs ($p < 0.001$).

Conclusion: In this population of pediatric subjects with acute concussion and headache, individuals who used headache medications, like NSAIDs, for post traumatic headache did not report a statistically significant improvement in headache symptoms at 3 months versus those who did not use medication. Furthermore, although the number was small, all subjects using only triptans reported persisting headache at 3-months. Presumptions that early aggressive acute treatment of PTH may need to be reconsidered. Further research that focuses on PTH phenotype, potential biomarkers, treatments, and outcomes is indicated.

Disclosure of Interest: None Declared.

IHC-PO-223

Post-traumatic headache: magnetic resonance diffusion tensor imaging analysis

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Objective: Post-traumatic headache is a complicated disorder. Magnetic resonance imaging (MRI) typically shows no or mild injury despite patients complaining of severe sustained headache. We applied a new MRI technique involving diffusion tensor imaging (DTI) and neurite orientation density dispersion imaging (NODDI). The purpose of this study was to establish an objective diagnostic method for post-traumatic headache and to discover its pathophysiology.

Methods: Seven post-traumatic headache patients were included in this study (3 male and 4 female patients; 42 to 81 years old). Whole-brain DTI and NODDI scans were analyzed using tract-based spatial statistics (TBSS) for all patients. Regions of interest (ROIs) were placed at the splenium, body and genu of the corpus callosum, and the mean fractional anisotropy (FA) was measured. Seven healthy age- and sex matched volunteers underwent the same imaging.

Results: There were no marked difference in the age and sex between patients and healthy volunteers ($p > 0.05$). TBSS and ROI analyses showed no significant differences in DTI findings and the FA between patients and healthy volunteers. NODDI demonstrated low orientation dispersion at bilateral cerebral and brain stem tract in patients.

Conclusion: NODDI may be useful to evaluate the pathology in the patients with post-traumatic headache.

Disclosure of Interest: None Declared.

IHC-PO-224

Studying post-traumatic headache in animal models of traumatic brain injury

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Objective: Post-traumatic headache (PTH) after traumatic brain injury (TBI) is debilitating and hard to diagnose. Unfortunately, PTH is highly prevalent in active duty personnel, Veterans, as well as in sport athletes. The high incidence and chronic nature of PTH underscores the need to study these problems in animal models in order to develop new and effective treatments. The foundation of our study is the fact that PTH has many symptoms of chronic migraine.

Methods: We proposed to evaluate photosensitivity (light-aversion assay), tactile hypersensitivity (periorbital and plantar von Frey assays) and facial signs of discomfort (mouse grimace scale) in two mouse models of mild TBI: the blast-induced TBI model and the closed-head injury (mCHI) model induced by weight drop.

Results: Here we show that neither model can induce spontaneous photophobia or facial signs of discomfort. However, blast-injured animals develop both cephalic and extra-cephalic allodynia starting 1 week after the injury and persisting for at least 9 weeks. In the mCHI model, injured mice only develop cephalic hypersensitivity between day 1 and day 5 after the injury. We also investigated the repercussions of fox urine exposure (predator) and of subthreshold administration of calcitonin gene-related peptide on the previously mentioned symptoms.

Conclusion: In sum, we report here for the first time the development of a chronic pain phenotype following TBI in mice. Other phenotypes need to be explored to finish characterizing those models.

Disclosure of Interest: None Declared.

IHC-PO-463**Rationale and study design for a randomised, single-centre, double-blind, sham-controlled study of non-invasive vagus nerve stimulation for the treatment of post-traumatic headache**

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Objective: Worldwide, ~69 million people per year sustain a traumatic brain injury (TBI), and post-traumatic headache (PTH) is common after such injuries. There has been little study of treatments for mild TBI (mTBI) or PTH, and clinicians often use drugs approved for primary headache disorders. Many patients self-treat with over-the-counter agents or non-steroidal anti-inflammatory drugs, which often provide suboptimal relief. We initiated a randomised, double-blind (DB), sham-controlled, parallel-group pilot study of non-invasive vagus nerve stimulation (nVNS) to treat PTH.

Methods: The study is enrolling adults who present 1–4 weeks after a head injury, meet ICHD-3 criteria for acute headache attributed to mTBI, and have ≥ 2 headaches/week with a migraine or probable migraine phenotype. After a 2-week run-in period, subjects will be randomly assigned (1:1) to receive daily preventive therapy and as-needed acute treatment with nVNS or a sham device. Preventive therapy will consist of two 120-second stimulations given 3 times daily. Acute treatment will comprise 2 stimulations delivered at headache onset, followed by 2 stimulations 20 minutes after the start of initial treatment. Subjects are not to use acute rescue medication for 120 minutes post-treatment. Up to 80 subjects will be enrolled at 1 North American site. The expected duration is 12 months (9 months for enrolment, 14 weeks for active participation).

Results: The primary effectiveness endpoint is the decrease in pain (on a 7-point numeric scale) at 60 minutes post-treatment for all treated headache attacks. Secondary endpoints include decrease in the frequency of headache days between the run-in period and the last 2 weeks of the DB period and responder rates (ie, percentages of subjects with $\geq 50\%$ decrease in attack frequency). The primary safety endpoint is the incidence of treatment-related serious adverse events.

Conclusion: This study is designed to assess the efficacy and safety of nVNS as a novel therapy for PTH.

Disclosure of Interests: B. Vargas has received advisory board fees from Amgen, Novartis, Allergan, Alder, Teva, Lilly, Upsher-Smith, Biohaven, Promius, and Xoc and has received speaker fees from ATI. He serves on the board of directors for the American Headache Society and the

Headache Cooperative of the Pacific and is an editorial board member for *Neurology Today*.

E. Liebler is an employee of electroCore, Inc., and receives stock ownership.

S. Bunt has no financial conflicts of interest to declare.

C. Supnet has no financial conflicts of interest to declare.

IHC-PO-464**A case of sluder's syndrome treated with block of sphenopalatine ganglion**

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Objective: We present a case report of a 24 years old healthy patient, who has been referred to outpatient care for atypical facial neuralgia. He has an history of maxillo-facial trauma with multiple fractures stabilized with plate osteosynthesis 3 years before, followed by a complete removal of the plates. He has been experiencing chronic facial neuralgia with multiple episodes per day with Numerical Rating Scale (NRS) 10, localized to the right hemiface, associated with chemosis, lacrimation and rhinorrhea, and exacerbated by environmental temperature changes, mastication and by the intake of both hot and cold food and drinks. Based on the medical history, clinical examination and a head MRI we performed, Sluder's syndrome has been diagnosed in January 2019. At the time of our first medical examination he was being treated with prednisone and carbamazepine with inadequate pain relief. We suggested the transnasal block of the right sphenopalatine ganglion with bupivacaine through a mini-invasive technique.

Methods: A cycle of ten blocks of the right sphenopalatine ganglion with bupivacaine 0.5% 0.3ml using the "TX360 Nasal Applicator" (Tian Medical, LLC) on alternate days has been planned, starting on February 13th 2019. The intensity of pain measured with NRS, the number of pain episodes per day and the extent of autonomic signs have been assessed before and after every block.

Results: We performed a cycle of only six nasal blocks every other day. Since the first administration, NRS has decreased from 9 ± 1 to 2 ± 1 and the number of episodes per day has decreased from 8 ± 2 to 1 ± 1 . Autonomic signs disappeared after the first block. After the third administration the daily episodes disappeared with marked improvement in the patient's quality of life. We continued the treatment until the sixth block, but due to the disappearance of the symptomatology it was decided

to suspend the therapy. After about two months the patient reports absence of pain and autonomic signs without any relapse.

Conclusion: Mini-invasive transnasal block of sphenopalatine ganglion may be a successful therapy in the treatment of Sluder's syndrome.

Disclosure of Interest: None Declared.

Psychological and Behavioural Factors and Management

IHC-PO-225

Individual-level patterns of perceived stress throughout the migraine cycle: A longitudinal cohort study using daily prospective data

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Objective: To determine individual patterns of perceived stress across stages of the migraine cycle.

Methods: Individuals with migraine registered to use the mobile headache diary NI-Headache[®] and completed 90 days of daily data entry, including perceived stress, rated on a 0–10 scale. Days were categorized into phases: P1 = prodromal (2 days prior to the first day with migraine), P2 = migraine (migraine days per International Classification of Headache Disorders-3 definition), P3 = postdromal (2 days following the last migraine day with migraine), P0 = interictal days (other days). Individuals with at least 5 days in each phase were eligible and data from their first 90 days were used. The odds of stress were modeled with a multinomial regression model using sex, age and phase as covariates. A two-step cluster analysis (hierarchical and a k-means) was used to determine the number of patterns of stress variation.

Results: In 730 participants (n = 730), the mean perceived stress rating was 3.4 (standard deviation = ± 2.4) and the median was 3.0 (interquartile range = 3.0). The odds of high perceived stress scores increased in P2 and to a lesser extent in P1 relative to P0 (p < 0.0001), in females relative to males, and decreased with age (p < 0.05). Cluster analysis uncovered 6 dominant patterns of stress variation. Although P2 had the highest odds of elevated perceived stress scores in the regression model, results of the cluster analysis indicate that this is only true for 3 clusters of participants (cluster 1: n = 205, cluster 3: n = 78 and cluster 6: n = 156). Other interesting and

distinct patterns were seen in clusters 2 (n = 79), 4 (n = 136) and 5 (n = 75).

Conclusion: Although on an aggregate level perceived stress peaks during the pain phase, in individuals there appear to be 6 distinct dominant patterns of stress variation across the migraine cycle. A better understanding of how stress and other related factors vary across the migraine cycle in individuals may allow for insights into disease biology and facilitate targeted individualized treatment plans in the future.

Disclosure of Interests: Serena Orr: Receives royalties from Cambridge University Press.

Marina Vives-Mestres: Is a consultant for Curelator, Inc.

Stephen Donoghue: Is a consultant for Curelator, Inc.

Kenneth Shulman: Is a consultant for Curelator, Inc.

Alec Mian: Is the founder and CEO of Curelator, Inc.

IHC-PO-226

A Pilot Randomized Controlled Trial to Assess the Impact of Motivational Interviewing on Initiating Behavioral Therapy for Migraine

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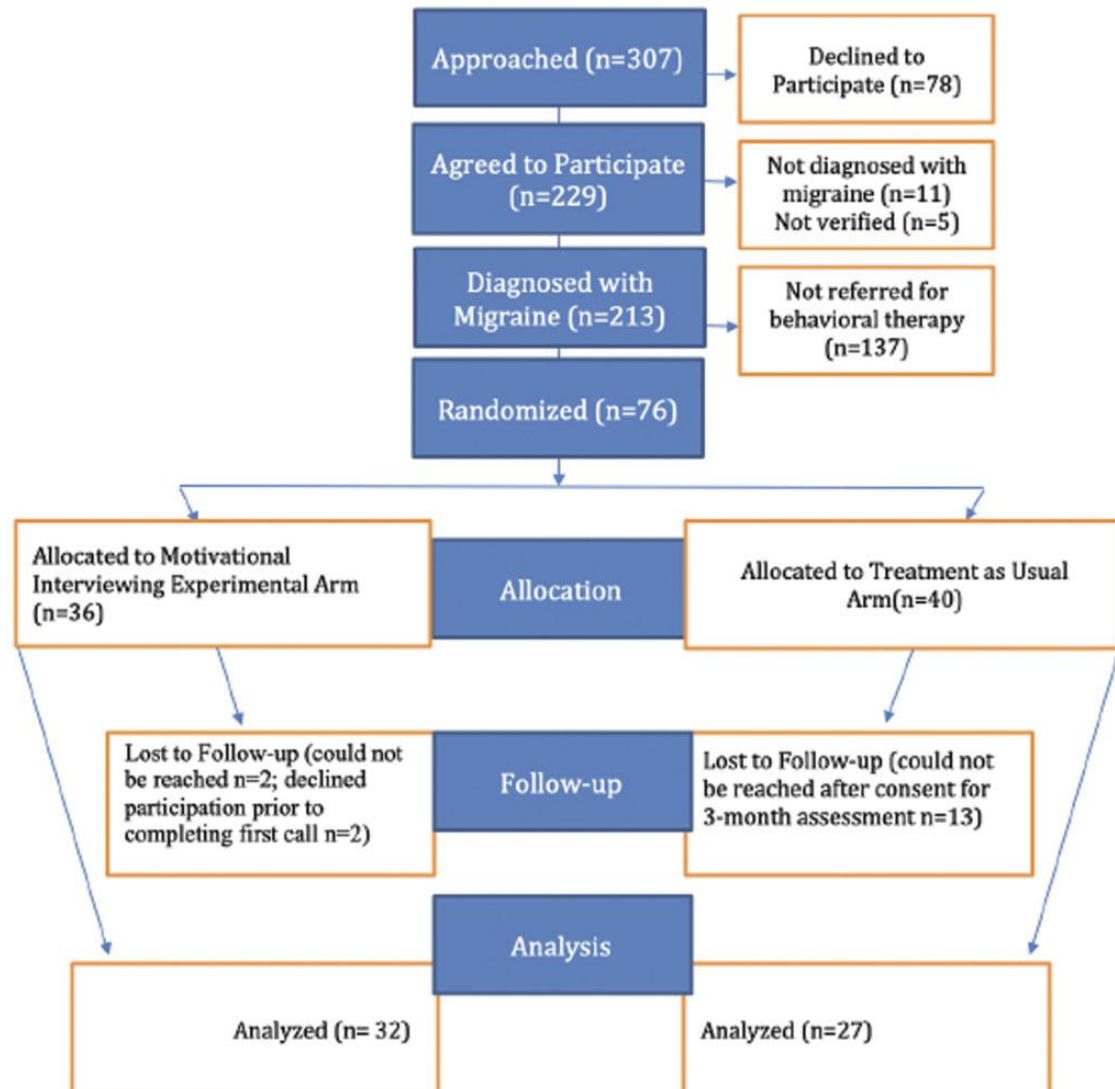
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Objective: Relaxation, biofeedback, and cognitive behavioral therapy are considered grade-A, evidence-based behavioral therapies (BT) for migraine. Despite the efficacy of these BTs, only ~50% of patients initiate BT recommended by their headache specialists. Motivational interviewing (MI) is a BT to help patients explore and overcome ambivalence to enact positive change in their lives. We tested whether telephone-based MI improves initiation, scheduling, and attending BT for migraine prevention.

Methods: Participants, consecutively recruited during their appointments with headache specialists, participated in a single blind randomized controlled trial comparing telephone-based MI to treatment as usual (TAU). Inclusion criteria: age 16–80, ICHD criteria migraine diagnosis, and referral for BT for migraine prevention during the same appointment. Exclusion criteria: participation in BT for migraine in the past year. Non-clinicians trained in MI conducted MI calls. MI group participants received max 5 MI calls. Both groups were called ~3 months to collect data. Statistical analyses: descriptive statistics, t-tests and logistic regression.

Results: 76 patients were enrolled and randomized (n = 36 MI, n = 40 TAU), mean age: 39 ± 12, 95% female, all had health insurance. Mean number of headache days/month: 12.0 ± 9.0. 70.9% were moderately-severely



Abstract number: IHC-PO-226

disabled (via migraine disability assessment scale (MIDAS)). The mean number of MI calls/participant: 2.69 ± 1.56 [0–5], mean call time: 12.10 ± 5.13 [4–28] mins. MI group participants were more likely to initiate making an appointment (65.6% vs. 40.7%, $P=0.03$), no difference in scheduling (34.4% vs. 22.2%, $P=0.30$) or attending (21.9% vs. 22.2%, $P=0.97$).

Conclusion: Telephone-based MI improved initiation rates for BT, but not rates of attendance or scheduling appointments. Many barriers identified in prior studies seem to lessen the effect of telephone-based MI on scheduling and attending BT appointments. Future studies might be conducted to combine MI and problem-solving approaches targeting other patient barriers to following BT recommendations.

Disclosure of Interests: Mia Minen, MD, MPH- salary support funding from NCCIH, travel funds to meetings of

the American Academy of Neurology Guidelines Development, Dissemination and Implementation Subcommittee, as she is a member, and travel funds to the American Headache Society's meetings as she is an AHS General Board member. A Co-Section Head of the Headache Section of Pain Medicine and an Associate Editor of the journal *Headache*.

Gabriella Sahyoun-none.

Ariana Gopal-none.

Valeriya Levitan, MD-none.

Elizabeth Pirraglia, MA-none.

Naomi M. Simon, MD. MSc.

Audrey Halpern, MD-pharmaceutical speaking disclosures.

IHC-PO-227**Allostatic load in migraine patients: a pilot study using an integrated psychosomatic and biochemical approach**

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Objective: Migraine may be considered a disorder of Allostatic Load (AL). The aim of our study was to assess the relationships between AL, psychological and psychosomatic variables in a group of episodic (EM) and chronic migraine (CM) outpatients compared to healthy controls (HC).

Methods: AL was calculated based on a composite index of 20 biomarkers reflecting neuroendocrine, cardiovascular, metabolic, immune systems and anthropometric status. Relationships between AL index, psychosomatic syndromes (Diagnostic Criteria for Psychosomatic Research; DCPR), psychopathology (Structured Clinical Interview for DSM-5; SCID-5-CV), perceived stress (Perceived Stress Scale; PSS) were assessed in migraine patients and in HC. Patients with EM were divided into 2 categories: low/moderate-frequency migraine (1 to 9 days of headache/month) and high-frequency migraine (10 to 14 days of headache/month). Fisher's exact test was used for the comparisons between migraine patients and HC. Spearman's rho was used to evaluate the correlations between AL and psychological and psychosomatic variables. P-value <0.05 was considered significant.

Results: 41 migraine patients (32 with EM; 9 with CM) and 34 HC were enrolled. Most of patients showed moderate AL (46%) and high AL (27%) versus HC (35% and 18%). High AL was more prevalent in high-frequency EM (50%) compared to CM patients (33%). Demoralization and allostatic overload (DCPR syndromes), depressive and anxiety disorders (SCID), higher perceived stress scores (PSS) were mostly reported by migraine patients than HC.

Conclusion: Our preliminary results showed a migraineurs' trend to report a higher AL index and more SCID and DCPR syndromes. Despite this, there was no statistically significant difference because of the small sample size. This is an ongoing study that suggests to examine the role of AL and its correlation with psychological and psychosomatic factors in migraine patients.

Disclosure of Interests: Prof Cortelli has received honoraria for speaking engagements or consulting activities until 20th September 2018 with Abbvie, Lilly, Teva,

Novartis, UCB Pharma S.p.A, Chiesi Farmaceutici. Dr Pierangeli has received honoraria for speaking engagements or consulting activities with Teva, Allergan, FB Health. Dr Di Tillo, Dr Cevoli, Dr Zenesini, Mrs Fontana, Prof Grandi, Prof Tossani have nothing to disclose.

IHC-PO-228**Triptan and/or ergotamine-associated overdoses in the United States: Analysis of the National Poison Data System**

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Objective: Suicidal ideation and behaviors are overrepresented in migraine. The objectives of our study were to examine the clinical outcomes of intentional overdoses involving triptans and ergotamines, and describe effects of triptan and ergotamine toxicity.

Methods: This is a 5-year retrospective study (01/2014–12/2018) using data from the National Poison Data System (NPDS). Demographics, exposure characteristics, and outcomes were described. Univariate logistic regression was used to estimate the odds ratio for major effect or death vs minor, moderate, or no effect. A multivariable logistic regression model with inclusion criteria of $p < 0.1$ in univariate analysis was implemented with backwards selection. All hypotheses were two-sided with $p < 0.05$ considered significant.

Results: In this population ($n = 1489$), multiple exposure was most common ($n = 1145$). The mean age was 31.2 years and 80.4% were female. Suicidal intention was suspected in 80.9%. Multiproduct overdoses included benzodiazepines (23.1%), tricyclic antidepressants (TCAs, 12.6%), opioids (19.9%), and butalbital (0.2%). Major effects were seen in 6.5% and death in 0.4%. Sumatriptan was the most common triptan (76.16%). Features of isolated triptan ingestion ($n = 328$) included: hypertension (14%), tachycardia (10.7%), drowsiness (11%), nausea (6.4%), vomiting (4.6%), vertigo (4%), non-cardiac chest pain (3.7%), and diaphoresis (2.4%). The most common symptoms in isolated ergotamine ingestion ($n = 16$) were abdominal pain (16%), vomiting (12.5%), numbness (12.5%), nausea (6.3%), diarrhea (6.3%), and vertigo (6.3%). Multivariable logistic regression found significantly increased risk of major event or death due to age [OR(95% CI) 1.02(1.01, 1.04), $p = 0.004$], multiple product exposure [OR(95% CI) 9.50(2.29, 39.48), $p = 0.002$], and concomitant benzodiazepines [OR(95% CI) 1.71(1.05,

2.78), $p = 0.032$] or TCAs [OR(95% CI) 3.16(1.88, 5.31), $p = <0.001$].

Conclusion: The risk of major effect or death was overall low, and predicted by age, multiple product exposure, and concomitant benzodiazepines or TCAs. The triptan toxidrome consists of hypertension, tachycardia and drowsiness. The toxic effects of ergotamine were acute gastrointestinal syndrome with vertigo and numbness.

Disclosure of Interest: None Declared.

IHC-PO-229

The Cluster Headache Scales (CHS) – Development and Psychometric Evaluation of a Self-Report Questionnaire

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Objective: Cluster headache (CH) is a primary headache disorder characterized by recurrent unilateral attacks of severe headaches. The disorder is associated with several psychological factors such as emotional and functional disability, psychological strain, and different ways of coping. We aimed to develop a self-report questionnaire that measures a broad range of psychological relevant aspects of the cluster headache disorder – the Cluster Headache Scales (CHS).

Methods: The CHS were constructed based on literature as well as semi-structured interviews with patients and practitioners. It consists of three parts: (I) socio-demographic data, (II) disorder characteristics (type, duration, current disorder activity, treatment, trigger), and (III) psychological aspects with the assumed core areas (a) strain, (b) disability, and (c) coping. The questions of part III (95 items in the study version) are to be answered on a 5-point Likert scale (strong rejection to strong agreement). An online survey including the CHS and other questionnaires (e.g. the Headache Disability Inventory) was conducted with $N = 302$ CH sufferers.

Results: Explorative factor analysis of part (III) yielded five subscales, each with a good to excellent Cronbach's alpha (α). We labeled the subscales as (a) disability, $\alpha = .90$, (b) anxiety/fear, $\alpha = .91$ (c) aggression, $\alpha = .81$, (d) medical care, $\alpha = .83$ (e) sleep $\alpha = .83$. Thus, CHS part III could be reduced to 29 items. The correlation between subscales of the CHS and scales of other relevant measures was moderate or strong ($r = .39$ to $.79$) and statistically significant.

Conclusion: Our results support the use of the CHS as a reliable and valid self-report questionnaire for assessing CH disorder associated psychological factors. This tool could be used for clinical research and for treatment

planning. Future research should aim to determine retest reliability.

Disclosure of Interests: Timo Martin Klan, Annabella Vales, Michael Witthöft: None.

Charly Gaul has received honoraria for consulting and lectures within the past three years from Allergan Pharma, Ratiopharm, Boehringer Ingelheim Pharma, Lilly Germany, Novartis Pharma, Desitin Arzneimittel, Cerbotec, Bayer vital, Hormosan Pharma, electroCore, Grünenthal, Reckitt Benckiser, and TEVA.

Eva Liesering-Latta has received honoraria for lectures within the past two years from Allergan Pharma, Lilly Germany, Reckitt Benckiser.

IHC-PO-230

ACT for Migraine: Effect of Acceptance and Commitment Therapy (ACT) for High Frequency Episodic Migraine without Aura: A phase-II, multicentric, randomized, open-label study

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Objective: Patients with High Frequency Migraine without Aura are particularly exposed to the risk of chronification and they need a multidisciplinary approach to manage their problem before than a chronic condition is induced. Recently, non-pharmacological approaches showed efficacy in treatment of pain conditions and migraine, comparable to pharmacological prophylaxis at long-term. The goal is to create in the patients psychological flexibility to improve mental and physical states, disability, and favorably impact in pain conditions. Aim of the study was to assess the feasibility and effectiveness of a novel ACT model for patients with High Frequency Migraine without Aura (with/without Medication Overuse).

Methods: Twenty-four patients with High Frequency Migraine without aura were included and randomized for the study. Two treatment conditions: 1) TAU (Treatment as Usual): pharmacological prophylaxis (topiramate, amitriptyline, beta-blocker, Ca-channel blockers) (11 patients); 2) TAU + ACT (13 patients). ACT consisted of six 90 minutes weekly sessions, and two booster sessions, every 15 days; small groups of patients (7–10 patients each). Sessions included: psycho-education, discussions, experiential exercises and home assignments.

Results: All patients arrived to the 6month follow-up visit. Results showed a decrease in days of headache /month in the ACTgroup (10 vs 7.2; -3.8 the difference between pre and 6month); in the TAUGroup the days of headache per month did not change (9.2vs 9.4; $+0.2$ the difference between pre and 6month). Also a decrease of medications intake per month was observed in the ACT Group (9.2 vs 5.5; -3.7 the difference between pre and 6month). A slight decrease was observed in the TAUGroup (9.9 vs 8.2; -1.7 the difference between pre and 6month). Patients in the ACT group were actively involved and participated regularly at the sessions.

Conclusion: Although preliminary, results show that ACT seems beneficial for this category of patients. An integrated and flexible treatment program combining different approaches may be more effective than drugs alone to alleviate pain, to reinforce clinical improvement.

Disclosure of Interest: None Declared.

IHC-PO-231

Detecting factors associated with “low” and “high” headache pain days in individuals with chronic migraine

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Objective: We previously used Cox models to identify individual factors associated with migraine attack occurrence. However in individuals with chronic migraine (CM) this methodology fails because of inability to identify distinct attacks when there are more days with headache than with no pain. We describe an alternative statistical method to determine factors associated with 1) more severe pain (“high” pain days) and 2) less severe pain “low”, pain days) in individuals with CM.

Methods: Individuals with migraine used a digital health platform (NI-Headache[®]) daily for 90 days, entering headache details and peak pain severity (none/mild/moderate/severe). In those retrospectively classed as having CM (ICHD-3 criteria) associations between daily self-reported factors and a) “low” pain days (peak severity = none or mild pain) and b) “high” pain days (moderate or severe pain) were determined using univariate logistic models.

Results: Data from 141 CM individuals were analysed: 90.1% female; mean (SD) age 43.9 (13.7); average headache days/month 23.4 (4.5), of which 19.4 (5.7) were migraine days. Overall we found one or more factors associated with “high” pain days in 95% individuals. For comparison, the Cox model identified one or more factors associated with attack occurrence in only 54.6%. The top five factors associated with “high” pain days were: light sensitivity

(66.6% individuals), noise sensitivity (50%), poor concentration (46.2%), allodynia (39.7%) and neck pain (36.2%). The top five associated with “low” pain days were: happiness (33.3%), feeling refreshed after sleep (31.8%), sleep quality (21.2%), relaxedness (15.8%) and white wine intake (13.3%). Considerable inter-individual variability demonstrates the need for analysis at the individual level.

Conclusion: Our method identifies factors associated with pain intensity in CM individuals. The most common factors associated with “high” pain days were all typical migraine attack symptoms; for “low” pain days top factors were related to good sleep, good mood and white wine. Whilst causality has not been determined, individuals may be able to use this information to make lifestyle changes which improve (self) management of their condition.

Disclosure of Interests: S Donoghue, M Vives-Mestres and K Shulman are Consultants to Curelator Inc.

IHC-PO-232

Is stress associated with pain severity in chronic migraine?

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Objective: To determine in individuals with chronic migraine (CM) 1) how many suspect stress as a trigger and 2) for how many an association between stress and migraine severity can be identified statistically.

Methods: Individuals with migraine registered to use NI-Headache[®] and answered questions about factors they suspect contribute to attack occurrence, including stress, and their importance (1 = low; 10 = maximal). They then used Curelator Headache[®] daily for 90 days, entering details of headaches and tracking daily factors possibly associated with migraine attack risk: self-reported stress was determined using a single question and a 0–10 scale. After 90 days all factors were analyzed for each individual retrospectively classed as having CM (ICHD-3 criteria). The association between daily self-reported stress and peak migraine severity comparing a) “low” pain days (peak severity = none or mild pain) vs. b) “high” pain days (moderate or severe pain) was determined via a univariate logistic regression.

Results: Of 136 individuals with chronic migraine, stress was suspected as a trigger by 125 (91.9%): mildly suspected (1–3) by 9.6%; moderately (4–6) by 19.1%; strongly (7–10) by 63.2%. Only one did not suspect it; 9 did not answer. In 120 (88.2%) of these individuals who suspected stress and who entered sufficient daily data for analysis, stress was shown to be associated with increased risk of a “high” pain day in 34 (28.3%), with no association found in

the other 86 (71.7%). In nine who did not answer the question about suspecting stress, associations with severity were found in two, and no association in seven.

Conclusion: Stress is commonly suspected to be a trigger of migraine attacks. However determining statistical associations with attack occurrence in individuals with chronic migraine is often not possible because attacks are not distinct. Using an alternative approach we determined the association of stress with “high” and “low” pain severity days and showed that in more than one-quarter of individuals, stress is associated with “high” pain days. Further work is needed to determine causality.

Disclosure of Interests: S Donoghue, K Shulman and M Vives-Mestres are Consultants to Curelator Inc.

IHC-PO-233

Does the Evidence Support “Migraine Diets”?

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Objective: “Migraine diets” are used as a lifestyle modification treatment for migraine. This study reviews the evidence for gluten free, IgG elimination, anti-histamine or IgE allergy avoidance, tyramine-free, ketogenic, high

omega-3/low omega-6 (H3/L6), sodium, low fat, and low glycemic index diets.

Methods: A literature search was done using MEDLINE March 2019. MeSH terms included Headache, Migraine, and Diet as well as a manual review of references. Relevant results are reviewed.

Results: There were 748 articles including 2 systematic reviews, 9 randomized controlled trials (RCT), 8 prospective and 1 retrospective studies. There is support for gluten free diets in celiac disease. Anti-histamine and IgE avoidance but not tyramine-free diets are supported. Ketogenic and low fat diets are supported. The H3/L6 and low glycemic index diets are supported, but low sodium & IgG diets are inconsistently supported. See table 1.

Conclusion: The current evidence for migraine diets is suboptimal despite positive trials, and not sufficiently supported to recommend clinically. It is unclear if individual genetic responses to certain diets or improved eating habits are the underlying factor.

Disclosure of Interests: Robblee: No disclosures.

Starling: Alder, eNeura, Amgen, Eli Lilly & Company, Novartis.

Table 1. “Migraine Diets”

Diet	Studies	Population	Outcomes
Gluten Free	1 Systematic review	Celiac Disease ± HA/migraine (n=42,388)	↓Frequency
IgG	3 RCT	1) Migraine + IBS (n=21) 2) Migraine (n=30) 3) Migraine (n=167)	↓HA days & abortive use ↓ HA & Migraine days ∅ Response
Histamine	1 Prospective	Chronic daily Headache (n=28)	↓Frequency by >50%
IgE	1 Prospective	Migraine with +/- Skin Prick test	↓Frequency in + skin prick test group
Tyramine	1 Prospective	Migraine (n=24)	∅ Response
Ketogenic	1 RCT 2 Prospective	1) Migraine & Overweight (n=96) 2) Migraine (n=18) 3) HA in teens (n=8)	↓Frequency & abortive use ↓Frequency & duration ∅ Response
H3/L6	1 Systematic review 1 RCT	1) Migraine (diet or supplement) 2) Chronic migraine	↓Frequency, duration & severity ↓Frequency
Sodium	1 Retrospective 2 Prospective	1) Migraine (n=8819) 2) Hypertension (n=976 + 399)	↑sodium: ↓migraine probability ↓sodium: ↓frequency & severity
Low Fat	2 RCT 1 Prospective	1) Migraine (n=42) 2) Migraine (n=83) 3) Migraine (n=54)	↓Severity, but not frequency ↓Frequency & severity ↓Frequency, duration, severity & abortive use
Low glycemic	RCT	Migraine (n=350)	↓Frequency & severity (Diet & Preventive groups)

mo=months, wks=weeks, d=days, HA=headache

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Diet	Studies	Population	Outcomes
Gluten Free	1 Systematic review	Celiac Disease ± HA/migraine (n=42,388)	↓Frequency
IgG	3 RCT	1) Migraine + IBS (n=21) 2) Migraine (n=30) 3) Migraine (n=167)	↓HA days & abortive use ↓ HA & Migraine days Ø Response
Histamine	1 Prospective	Chronic daily Headache (n=28)	↓Frequency by >50%
Tyramine	1 Prospective	Migraine (n=24)	Ø Response
Ketogenic	1 RCT 2 Prospective	1) Migraine & Overweight (n=96) 2) Migraine (n=18) 3) HA in teens (n=8)	↓Frequency & abortive use ↓Frequency & duration Ø Response
H3/L6	1 Systematic review 1 RCT	1)Migraine (diet or supplement) 2)Chronic migraine	↓Frequency, duration & severity ↓Frequency
Sodium	1 Retrospective 2 Prospective	1) Migraine (n=8819) 2) Hypertension (n=976 + 399)	sodium: ↓migraine probability ↓sodium: ↓frequency & severity
Low Fat	2 RCT 1 Prospective	1) Migraine (n=42) 2) Migraine (n=83) 3) Migraine (n=54)	↓Severity, but not frequency ↓Frequency & severity ↓Frequency, duration, severity & abortive use
Low glycemic	RCT	Migraine (n=350)	↓Frequency & severity (Diet & Preventive groups)

Abstract number: IHC-PO-233

IHC-PO-234

An Interdisciplinary Cognitive Behavioral Program for adults with severe migraine in a Headache center of a General Hospital

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Objective: The purpose is to describe an interdisciplinary headache program, to report on patient perceptions and patient treatment outcomes on an impact scale of migraine. We believe that every patient has to become his own migrainespecialist to make the best choices in life and cope with their migraine (self-management). An interdisciplinary approach where all health-practioners speak the same “language” was created. The program is semi-structured and uses up-to-date information.

Methods: The self-management program “Grip on your Migraine” is developed in close cooperation with relevant specialists of the Headachecenter. There where 12 groups of mean 7 adults (mostly women). It’s a closed group with a semi-structured program, 6 sessions of 2 hours and an evaluation-session after 3 months. Fixed parts of the program; up-to-date education about phenomenology, pathophysiology, “learning to cope triggers”, CBT-elements, lifestyle counselling and different relaxation-exercises. Relevant specialists (neurologist, psychologist,

gynecologist, pharmacist, physiotherapist) joined the program. All questions from patients were answered. Patient perceptions of the program were obtained with questionnaires, an overall rate and using HDI-scores.

Results: The perception of the patients of the interdisciplinary treatment was very positive (high scores) and the participation of the specialists was highly appreciated. The compliance was good. Elements described as positive are; acknowledgement, counseling, a positive approach to self-management, up-to-date information, CBT elements and relaxation. The HDI-score for the 12 groups overall were not significantly reduced, but a closer look shows very different results. The program elements described as influential for life changes were different for patients (from medication to relaxation, to CBT and learning to cope).

Conclusion: This interdisciplinary program is described as very high appreciated by patients with severe migraine. The program with cooperation of different specialists was received as beneficial. Up-to-date education, relaxation and learning to cope with triggers where the most appreciated parts. Optimal acknowledgement helped to accept a psychological approach and opens new ways for patients.

Disclosure of Interest: None Declared.

IHC-PO-235**Role of maternal stress and alexithymia in children's migraine severity and psychological profile**

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Objective: Recent studies showed that patients' attachment style and maternal alexithymia traits may impact on psychological profile and pain expression in children/adolescents suffering from migraine. So far, very few studies explored the relationship between maternal stress, children's psychological profile and migraine severity. Aims of our study were to explore the role of maternal parenting stress and alexithymia on: 1) children's headache severity (frequency); 2) maternal perception of children's psychological conditions and 3) children's psychological profile.

Methods: We studied 51 migraineurs (mean age 11.6 ± 2.1 years; 22 M and 29 F). Patients were divided in two groups according to the headache attacks frequency (high and low). Maternal stress and alexithymia levels were evaluated by PSI-SF and TAS-20 questionnaires. We used SAFA "Anxiety" and "Depression" scales to explore children's psychological profile. To evaluate maternal perception of children's psychological conditions CBCL 6/18 was employed.

Results: We found a correlation between maternal stress and CBCL Internalizing ($p = 0.00$), Externalizing ($p = 0.00$) and Total scales ($p = 0.00$). A positive correlation has been identified between mothers' PSI Total score and SAFA-D Total score ($p = 0.03$). In particular, a positive correlation was found between "Parental distress" and children's SAFA-D "Feeling of guilt" subscales ($p = 0.04$). Maternal stress and alexithymia did not show significant differences among the two migraine frequency groups ($p > 0.05$). However, in high frequency group, PSI Total score showed a positive correlation with Internalizing scale ($p = 0.00$). No relationships were found between TAS-20, CBCL, SAFA and migraine frequency.

Conclusion: Maternal stress has no relationship with children's migraine frequency. However, it shows a relationship with maternal perception of children's psychological

profile and patients' depressive symptoms, which in turn may impact on migraine severity.

Disclosure of Interest: None Declared.

IHC-PO-236**Psychosocial risk factors for headache in slovenia**

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Objective: Headache is a common disabling condition related to high health system burden. It can be deleterious for psychological and social well-being. In Slovenia psychosocial factor for headache are not well established. To identify population groups at very high risk for headache and thus enable more focused prevention actions in Slovenia.

Methods: Data originate from the national survey carried out in 2012 which was a part of the CINDI program. A self-administered postal questionnaire were used. Multiple logistic regression was used to determine the impact of gender, age, education, employment, self-assessed social class, type of residence community, stress perception, coffee drinking behaviour, sleep behaviour on headache.

Results: We noticed high odds for risky stress behaviour (OR yes vs. no = 1.99; $P < 0.001$), sleep behaviour (OR < 6 vs. 8 hours/day = 1.23; $p < 0.001$) and coffee drinking behaviour (OR > 1 cups vs. no cups/day = 1.58; $p < 0.001$) in headache subjects. In addition, we found the highest odds in women (OR women vs. men = 1.99, $P < 0.001$), aged 25–29 years (OR 25–29 vs. 70–74 = 6.10, $P < 0.001$), participants with the lowest (OR primary vs. postgraduate = 1.34, $P = 0.082$). Regarding kind of work we detected higher odds in intellectual/leading positions (OR intellectual/leading positions vs. pensioners = 1.39, $P = 0.014$), participants self-classified in the lowest social class (OR lower vs. upper-middle = 1.65, $P = 0.005$), and in persons under 18 in household (OR yes vs. no = 1.15, $P = 0.028$).

Conclusion: In Slovenia, intellectual/leading position women, aged 25–29 years, were identified as the largest population sub-group at high risk for frequent headache disorders with stress behaviour.

Disclosure of Interest: None Declared.

IHC-PO-237**Assessment of the Factor Structure of the Pediatric Pain Coping Inventory (PPCI) in Youth with Headache Disorders**Kristine Woods^{1,*} and Sarah Ostrowski-Delahanty¹¹Akron Children's Hospital, Akron, United States

Objective: Assessing preferred coping strategies in youth with headaches is important in adequately treating pain, potentially reducing functional and emotional concerns. The PPCI is a pain coping measure validated in youth with rheumatologic disorders and it's unclear whether the PPCI is valid for headache pain. The purpose of this study was to examine the factor structure of the PPCI in youth with headaches.

Methods: This is a retrospective review of headache patients seen for behavioral health evaluation from 3/2013 to 8/2016. Participants completed the PPCI and other psychological measures given as part of standard clinical care. Statistical analyses on study variables included frequency analyses, principal components analyses (PCA), Pearson product-moment correlation coefficients, and independent t-tests.

Results: Participants were primarily Caucasian (89.9%) females (74.9%) with a mean age of 14.5 years. Migraine (with and without aura, chronic) was the most common diagnosis (63.4%). Results of the PCA suggest that original 5 factor model explained 39.3% of the variance. The Scree plot showed a better fit with 8 factors, explaining 49.07% of the variance. The components identified were not consistent with the scales identified by Varni et al. (1996). Factor I was the largest factor and included items from the Cognitive, Distraction, and Catastrophizing subscales with factor loadings ranging from 0.76–0.46. Examination of the parent reported PPCI items produced similar findings.

Cronbach's alpha for the total PPCI suggests the items are internally consistent (child = 0.85 for and parent = .80). Examination of the 5 PPCI scales revealed poor to acceptable internal consistency (child: .61-.68; parent: .54-.73). Correlation analyses revealed that youth FDI score was correlated with all PPCI scales except Distraction (child: $r = .079$, $p = .07$; parent: $r = .034$, $p = .44$).

Conclusion: Our results suggest the 5-factor model of the PPCI is not parsimonious for headache patients. Although an 8-factor model was more parsimonious, individual items did not load on the same factors as Varni et al.'s study. Assessing and understanding how youth with headache cope with their pain is an important undertaking; however, our results suggest the PPCI is not the

most appropriate measure for assessing pain coping in this population.

Disclosure of Interest: None Declared.

IHC-PO-465**Everyday life social cognition in chronic migraine**Sara Bottiroli^{1,2,*}, Elena Cavallini³, Serena Lecce³, Grazia Sances¹, Marta Allena¹, Elena Guaschino¹ and Cristina Tassorelli^{1,3}¹IRCCS MONDINO FOUNDATION, Pavia²Giustino Fortunato University, Benevento³University of Pavia, Pavia, Italy

Objective: The ability to attribute mental states to oneself and others is an important aspect of social cognition, also known as Theory of Mind (ToM). The ability to make social cognitive inferences is indeed crucial for successful social behaviours because they mediate an understanding of the intentions and dispositions of others and lead to the correct prediction of behavior. Previous evidences have shown pathological scores in ToM in chronic migraine. Given the relevance of Theory of Mind in social interactions, it is important to assess it by using tests approximating the demands of everyday life social cognition, which is lack in previous studies. Keeping this in mind, the present study is aimed to evaluate whether chronic migraine is associated to deficit in ToM and in other aspects of social functioning, by using a video-based instrument, the Movie for the Assessment of Social Cognition (MASC), requiring subjects to make inferences about video characters' mental states.

Methods: 40 patients suffering from chronic migraine (CM) (79.5% female, Age: 47.3 ± 11.1) and 37 patients suffering from episodic migraine (EM) (83.8% female; Age: 41.0 ± 11.4) were evaluated using a battery of ToM tasks comprising the MASC and the Reading the Mind in the Eyes Test (RMET), as well as questionnaires on their social functioning. Chronic migraine diagnosis was operationally defined according to ICHD-III β . Data were analyzed with analysis of variance.

Results: Compared with EM, CM patients had significantly lower scores in the MASC (CM = 17.7 ± 14.7 , EM = 22.9 ± 14.0 , $p < .05$), and these differences resulted also when distinguishing between cognitive (CM = 9.9 ± 9.4 , EM = 14.6 ± 9.1 , $p < .05$) and affective (CM = 5.8 ± 5.5 , EM = 8.3 ± 5.2 , $p < .05$) components. EM also had higher scores in the RMET (CM = 21.7 ± 3.1 , EM = 24.4 ± 3.8 ,

$p < .005$), and believed to be abler to understand ones and others' feelings in comparison to chronic migraineurs.

Conclusion: Our results indicate that CM patients have more difficulties in understanding others' mental states than EM, which is highlighted also by tasks reflecting every-

Table 1. Outcome Measure Results

	N	Mean Change	SD	P-value
HMSE	23	27.12	33.92	<0.001
HIT-6	44	-8.32	7.77	<0.001
COPM (performance)	42	2.99	1.40	<0.001
COPM (satisfaction)	42	3.42	1.68	<0.001

day life competences. This evidence suggests the existence of a link between this chronic condition and social competent behaviours and abilities.

Disclosure of Interest: None Declared.

IHC-PO-466

An Interdisciplinary Team Approach for Treatment of Headache Disorders: A Retrospective Review of a case series from an Academic Headache Center

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Objective: There is consensus among headache specialists that a multidisciplinary or interdisciplinary model of care has advantages and results in better outcomes. Most commonly, this team includes a headache specialist, physical therapy (PT) and pain management. At the USC Keck Medical Center, an interdisciplinary team of neurologists, PTs and pain psychologists has successfully incorporated occupational therapists (OTs) as key members of this model for treating headache disorders and this model has been described in a previous publication (Sahai-Srivastava et al, 2017). The aim of this study is to report our real-life experience of an interdisciplinary approach with a series of patients with headache disorders and the effects on pain, quality of life, function and self-efficacy.

Methods: This was a retrospective analysis of 97 patients who participated in interdisciplinary team care as part of their usual plan of care. Patients were included in the data analysis if they 1) had a headache disorder diagnosis, the most common being migraines, 2) were treated by

neurology, OT and PT, and 3) completed pre and post outcome data. The following outcome measures were administered to assess functional progress: Headache Impact Test-6 (HIT-6), Headache Management Self-Efficacy Scale (HMSE), and the Canadian Occupational Performance Measure (COPM).

Results: Our patient sample has a mean age of 38 years old and was predominantly female (80%) and white (80%). Paired T-test was used to determine clinically significant changes from pre and post outcome data. STAT/IC 14.2 was used to analyze the data. We found that there was a statistically significant improvement in measures of quality of life and self-efficacy with the team approach in headache patients. Results can be found in Table 1.

Conclusion: For patients with headache disorders, interdisciplinary team care including neurology, OT and PT results in clinically significant improvements in quality of life, functional impact of headache, and self-efficacy in managing headaches. Further studies comparing team approach with traditional treatment approaches should be done to confirm these findings.

Disclosure of Interest: None Declared.

IHC-PO-467

Chronic Headache Self-Efficacy Scale (CHASE): Preliminary Assessment of Measurement Properties

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Objective: Chronic headaches are debilitating.¹ Higher self-efficacy, or the belief in one's ability to manage and control headaches, is correlated with lower depression, anxiety, and physical symptoms in patients with chronic headaches.² The Chronic Headache Self-Efficacy Scale (CHASE) is a 14-item patient report scale developed to identify and measure self-efficacy related to elements of daily activities in patients with chronic headaches. The purpose of this study is to evaluate psychometric properties of CHASE.

Methods: Participants (n = 21) diagnosed by a neurologist with chronic headaches were included. Participants completed CHASE, Headache Management Self-Efficacy Scale (HMSE), and Headache Impact Test-6 (HIT-6), at three time points: initial encounter (T1), post-24 to 72 hours (T2), and post-12 weeks (T3). Reliability was assessed with Interclass Correlation Coefficient (ICC_{3,1}). Error was determined with Standard Error of Measurement (SEM) and Minimal Detectable Change at 90% confidence interval (MDC₉₀). Validity was assessed by relationship between CHASE, HIT6 and HMSE at T1 and change

(T1–T3) in CHASE compared to HIT6 and HMSE. Global rating of change (GROC) at T3 was used to assess overall change. Responsiveness of CHASE was assessed by comparing the score on CHASE, HIT6, and HMSE between patients who reported at least moderate changes ($GROC \geq 4$) in their headache symptoms at T3 and patients who did not.

Results: $ICC_{3,1} = 0.87$ (CI: 0.62, 0.96); $SEM = 7.3$ pts; $MDC_{90} = 16.9$ pts. At T3 CHASE was correlated with HIT6 ($r = -0.68$, $p < 0.01$) and HMSE ($r = 0.70$, $p < 0.01$). There was a correlation between the change scores (T1–T3) of CHASE with HIT6 ($r = -0.41$, $p = 0.06$) and HMSE ($r = 0.45$, $p = 0.04$). Patients who reported at least moderate change in headache symptoms from T1 to T3 had high scores on HIT6 (mean difference [MD] = -11.2 ; CI: -15.9 , -6.3 , $p < 0.01$) and CHASE (MD = 26.7 , CI = $12.8, 40.6$, $p < 0.01$) but not HMSE (MD = 16.9 , CI = $-4.0, 37.7$, $p = 0.11$).

Conclusion: Preliminary results indicate excellent reliability, acceptable error and validity, and moderate responsiveness. Participant recruitment continues to fully assess reliability, validity, error, and responsiveness of CHASE. The CHASE scale may provide clinicians a means to assess self-efficacy and behaviors specific to management of chronic headaches.

Disclosure of Interest: None Declared.

IHC-PO-468

Is chocolate associated with more severe days in chronic migraine?

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Objective: To determine in individuals with chronic migraine (CM) 1) how many suspect chocolate as a trigger and 2) for how many can a statistical association be verified between chocolate ingestion and severity of migraine.

Methods: Individuals with migraine registered to use NI-Headache[®] and answered questions about their suspected triggers, including chocolate, and their importance (1 = low; 10 = maximal). They then used NI-Headache daily for 90 days, entering details about headaches and tracking factors that may affect the severity of their migraine attacks. After 90 days all factors were analyzed for each individual retrospectively classed as having CM (ICHD-3 criteria). The association between daily self-reported chocolate ingestion (no/some/a lot) and peak migraine severity comparing a) “low” pain days (no or mild pain) vs. b) “high” pain days (moderate or severe pain) was determined via a univariate logistic regression.

Results: Of 136 individuals with CM, chocolate was suspected as a trigger by 68 (50.0%): mildly suspected (1–3) by 25.0%; moderately (4–6) by 14.7%; strongly (7–10) by 10.3%. Overall, of 109 (80.1%) entering data with sufficient variability for analysis, chocolate was associated with pain severity in only 9 (8.2%). Of 55 (40.4%) individuals with analyzable data who suspected chocolate as a trigger, chocolate was associated with “high” pain days in 2 (3.6%), “low” pain days in 3 (5.5%) and not associated with pain severity in 50 (90.1%). Of 44 (32.4%) with sufficient data who did NOT suspect chocolate as a trigger, chocolate was associated with “high” pain days in 1 (2.3%), “low” pain days in 2 (4.5%) and there was no association in 41 (93.2%). Of 10 (7.4%) with sufficient data who did not answer the question, chocolate was associated with “high” pain days in 1 (10.0%).

Conclusion: There was no clear association between degree of suspicion of chocolate and the proportions of individuals in whom an association was scientifically identified. Chocolate is widely suspected as a trigger, but an association with migraine attack severity was identified statistically in very few, with no difference in “high” and “low” pain days. Results were similar to prior analysis of chocolate association with attack occurrence in episodic migraine using a Cox model.

Disclosure of Interests: K Shulman, S Donoghue and M Vives-Mestres are Consultants to Curelator Inc.

IHC-PO-469

The Lived Experience of Women living with Hemiplegic Migraine

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Objective: The aim of this study was to explore the lived experience of women living with a diagnosis of hemiplegic migraine.

Methods: In-depth, semi-structured interviews were carried out with eight women living with hemiplegic migraine. Participants were selected by purposive sampling and the Migraine Association of Ireland was the primary recruitment source. All the women lived in the Republic of Ireland and were between the ages of 23 and 54 years. The interviews were analysed using Interpretative Phenomenological Analysis.

Results: Three main themes emerged reflecting participants' experiences: “What is it?”- Making sense of hemiplegic migraine, “Taken its toll” – The impact of hemiplegic migraine and “Deal with it”- Finding ways to cope with hemiplegic migraine. Hemiplegic migraine is experienced as a poorly understood and under recognised condition. Feeling dismissed or doubted was a common experience

among participants. Hemiplegic migraine negatively impacted on the women's sense of self, relationships, and their engagement in normal, everyday activities. Several participants regarded themselves as a burden, while some felt that life with hemiplegic migraine was not a life. Living with the unpredictability of the condition was identified as particularly problematic. Participants employed a variety of methods to minimise both the risk of an attack, and the impact of those that occurred. Psychological therapy, family support, and spending time in nature and with animals were regarded as lifelines in helping participants to live with their condition, while acceptance of their condition and having hope for the future were also regarded as helpful.

Conclusion: This study, the first to date to investigate the lived experience of hemiplegic migraine, highlights the necessity for increased awareness and education in relation to the condition. It also highlights the need for health care practitioners to enquire about the emotional impact of hemiplegic migraine when working with patients with this condition.

Disclosure of Interest: None Declared.

IHC-PO-470

Chronic headache patients in the Republic of Moldova health care system: barriers and perceptions

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Objective: Chronic headache impose an important burden on patients and health care system. Republic of Moldova lack an integrated multidisciplinary headache care. The aim of the study was to evaluate the barriers and pathways of the patients with chronic headaches in health care system.

Methods: An observational mixt design (quantitative and qualitative) study was conducted. In the quantitative part 176 patients with chronic headaches (according to ICHD – 3 criteria) from January till May 2018 was included. Patients fulfill a structured questionnaire about headache, coping strategies, personal burden and health care utilization. Qualitative part included in depth interviews and focus – groups. All quantitative data was analyzed using SPSS software.

Results: Mean age in the study group was 55.34 ± 10.26 years, 80.1% was females and 19.9% – males. The patients suffered pain – 10.27 ± 9.07 years, 61.1% had every day pain, 53% – took pain medication every day. Only 35.2% know about chronic headache, 36.4% know about prophylactic treatment, 17% know a headache specialist. The pain

medication was efficient in 29% of them, partially efficient in 59.7% and not useful in 11.4% of patients. Only 38% of patients used non – pharmacological methods of treatment. Chronic headache affected every day activities a lot in 39.2% of patients, sometimes affected – 51.7% and not affected in 9.1% of patients. Patients were satisfied about headache care in 2.8%, partially satisfied in 72.2% and were not satisfied in 25%. A chronic headache patient called emergency – 0.95 ± 1.65 times last year, saw a general practitioner – 5.55 ± 5.68 times last year, consulted a specialist – 2.81 ± 2.66 times last year. When asked about problems they faced in headache care patients mentioned: pain medication very expensive – 74.4%, waiting time for investigation too long – 56.6%, waiting time to consult a specialist too long – 45.9%, long distance to see a specialist or take a treatment – 43.9%.

Conclusion: Chronic headache patients in Republic of Moldova health care system encounter barriers: geographic accessibility, availability, affordability and acceptability of the services. Patients are not informed about their condition, treatment options and are partially or not satisfied about their treatment.

Disclosure of Interest: None Declared.

IHC-PO-471

Exploratory analysis on missed appointments in a headache clinic

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Objective: Frequent follow-up is usually needed in the approach of patients with headache. Missed appointments lead to resource inefficiency and are associated with worse prognosis. Our aim was to identify risk factors for absenteeism in our Headache Clinic (HC).

Methods: A retrospective study was conducted, with the collection and analysis of data from a tertiary hospital database. Appointments to the headache clinic, between June 2017 and February 2019, were included. A descriptive analysis on patient and appointment characteristics and the association with absenteeism was conducted. Estimates of frequency and inferential analysis are presented (SPSS 25).

Results: 167 patients were referred to the HC. There were more females (83.2%, $n = 139$) and the median age was 39 years (range 17–86). Of these, 39 (23.4%) missed the first visit. In the group with subsequent scheduled appointments, 61% (79 out of 129) had at least one failed appointment. The overall frequency of absenteeism was 23.3% (84 in 360).

Overall, the absenteeism group was younger (median age 35.5 vs 44, $p = 0.011$), less frequently married (49.3% vs 65.8%, $p = 0.046$), with more appointments scheduled in the summer (22.6% vs 10.8%, $p = 0.042$) and during the morning period (89.3% vs 77.1%, $p = 0.035$). Patients with migraine diagnosis were more regular (46.4% vs 63.9%, $p = 0.024$).

In-hospital referrals (48.7% vs 69.5% referred by the general practitioner, $p = 0.017$) and important medical comorbidity (40.0% vs 13.3%, $p = 0.008$) was associated with no-shows to the first appointment. In a multivariate analysis, missed first appointments remained significantly associated with the summer period ($p = 0.009$) and in-hospital referrals ($p = 0.023$).

There was no association between missed appointments and waiting list time (119 days vs 102, $p = 0.162$); gender; labor; duration or frequency of headache; coexistence of medication overuse headache or psychiatric disease nor with a bank holiday during the appointment's week.

Conclusion: Several sociodemographic factors seem to be relevant for absenteeism. Nevertheless, their possible collinearity determined that only appointments during the summer and in-hospital referrals were associated with no-shows. A closer bond with the general practitioner may explain why primary health care referrals missed less appointments.

Disclosure of Interest: None Declared.

IHC-PO-472

Migraine patient school (MPS) – A structured multimodal educational programme for patients with high frequency and chronic migraine

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Objective: High frequency and chronic migraine is disabling, leads to loss of function and affects family and working life. The effect of MPS on migraine situation was studied analysing various health related aspects.

Methods: Participants, 30 patients with severe migraine, 18–65 years old, recruited consecutively into 4 groups,

filled in questionnaires (HIT-6, PSS, MSQoL, HAD, PIPS) and headache diaries for 4 weeks prior to and after the MPS. The MPS program involved 7 sessions 1–2 week apart held by a neurologist (headache specialist) and a physical therapist specialized in pain. The session themes, (developed by K Hedborg, Ups J Med Sci. 2011;116:169), were: Stress and calm, Exercise, Diet, Thought pattern, Handling of emotions, Approach to yourself and your environment, and Summary. The topic theme was discussed, and home assignments were given at each session. Participants missing a session received the corresponding material by email. Every session included a theoretical part on different aspects of migraine and ended with a 30-min practical physical therapy session with body awareness, breathing and relaxation exercises.

Statistics: Median values; Wilcoxon's Signed Rank test.

Results: Twenty-three female and 1 male of the 30 included patients fulfilled the MPS. A reduction in median values were seen in HIT-6 (65 to 62; $p = 0.002$), PSS (30 to 26; $p = 0.01$), PIPS (avoidance) 33 to 30; $p = 0.025$), while median MSQoL increased (39 to 50; $p = 0.036$). PIPS (fusion) and HAD (anxiety, depression) showed no significant changes.

Conclusion: The MPS seems to add some strategies to handle the situation for the patients with the severest form of migraine (high frequency-chronic).

Disclosure of Interest: None Declared.

IHC-PO-473

A pilot investigation of mindfulness meditation for adolescents with frequent migraine: Interim findings

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Objective: Approximately 2% of adolescents experience chronic migraine (CM) & many more have "high frequency" migraine. Pharmacological prophylactic therapies provide relief for certain adolescents, but leave many insufficiently helped. Research supports the utility of mindfulness-based approaches (MF) for adults with headache, but whether this is effective with adolescents is unknown. We present interim findings from our pilot investigation of MF treatment for this group of patients.

Methods: Twenty-two adolescents (21 females/1 male; aged 12–17) with CM (≥ 15 migraine days/mo) or high-frequency migraine (9–14 migraine days/mo) are currently enrolled in our trial. Treatment consists of 7 45-minute

weekly group sessions of MF (augmented by home practice) to enhance sustained non-judgmental present moment awareness. Multiple outcome measures are collected, with monthly headache frequency & medication intake constituting our primary measures, while catastrophizing attitudes (Pain Catastrophizing Scale), disability (PedMIDAS), depression (Children's Depression Inventory), & anxiety (State-Trait Anxiety Inventory) are our secondary measures.

Results: Ten adolescents (9 females/1 male) have completed treatment & a planned 6-month follow-up thus far. Number of headache days has decreased by 68% (16→5.0) with similar improvement for medication intake—60% (7→2.8) from pre-treatment to the 6-month follow-up. Catastrophizing attitudes showed similar reductions at 6 months—47% (29.3→15.4), as did the levels of disability—57% (42.7→25.5) & depression—43% (12.5→7.1), with no decrease for anxiety.

Conclusion: Treatment was well accepted (no problems or adverse side effects reported) with high levels of adherence. Our interim data show significant benefits for all measures (except anxiety). We are continuing to complete treatment & collect a minimum of 1-year follow-up for all enrolled adolescents. At that point we will be able to make more definitive claims about the feasibility, acceptability & clinical effectiveness for this relatively new form of treatment for adolescents presenting with frequent forms of migraine.

Disclosure of Interest: None Declared.

IHC-PO-474

Depression, Anxiety, Stress and Coping in Chronic Daily Headache

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Objective: Headaches are one of the most disabling conditions second only to low-back Pain. Evidence clearly suggests that CDH is more disabling than episodic headaches. Limited efforts have been made to understand the psychosocial variables in chronic daily headaches. They are mostly discussed in combination with episodic headaches. This study aims to understand depression, anxiety, stress and coping among chronic daily headache from an Indian perspective.

Methods: A total of 40 patients with CDH (Chronic Daily Headache) (according to ICHD-III β version) were recruited from the Out-patient department of Neurology, NIMHANS. The inclusion criteria was individuals between the ages of 18–60 years with a primary

diagnosis of chronic daily headache willing to participate in the study. The scales used in the study were socio-demographic schedule, Perceived stress scale, Hamilton depression scale (HAM-D), Generalized Anxiety Scale (GAD-7), and Brief cope (Carver).

Results: The average age of the participants was 34 years, majority (70%) were females. The average duration of chronic headache was found to be 5 years. The average duration of an episode was found to be 8 hrs/day for 20 days/month. The common triggering factors identified are lifestyle factors, such as poor eating habits and sleeping habits. Anxiety about the headache episodes and anticipation of episodes were also observed. On Perceived stress scale, average score was 21(±7.2) indicating moderate stress. Participants reported average score of 7(±3.42) and 14(±4.02) respectively on GAD-7 and HAM-D. The common coping strategies used were self-distraction and behavioural disengagement.

Conclusion: Headache disorders have a major impact on the overall quality of life of the person. It impacts on an individual, familial and social level. Understanding these different dimensions will aid in creating wholistic and effective interventions.

Disclosure of Interest: None Declared.

IHC-PO-475

Triggers of Primary Headaches: What are the Issues, and the Ways Forward?

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Objective: The literature on the triggers of primary headache was reviewed to highlight the issues in the triggers literature, and to determine ways forward.

Methods: The literature review involved searching with key terms, as well as considering all the papers cited in the identified publications.

Results: The triggers of primary headaches have considerable significance for our understanding and management of headaches. Triggers explain the variance in headaches – why they occur when they do. Trigger management is generally viewed as an important component of a comprehensive treatment approach for headaches. Yet paradoxically, triggers do not have a prominent place in the headache literature. This perhaps reflects the fact that headaches tend to be de-contextualised in the literature as the focus is mainly on what happens in the brain rather than what triggers off the neurobiological processes. This review focused on identifying issues that have held back the development of the literature on the triggers of primary headaches, starting with the definition of a trigger and how specific triggers are labelled. Consideration was

then given to classification systems for triggers. The review considered next the evidence relating to whether self-reported triggers can indeed precipitate headaches, and how that capacity to elicit headaches may be acquired or extinguished. Attention was given to the very important clinical issue of trigger management.

Conclusion: Perhaps the most useful thing to accomplish at this point in time would be agreement on a definition of headache triggers, a list of triggers, and a classification system for triggers. This would greatly assist comparing research on triggers from different research groups as well as eliminating some of the issues identified in this review. An authoritative body like the International Headache Society, could establish a committee that would complete these tasks just as it set up a committee over 30 years ago to develop a new headache classification system. Consideration should also be given to incorporating triggers into ICHD as an axis or via the use of codes, as this would raise the profile of the importance of triggers in assessment and management.

Disclosure of Interest: None Declared.

IHC-PO-476

Biofeedback Training in the Treatment of Headache and Anxiety

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Objective: The objective of the study was to determine if biofeedback training is an effective treatment modality in the treatment of headache in patients with anxiety.

Methods: Inpatients at a headache center participated in six biofeedback sessions during the course of their hospital stay. Each participant completed a self-reported Headache Pain Level Diary to record pain levels prior to and after each biofeedback session. In order to assess anxiety patients completed a Severity Measure for Generalized Anxiety Disorders in Adults from the Diagnostic and Statistical Manual of Mental Health (DSM-5). This measure was administered just prior to the first and at the conclusion of the sixth biofeedback sessions. Ninety-six participants were included in the study. Twenty-one participants reported a history of generalized anxiety disorder. Thirteen participants reported a history of anxiety disorder, unspecified. One participant reported a history of panic disorder without agoraphobia. Sixty-one participants reported having symptoms of anxiety but no formal anxiety diagnosis. The majority of participants were diagnosed with chronic migraine (82), with additional headache diagnoses including new daily persistent headache (7), headache (2), chronic post-traumatic headache (2), chronic

cluster headache (2), and chronic paroxysmal hemicrania (1).

Results: Mean pain level at the beginning of biofeedback training and at the conclusion of biofeedback training were compared. In addition, mean anxiety level at the beginning of biofeedback training and at the conclusion of biofeedback training were compared. Paired t-tests revealed that the change in pain and anxiety were both significant from the beginning to the conclusion of biofeedback training.

Conclusion: Our findings illustrate that biofeedback training is an effective treatment modality for both headache pain and anxiety.

Disclosure of Interest: None Declared.

IHC-PO-477

The impact of shift work on migraine: a case series and narrative review

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Objective: Numerous modifiable factors can lead to chronification of migraine and to increased headache-related disability. These include, among others, obesity, depression, overuse of acute medications, ineffective acute treatments, and stressful life events. Sleep disruptions and disorders are also felt to increase risk for transitioning from episodic to chronic migraine.

We present a case report of two migraine patients engaged in shift work, followed by a narrative review, to assess whether shift work influences headache-related disability and chronification of migraine. We hypothesize that shift work, which leads to atypical or irregular sleep cycles by definition, along with poor quality sleep, is a risk factor for chronification of migraine.

Methods: We present the case histories of two shift workers with migraine as per ICHD-III criteria, seen at a large, busy academic headache center, followed by a narrative review of the literature.

Results: Previous literature regarding the relationship between shift work and migraine is sparse and conflicting, with more recent studies suggesting that shift work may be a risk factor for migraine-related disability. In our case series, both patients initially reported severe migraine headache-related disability. Both patients had noted a worsening of their headaches after beginning night shift work. Both improved when switched back to only day shifts, then worsened upon being put back on night shifts. They finally reverted from chronic to episodic migraine after eliminating night shifts completely and maintaining a good sleep routine.

Conclusion: In the two cases presented, shift work was associated with chronification of migraine and increased headache-related disability despite optimal headache management and good patient adherence. A switch to only day shifts promoted transition to an episodic, less disabling pattern of migraine. It is clinically important to take a detailed sleep history in headache patients, and when appropriate, provide support for workplace accommodations. Further larger-scale, rigorous studies are needed to more clearly delineate the relationship between shift work and migraine.

Disclosure of Interest: None Declared.

Tension-type Headache

IHC-PO-238

School and family psychological profile of adolescents affected by tension-type headache

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Objective: To study the role of school anxiety and family relationships in the development of tension-type headache (TTH) in adolescents.

Methods: A total of 270 adolescents with TTH have been under study. We formed three groups: 1st – adolescents with episodic TTH (ETTH); 2nd – with chronic TTH (CTTH); 3rd – control group (adolescents without headache). The study of the level of school anxiety (Phillips scale), and the level of psychosocial stress, and emotional/social support to adolescents (the questionnaire “Interaction parents-child” (I. M. Markovskaya)) was performed.

Results: The increased level of school anxiety was most pronounced in adolescents with ETTH. A low level of physiological stress resistance was observed with an increased frequency of headache episodes ($r = +0,45$, $p < 0,05$). We found that rates of very demanding mothers and increased severity of the measures that had been applied to adolescents were higher in patients with TTH compared with the control group ($13,5 \pm 2,6$ and $10,3 \pm 2,2$ points respectively, $p < 0,05$). Adolescents with ETTH, in contrast to the control group, indicated more often a mother’s strict control ($17,9 \pm 2,4$ and $11,1 \pm 2,2$ points respectively, $p < 0,05$). Adolescents with CTTH pointed out emotional distance, lack of cooperation, and a low degree of satisfaction with their current relationships with both parents more often than adolescents with ETTH ($p < 0,05$).

Conclusion: Adolescents with TTH have a high level of school anxiety and disturbed parental-adolescent relationships. Lack of basic security extends the individual significance of stress events for adolescents with TTH and leads to the formation of inadequate and limited pain coping strategies.

Disclosure of Interest: None Declared.

IHC-PO-239

Can we estimate the nociplastic pain mechanism of tension-type headache based on nonlinear multidimensional analysis (Deterministic chaos) EEG?

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Objective: To study pain mechanisms in adolescents with episodic and chronic tension-type headache (ETTH and CTTH).

Methods: 75 adolescents (ages 13–18) were examined. Three groups were formed: 1st group – patients with ETTH (26 pers.), 2nd – with CTTH (24 pers.) and 3rd – a control group (25 pers.). Estimation of brain dynamical systems during background activity and in the condition of mental stress (countdown in mind) was studied by the nonlinear multidimensional analysis (deterministic chaos) EEG and calculated Kolmogorov-Sinai entropy (KSE).

Results: Patients with CTTH, in comparison with 1st and 3rd groups, had a decrease in KSE in prefrontal, central and temporal leads (F3 – $-25,58\%$, C3 – $-17,22\%$, C4 – $-38,93\%$, T4 – $-21,71\%$, T6 – $-41,30\%$, $p < 0,05$), which corresponds to the projections of the limbic reticular system. These neurodynamic changes may indicate a decrease in the number of active parallel functional processes, a reduced capacity to self-organization and ability to form the adaptive ordered dissipative structures, i.e. a reduction in neuroplasticity, resulted in formation of a stable pathological dominant of excitability (reduction in the “level of chaos”), and a decrease in pain control – weak peripheral impulses from the pericranial muscle stiffness, vessels and other sources of an afferentiation are interpreted as nociceptive stimuli by the CNS.

Conclusion: Nonlinear EEG index (KSE) can be an objective quantitative measure of the neurodynamic characteristics of limbic-cortical-reticular structures which are involved in the formation of stable pathological dominant underlying nociplastic pain mechanism of CTTH.

Disclosure of Interest: None Declared.

IHC-PO-240

Fast disintegrating and quickly bioavailable aspirin formulations for the treatment of acute headache

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Objective: Aspirin and ibuprofen products are commonly used for the treatment of acute headache. Early onset of headache relief, e.g in migraine headache, is desirable as research has suggested a link between early treatment and better outcome. Formulation development can provide improvement in a medicinal products pharmaceutical and pharmacokinetic properties which in turn can support the efficacy of the product in clinical applications. Two new quickly disintegrating aspirin formulations have been developed for quick onset of action.

Methods: The relative pharmaceutical and pharmacokinetic performance of the two aspirin products were compared with two ibuprofen products (ibuprofen and ibuprofen-lysine tablets) by direct in vitro dissolution and in vivo disintegration followed by blood sampling for direct comparison of pharmacokinetics. Dissolution was investigated at three different pH (1.2, 4.5, 6.8) as requested by guidelines. Drill and fill method with ^{99m}Tc-DTPA scintigraph was used for disintegration; standard blood sampling and bioanalytics for pharmacokinetics.

Results: In vitro dissolution studies showed a substantial faster dissolution of the active ingredient acetylsalicylic acid from the two new aspirin products compared to ibuprofen- and ibuprofen lysinate-containing products. In vivo pharmacoscintigraphy showed a faster tablet disintegration (median time to completion of disintegration 9 and 5 min for aspirin and 37 min for both ibuprofen) and a substantial smaller active ingredient time to maximum plasma concentration of two new aspirin products compared to ibuprofen- and ibuprofen lysinate-containing tablets (median T_{max} 20 and 23 min for aspirin 500 and 1000 mg, respectively and 68 and 42 min for ibuprofen and ibuprofen-lysine, respectively).

Conclusion: The 500 and 1000 mg aspirin formulations demonstrated faster dissolution, disintegration and bioavailability than ibuprofen and ibuprofen-lysine formulations and consequently address important requirements for fast onset of action in pain relief. Therefore these formulations can be considered as appropriate for the fast relief of tension-type headache and migraine headache. However, this needs to be evaluated in further clinical research.

Disclosure of Interests: The work was sponsored by Bayer AG, Leverkusen, Germany. MV is an employee of Bayer. HS and FM are employees of BDD Pharma Ltd,

Glasgow UK. BDD Pharma received fees from Bayer for planning and executing the pharmacoscintigraphy study.

IHC-PO-240A

A new biofeedback approach for the control of the masseter and temporal myalgia: Utilization of an awake posterior interocclusal device

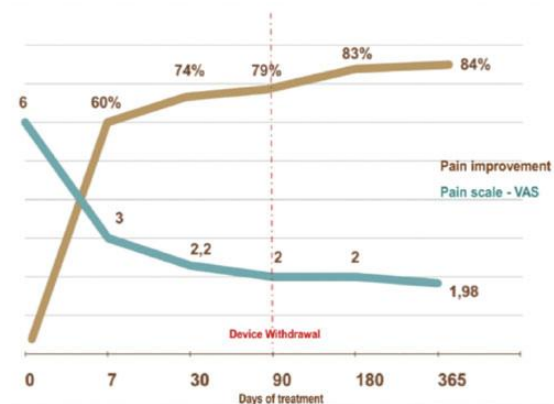
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Objective: The Objective of this study was to evaluate the improvement of reducing the pain of patients diagnosed with masticatory myofascial pain and bruxism, when undergoing treatment with a partial posterior interocclusal device (DIVA[®]) designed for the management and control of awake bruxism through biofeedback.

Methods: One hundred and sixty patients were evaluated during the periods: pre-treatment, seven, thirty, ninety, one hundred and sixty days and one year. The evaluation was carried out by measuring the pain (VAS) and reduction in pain using clinical and numerical scales.



Abstract number: IHC-PO-240A

Results: The majority of the patients who complained of masticatory myofascial pain, TMJ and neck pain experienced a significant reduction in pain between t0 and t30 ($p < 0.0001$). After 30 days of using the device, it was observed that the improvement remained at the same level, without any recurrence of pain up to t90. At t180 and t360 it was observed that even with the device withdrawal (at t90) the improvement remained at the same

Table 1. The division of patients by age and gender

Age, years	18–25	26–35	36–45	46–55
Gender				
Females, persons	12	17	13	9
Males, persons	10	5	6	8

level suggesting that the patients succeeded to control their awake bruxism.

Conclusion: The utilization of a posterior interocclusal device designed for the management and control of awake bruxism through biofeedback contributed to the reduction of pain in the majority of patients and that even with the device withdrawal (at t90) the improvement remained at the same level suggesting that the patients succeeded to control their awake bruxism.

Disclosure of Interest: None Declared.

IHC-PO-479

Clinical evaluation of application per-cutaneous electrical nerve stimulation in patients with chronic tension headache

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Objective: To assess the effect of percutaneous electrical nerve stimulation (PENS) in the treatment of chronic tension headache.

Methods: The study involved 85 patients treated between 2014 and 2016 at the 1st Republic Clinics under the Ministry of the Health of Uzbekistan. All patients underwent a comprehensive examination of pain and emotional status (VAS, hospital anxiety and depression scale) at the initial examination and six months after the prescribed treatment. The patients were divided into two groups. The first group included 39 patients who received only drug therapy for six months. The second group consisted of 47 patients using, as recommended drugs and portable PENS.

Results: The study showed that in the first group, the assessment of the intensity of headache – 5.4 ± 0.54 points during the initial examination; 6.3 ± 0.61 points at the second admission ($p \leq 0.001$). At the same time, according to the scales of anxiety and depression, during treatment was 11.2 ± 1.05 points, against the background of treatment 9.01 ± 0.86 ($p \leq 0.001$), depression – 8.9 ± 1.28 and $8.9 \pm 1, 02$, respectively ($p \leq 0.001$). In the second group, the level of headache intensity is 6.1 ± 0.50 points during the initial examination; 1.8 ± 0.39 points on the second admission ($p \leq 0.001$). At the same time,

according to the scales of anxiety and depression, during treatment was 12.1 ± 1.04 points, against the background of treatment 6.01 ± 0.63 ($p \leq 0.001$), depression – 11.2 ± 1.24 and $2.9 \pm 0, 95$, respectively ($p \leq 0,001$). In the group of patients using only drug therapy, nine (19.5%) developed tension headache. In patients who used portable BSEC in addition to the medical method of treatment, there were no cases of tension headache.

Conclusion: The use of portable PENS contributes to reduce the intensity of headache in patients with chronic hepatitis B, as well as prevent the development of strong tension headache. Furthermore, Percutaneous electrical nerve stimulation appears to be a useful complementary therapy to analgesic and antimigraine drugs for the short-term management of headache. Interestingly, the analgesic response to PENS therapy appears to be independent of the origin of the headache symptoms.

Disclosure of Interest: None Declared.

IHC-PO-480

Use of non-medication in the treatment of tension-type headache

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Objective: Background and Aims: The effect of the complex (acupuncture, d'arsonval currents and variable magnetic field) on the pain intensity of the patients having tension-type headache was investigated.

Methods: 80 patients aged from 18 to 55 (51 females and 29 males) having tension-type headache were observed. The pain was examined and measured according to the visual analogue scale (6 –7 points). All patients were observed (MRI, doppler ultrasound vessels of the head and neck, spondylography etc.). The patients were divided into two groups. The first group (62 patients) received in addition their basic medication and complex: acupuncture (individual points), variable magnetic field to the neck paravertebrally and d'arsonval current on the scalp and neck – shoulder region. The complete course was 10–12 procedures. The second group (control, 18 patients), received only the basic medication.

Results: The pain intensity of the patients in the first group was reduced after 6–7 days of treatment (96,7% patients) compared to the control group, where pain reduction after 12–16 days of treatment (44,4% patients); $p < 0,01$.

Conclusion: The addition of the acupuncture, variable magnetic field and d'arsonval current to the treatment of tension-type headache resulted in earlier remission.

Disclosure of Interest: None Declared.

IHC-PO-481

Does fast disintegration and quickly bioavailability of fast release Acetylsalicylic acid tablets result in improved gastrointestinal tolerability?

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Objective: Formulation improvement can lead to increased pharmaceutical and pharmacokinetic properties. Acetylsalicylic acid (ASA (Aspirin[®])) tablets were reformulated in 2014 to disintegrate and dissolve faster which result in faster onset of action and quicker pain relief in the self-medication of pain proven in three clinical studies and a pharmacy based survey (Cooper 2012, Voelker 2016, Theurer 2016).

Reformulated fast release ASA formulation showed good tolerability in clinical setting and under real world conditions overall and especially for gastrointestinal disorders (GI).

Methods: Data of three clinical studies and one real life study of reformulated ASA tablets were merged and closely scanned for GI disorders. Safety was evaluated by the incidence of treatment-emergent adverse events (TEAEs)

and the relation to study drug for this circumstance. Overall, 1938 subject data were analysed.

Results: Reformulated ASA tablets showed good tolerability. Reported TEAEs were mild or moderate in severity, no serious adverse event including bleeding was observed. 95.1%, 95.8%, 92.6% and 95.2% of study subjects reported no treatment emergent GI disorders.

Only one of three clinical efficacy studies showed a relation of ASA and the reported GI disorder, resulting in 1% of the study population (two subjects affected). One of the other two clinical studies presented TEAEs considered related to ASA.

Conclusion: Tolerability of ASA is still a matter of scientific debate. Short- and long-term application are mixed and tolerability of long-term application is often perceived as overall tolerability not only for bleeding risk but also for GI disorder.

Reformulated ASA tablets are indicated for short-term application in pain relief and show quick disintegration within 9 minutes (500 mg ASA), fast dissolution and short time to reach t-max in 20 minutes. Tablets as well as ASA itself have short physical contact with gastric mucosa.

The available data of reformulated ASA showed only a small number of GI disorders in clinical setting and under real life conditions. More than 92% of the patients tolerated Aspirin well and exhibit no gastrointestinal problem, more than 99% of clinical subjects discovered no gastrointestinal disorders related to Aspirin.

Disclosure of Interest: None Declared.

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**Cluster Headache and Other Trigeminal Autonomic Cephalalgias****IHC-OR-040****Efficacy and safety of fremanezumab for the prevention of episodic cluster headache: results of a randomized, double-blind, placebo-controlled, phase 3 study**

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Objective: To evaluate efficacy, tolerability, and safety of fremanezumab for preventive treatment of episodic cluster headache (ECH) in this study.

Methods: Eligible patients (pts) with a ≥ 12 -month (mo) history of ECH were randomized (1:1:1) to high-dose (HD) fremanezumab (mo 1/2/3, 900 mgIV/225 mgSC/225 mgSC), lower-dose (LD) fremanezumab (675 mgSC/PBO/PBO), or matched monthly PBO. The primary efficacy endpoint was mean change from baseline (BL) in weekly (wkly) average number of CH attacks during the first 4 weeks (wks). This study was terminated early for futility based on interim analyses (presented here).

Results: Prior to termination, 169 pts were randomized. With PBO, LD, and HD fremanezumab, BL wkly average numbers of CH attacks were 13.0, 13.3, and 12.7, respectively. The primary endpoint was not met; mean changes from BL in wkly average CH attacks during 4 wks were not significantly different for HD (-7.6) or LD (-5.8) fremanezumab vs PBO (-5.7 ; $P \geq 0.1$). The reduction in wkly average CH attacks at 3 wks with HD fremanezumab was -8.5 vs -5.8 with PBO ($P = 0.0930$). With HD fremanezumab vs PBO, there was also a significant decrease in acute medication use from BL during 12 wks and wkly

over the first 8 wks ($P < 0.05$, not multiplicity adjusted). No safety signals were identified.

Conclusion: Though this study was terminated because an interim analysis for the 4-wk primary endpoint demonstrated futility, results suggest that HD fremanezumab may have improved outcomes for ECH pts at wk 3. A low BL attack frequency, high PBO response, and the selection of wk 4 vs wk 3 for the primary endpoint may have contributed to the lack of separation between fremanezumab and PBO. Results also suggest CH may require higher monoclonal antibody doses than migraine. This negative study provides insight into the design of future studies in CH.

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Comorbidity of Primary Headaches

IHC-OR-028

Functional and metabolic changes in visual snow syndrome: a combined BOLD fMRI and MR-spectroscopy study

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Objective: Patients with visual snow (VS) suffer a pan-field visual disturbance described as continuous tiny flickering dots with frequent additional visual symptoms. A previous [¹⁸F]-FDG PET neuroimaging study in patients with VS showed increased glucose metabolism in the right lingual gyrus.

In order to understand more about the pathophysiology of visual snow and to confirm previous neuroimaging

results, we performed a combined magnetic resonance spectroscopy (MRS) and functional MRI study in patients with VS compared to healthy volunteers. By placing the MRS volume of interest over the right lingual gyrus, we investigated the neurochemical properties of this area. Blood oxygenation level dependent (BOLD) responses were studied in response to visual stimulation in all subjects.

Methods: Subjects with VS ($n=24$) and healthy volunteers ($n=24$), matched by age and gender, took part in the study. Scanning was performed on a 3T General Electric MR750 MRI scanner. For MRS, proton spectra were acquired using a point resolved spectroscopy (PRESS) protocol. BOLD responses were obtained with a single fMRI experiment consisting of a 40 seconds on/off block-design, characterized by a simulation of visual snow alternated with darkness. The study was approved by the London – City & East Research Ethics Committee (Reference number: 16/LO/0964). Imaging was analysed using SPM 12 and MRS using LC model.

Results: There was a significant increase in lactate concentrations in the VS group with respect to controls (0.64 ± 0.9 mmol/L vs. 0.08 ± 0.2 mmol/L; $p=0.006$). We found BOLD signal deactivation in VS patients but not controls in the left anterior insula in a whole brain analysis ($k=291$; $p=0.025$; $x=-34$, $y=12$, $z=-6$) and, following SVC, in the contralateral insula as well ($k=100$; $p=0.003$; $x=44$, $y=14$, $z=-2$). Furthermore, there was a significant negative correlation between lactate concentrations and BOLD response in the right lingual gyrus ($p=0.001$; $r=-0.46$), in VS patients only.

Conclusion: These results suggest that patients with VS have a localised disturbance in extrastriate anaerobic metabolism, which may cause a decreased metabolic reserve for the regular processing of external visual stimuli. As shown by the BOLD analysis, visual snow is also characterized by a difference in bilateral insular response in the on or off phase of a visual stimulus mimicking VS itself; this could be due to altered interoception and disruptions within the salience network.

Disclosure of Interest: None Declared.

Headache Pathophysiology – Basic Science

IHC-OR-032

Extracranial injections of onabotulinumtoxinA in combination with iv injection of atogepant attenuates activation of HT and WDR neurons by CSD

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Objective: The goal of the current study was to determine the effects of a combination therapy with onabotulinumtoxinA (BoNT-A) and atogepant (Ato) on the responsiveness of central (SpV) trigeminovascular neurons to CSD; a goal that partially depends on knowing BoNT-A effects on activation of nociceptors by CSD.

Methods: In the BoNT-A/Ato experiments, we studied responses to a single wave of CSD in 22 dura-sensitive neurons in SpV (11 HT, 11 WDR) of animals treated with saline (injected 7–11 d before recording) and vehicle (PEG 400) injected iv 1 h before CSD (control group), or BoNT-A and Ato injected at same timepoints (BoNT-A/Ato group). In the BoNT-A only experiments we studied responses to CSD in 54 C- and Ad-meningeal nociceptors pretreated with BoNT-A or saline.

Results: All central neurons: In control animals, a single wave of CSD activated 70% of all central trigeminovascular neurons, whereas in the BoNT-A/Ato group, it activated only 8.3% ($X^2=0.002$). In the control group, the mean firing increased >230% 1 and 2 h after CSD. In the BoNT-A/Ato group, the mean firing remained unchanged after CSD.

HT neurons: CSD activated 80% of the neurons in the control group, and 16.6% in the BoNT-A/Ato group ($X^2=0.035$). The mean firing increased 162.1 (1 h) and 251.1% (2 h) after CSD in the control group and remained unchanged in the BoNT-A/Ato group.

WDR neurons: CSD activated 60% of the neurons in the control group, and 0% in the BoNT-A/Ato group ($X^2=0.026$). The mean firing increased 542.9 (1 h) and 199.4% (2 h) after CSD in the control group and remained unchanged in the BoNT-A/Ato group.

BoNT-A only, C and Ad neurons: BoNT-A reduced significantly the prolonged firing of the C-but not the Ad fibers after CSD.

Conclusion: The combination therapy of BoNT-A and atogepant prevents the activation of both HT and WDR neurons by CSD. These findings raise the possibility that chronic migraine aura patients may benefit from treatment

approach that combines BoNT-A and blockade of CGRP signaling.

Disclosure of Interests: This study was supported by Allergan, and NIH grants R37-NS079678, ROI NS069847, ROI NS094198 (RB).

IHC-OR-036

Fremanezumab, an anti-CGRP monoclonal antibody, reduces stimulated CGRP release from rat cranial dura mater

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Objective: Calcitonin gene-related peptide (CGRP) is regarded as an important mediator in migraine. CGRP is released from trigeminal neurons during migraine pain, inhibition of the CGRP mediator system is therapeutic in migraine and infusion of CGRP can induce migraine-like headache in migraineurs. Most recent developments in migraine therapy aim at blocking CGRP or its receptor with monoclonal antibodies. To clarify the effects of CGRP sequestering in the trigeminal system, the stimulated release of CGRP from meningeal tissues was studied in an animal model.

Methods: Fremanezumab, an anti-CGRP monoclonal antibody (30 mg/kg) or an isotype control antibody was subcutaneously injected into adult Wistar rats. One, 3 and 10 days later rats were intraperitoneally injected with glycerol trinitrate (GTN, 5 mg/kg) or vehicle and 4 hours later sacrificed for measurement of CGRP release from the cranial dura mater in the hemisected head preparation stimulated by the TRPV1 agonist capsaicin (5×10^{-7} M). In addition, the total CGRP content of excised trigeminal ganglia was measured using an ELISA.

Results: The basal as well as the stimulated CGRP release were significantly lower in rats treated with fremanezumab compared to the isotype control. These differences were pronounced 3 days after antibody treatment, in animals injected with GTN and in females compared to males. The weight-normalized CGRP content in the trigeminal ganglia was not significantly different between fremanezumab and the isotype control but was higher after GTN treatment and in males compared to females.

Conclusion: Following treatment with fremanezumab, the CGRP release from meningeal afferents measured by ELISA is reduced, particularly when CGRP is upregulated after provocation with the “NO donor” GTN. Fremanezumab reduces the free CGRP and may interrupt

trigeminal afferent sensitization induced by high levels of CGRP in the tissue.

Disclosure of Interests: Kimberly Mackenzie and Jennifer Stratton are employed at Teva Biologics.

Headache Pathophysiology – Imaging and Neurophysiology

IHC-OR-029

Effect of pituitary adenylate cyclase-activating polypeptide-27 on cerebral hemodynamics in healthy volunteers: a 3T MRI study

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Objective: Pituitary adenylate cyclase-activating polypeptide (PACAP) has emerged as an important signaling peptide in migraine pathogenesis. Recently, we have shown that the less-abundant PACAP isoform, PACAP27, induced migraine and headache in patients equipotently to PACAP38. The present study examined the effect of PACAP27 on cerebral hemodynamics in healthy volunteers using high resolution magnetic resonance angiography (MRA).

Methods: Eighteen healthy volunteers received infusion of PACAP27 (10 pmol/kg/min) or placebo over 20 min and were scanned repeatedly in fixed intervals for 5 hours in a double-blind, randomized, placebo-controlled study. The circumference of extra-intracerebral arteries was measured and compared with PACAP38 data.

Results: We found significant dilation of middle meningeal artery (MMA) ($p=0.019$), superficial temporal artery ($p=0.001$) and external carotid artery ($p=0.039$) after PACAP27 infusion compared to placebo. Whereas the middle cerebral artery (MCA) ($p=0.011$) and internal carotid artery (ICA) ($p_{ICA\text{cervical}}=0.015$, $p_{ICA\text{cerebral}}=0.019$) were constricted. No effects on basilar artery ($p=0.708$) and cavernous portion of ICA were found. Post hoc analyses revealed significant larger area under the curve for MMA after PACAP38 compared to PACAP27 ($p=0.033$). We also found that PACAP27 induced headache in nine out of twelve (75%) volunteers and one (17%) after placebo.

Conclusion: In conclusion, PACAP27 induced headache and dilated extracerebral arteries (>5 h) and slightly constricted MCA in healthy volunteers. Post hoc analysis of PACAP38 data compared with PACAP27 showed that

PACAP isoforms dilates MMA with significantly different magnitude.

Disclosure of Interest: None Declared.

IHC-OR-033

Central pain processing is altered in Persistent Idiopathic Facial Pain

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Objective: Persistent Idiopathic Facial Pain (PIFP) is a poorly understood chronic pain syndrome of the face, formerly known as atypical facial pain. It is characterized by a constant painful sensation without neurological abnormalities and without clinically objectifiable cause. Similarities to neuropathic pain conditions have been discussed and are currently thought to be relevant for the pathophysiology of this disease. In this study we aim to characterize the altered central pain processing in PIFP via functional magnetic resonance imaging (fMRI).

Methods: 22 patients suffering from PIFP and 15 healthy controls (HC) underwent a standardized and well-established paradigm of painful stimulation of the trigeminal nerve using gaseous ammonia. Functional images were acquired within a 3T MRI scanner using an optimized protocol for high resolution echoplanar brainstem imaging.

Results: PIFP patients show a significantly stronger activation to painful stimulation in the spinal trigeminal nucleus (sTN). Furthermore, our data point towards a bilateral activation of medial nuclei of the thalamus in these patients and in contrast to that towards a stronger activation of the insula in healthy controls as a response to painful stimulation. These two latter findings however did not reach statistical significance.

Conclusion: Our data suggest that abnormal central pain processing plays a role in the pathophysiology of PIFP. An integration of these findings into neuropathic pain models might help to gain a better general understanding of the pathophysiology of PIFP.

Disclosure of Interests: CZ received speaker honoraria and from Novartis, Teva, Allergan and Lilly and received consulting fees from Novartis and Teva. LHS received speaker and consulting fees from Allergan. AM is the editor-in-chief of Cephalalgia and reports no conflicting interests.

Migraine Acute Therapy

IHC-OR-038

Acute Treatment Patterns Among New Triptan Treatment Users and Potential Triptan-Insufficient Responders

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Objective: To examine real-world patterns of acute treatment of migraine among new triptan users and potential triptan-insufficient responder (TIR) patients.

Methods: Adult patients in the United States were selected if they had ≥ 1 triptan claim between 1/1/2013 and 31/12/2013 (first claim = index date) and 12 months of pre- and 24 months of post-index continuous enrollment in the 2012–2015 Clinformatics Data Mart (CDM)TM claims database. Patients were required to have ≥ 1 migraine diagnosis but no triptan claims in the pre-index period. Potential TIR patients were identified as patients who either (i) did not refill a triptan but used a nontriptan medication or (ii) refilled a triptan but augmented it with a nontriptan medication over the 24-month follow-up. Patients who continued filling triptan therapy only were categorized as triptan-only continuers. Treatment patterns of triptans, ergots, butalbital, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioids filled within 15 days of a medical claim with a migraine diagnosis were examined over 6-, 12-, and 24-month periods.

Results: Of 10,509 new triptan users, 3102 (29.5%) were potential TIR patients, 4371 (41.5%) were triptan-only continuers, and the remainder (29%) did not refill either triptans or other acute medications. In the overall sample, 6.5%, 9.5%, and 13.9% switched to or added a different triptan over 6, 12, and 24 months, respectively. Even among potential TIR patients, only 11% and 15% tried a different triptan within 6 and 12 months, respectively, which represents 3.3% and 4.5% of the overall sample. Opioids were the most commonly used nontriptan medication by TIR patients within the first 12 months: 52% filled an opioid medication, 69.5% of whom were new opioid users.

Conclusion: High rates of triptan discontinuation, minimal use of ≥ 2 different triptans, and high opioid use among new triptan users suggest potentially suboptimal response or tolerability issues with current standard of care and the need for new acute treatments.

Disclosure of Interests: Sponsorship: Allergan plc, Dublin, Ireland.

Anand S. Shewale is a full-time employee and shareholder of Allergan. Steven C. Marcus is a consultant for Allergan. Richard B. Lipton serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache. He has received research support from the NIH. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS, and has served as consultant or advisory board member for or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, and Vedanta. He receives royalties from Wolff's Headache (8th Edition, Oxford University Press), Informa, and Wiley. He holds stock options in eNeura Therapeutics and Biohaven. David W. Dodick, MD, within the last 36 months, reports personal fees from Acorda, Amgen, Alder, Allergan, Autonomic Technologies, Biohaven, Colucid, Eli Lilly, eNeura, Foresight Capital, Neuroief, Zosano, WL Gore, Vedanta Associates, Promius Pharma, Magellan Healthcare, CC West Ford Group, Nocira, Novartis, NuPathe, Supernus, Electrocore, Tonix, Teva, Alcobra, Insys, Ipsen, Charleston Laboratories, Biocentric, Theranica, Xenon, and ZPOpco; travel expense reimbursement and speaking fee from Sun Pharma; anticipated income from consulting within the next 3 weeks not previously reported from Impel Pharmaceuticals (currently under review by Mayo Clinic Medical Industry Relations Committee); compensation for activities related to a data safety monitoring committee from Axsome; speaking fees or fees related to CME content development from Healthlogix, Medicom Worldwide, Medlogix Communications, MedNet, Miller Medical Communications, PeerView Operation Services America, Web MD/Medscape, American Academy of Neurology, American Headache Society, PeerView Institute for Medical Education, Chameleon Communications, Academy for Continued Healthcare Learning, Universal Meeting Management, Haymarket Medical Education, Global Scientific Communications, UpToDate, and Meeting LogiX; royalties from editorial or book publishing from Oxford University Press, Cambridge University Press, Wiley Blackwell, Sage, and Wolters Kluwer Health; and a consulting use agreement through his employer with NeuroAssessment Systems and Myndshft. He holds equity in Aural Analytics, Healint, Theranica, Second Opinion/Mobile Health, and Epien, and serves on the board of directors of King-Devick Technologies and Ontologics. Hema N. Viswanathan is a full-time employee and shareholder of Allergan. Jalpa A. Doshi is a consultant for Allergan.

IHC-OR-041

Acute Treatment with Rimegepant 75 mg Confers Clinically Relevant Improvement in Migraine-Related Disability: Results from a One Year, Open-Label Safety Study (BHV3000-201)

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Objective: Epidemiologic studies have shown that migraine is among the most disabling neurologic conditions, burdening adults in their most productive years. The effect of rimegepant 75 mg oral tablet on migraine-related disability was assessed over 52 weeks of use as an acute treatment.

Methods: BHV-3000-201 is a multicenter, 1 year, open-label safety study of rimegepant 75 mg oral tablet. Eligible subjects include adults with ≥ 1 year history of migraine (ICHD-3 beta) who have been instructed to treat migraine attacks of any pain intensity with rimegepant 75 mg up to once daily as-needed for up to 52 weeks. Disability was assessed at baseline and Weeks 12, 24, 36, and 52 via the Migraine Disability Assessment (MIDAS), a validated 5-item instrument that queries migraine-related absenteeism and lost productivity at work, school, and home, as well as missed family, social, and leisure activities. Mean changes from baseline in total scores were analyzed post-hoc with paired t-tests, with decreasing scores signifying benefit.

Results: A total 1789 subjects was assessed. At Weeks 12, 24, 36, and 52, populations of 1631, 1211, 1085, and 917 subjects respectively were analyzed. Baseline mean total MIDAS score was 33.0 ± 0.8 (SEM) corresponding to the grade of severely disabled. Mean [95% C.I.] change from baseline in total MIDAS score was -12.5 [$-13.9, -11.1$] at Wk 12; -14.2 [$-15.8, -12.6$] at Wk 24; -14.8 [$-16.6, -13.1$] at Wk 36; and -14.1 [$-15.9, -12.2$] at Wk 52. Improvements in migraine-related disability were clinically and statistically significant at all time points $p < .0001$).

Conclusion: Acute treatment with rimegepant 75 mg confers significant improvement in migraine-associated disability, transitioning patients from severe to moderate disability within 3 months. This improvement was sustained out to one year. Observed changes exceeded the minimum clinically important difference (5 disability days/3mos) by nearly three-fold at all time points. These benefits would favorably impact healthcare costs, workplace productivity, and patient wellbeing.

Disclosure of Interests: GL, RC, ES, CJ, VC are employees and shareholders of Biohaven; RL is a consultant and shareholder to Biohaven.

IHC-OR-043

Long-term Safety of Qtrypta for the Acute Treatment of Migraine – 1-year Safety Results of Nearly 6,000 Treated Attacks

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Objective: Qtrypta is an intracutaneous microneedle formulation of zolmitriptan developed for acute migraine. Efficacy for freedom from pain and most bothersome symptom (MBS) at 2 hours was demonstrated in a previous randomized double-blind placebo-controlled trial. Our objective was to evaluate the safety of repeated use of Qtrypta 2×1.9 mg for migraine attacks.

Methods: During a 2-week run-in, migraine diagnosis and attack frequency of at least 2/month were confirmed via e-Diary. Subjects then recorded migraine symptoms, treatment effectiveness, and application site skin observations at 30 minutes, 2, 12, 24, and 48 hours post-dose. They completed the Migraine Assessment of Current Therapy (M-ACT) at all scheduled visits. Standard safety procedures and investigator assessment of application sites were done at each visit. Labs and ECGs were performed at beginning and end of study.

Results: In all, 342 subjects qualified, 335 treated at least one attack, 257 completed 6 months, and 127 completed 12 months. The average number of treatments/month was 1.9. The most frequent reason for premature discontinuation was not having 2 attacks/month ($n = 79$). Sixty subjects discontinued between 6 and 12 months once goals were achieved. Sixteen subjects discontinued due to adverse events (AEs); 5 of these were application site reactions, all of which were mild lasting one day or less. The most commonly reported AEs were mild erythema and swelling at the application site (approximately 90% of subjects); more than 80% of both resolved by 48 hours. Application site pain was reported by 14% of subjects on the first treatment, but by only 1% on the 25th. Grading of skin findings did not change appreciably across the 1st, 5th, 15th or 25th treatment. No neurologic adverse event exceeded 2%. Dizziness was reported by 1.8% of subjects. Pain freedom was achieved in 44% of attacks, and MBS freedom was achieved in 62%. M-ACT scores averaged 3.6 out of 4, demonstrating excellent efficacy and subject satisfaction.

Conclusion: Qtrypta was effective and well-tolerated throughout repeated use for the acute treatment of

migraine. The most common AEs were mild application site erythema and edema which resolved quickly.

Disclosure of Interests: SN is on the advisory board for Zosano. PS, JE and DK are employees of Zosano.

IHC-OR-027

Efficacy of IV Hydromorphone versus IV Prochlorperazine plus Diphenhydramine for Migraine-associated Symptoms

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Objective: Parenteral opioids are commonly used to treat migraines in acute care settings. We conducted a randomized trial of IV hydromorphone, an opioid, versus IV prochlorperazine, an anti-dopaminergic anti-emetic. The objective of this study is to compare improvement in migraine-associated symptoms (nausea, photophobia, and phonophobia) between the two groups.

Methods: This was a randomized, double-blind comparative effectiveness study conducted in two emergency departments in the Bronx, NY, USA. Patients who met ICHD3 criteria 1.1 for migraine without aura, or ICHD3 criteria 1.5.1 for probable migraine without aura were eligible for participation. Patients were excluded if they had used an opioid within the previous month. Participants received either hydromorphone 1 mg IV or prochlorperazine 10 mg IV plus diphenhydramine 25 mg IV. Diphenhydramine was administered to prevent akathisia (a common side effect of IV prochlorperazine). The outcomes of interest were sustained symptom relief for nausea, photophobia, and phonophobia. Sustained relief was defined as having that particular symptom at baseline with complete improvement within two hours after medication administration and no symptom relapse within the subsequent 48 hours.

Results: A total of 127 patients were enrolled, of whom 63 received prochlorperazine and 64 received hydromorphone. Of 49 patients in the prochlorperazine arm who reported nausea at baseline, 34 (69.4%) reported complete resolution without relapse versus 15 out of 49 (30.6%) in the hydromorphone arm (absolute risk reduction [ARR] = 38.8%, 95%CI: 20%–57%, $p = 0.001$). Of 55 patients in the prochlorperazine arm who reported photophobia at baseline, 23 (41.8%) reported complete resolution without relapse versus 13 out of 62 (20.9%) in the hydromorphone arm (ARR = 20.8%, 95%CI: 4.3%–37.3%, $p = 0.014$). Of 56 patients in the prochlorperazine arm who reported phonophobia at baseline, 25 (44.6%) reported complete resolution without relapse versus 16 out of 59 (25.4%) in the hydromorphone arm (ARR = 17.5%, 95%CI: 0.26%–34.8%, $p = .049$).

Conclusion: IV prochlorperazine plus diphenhydramine is significantly more effective than IV hydromorphone for the acute treatment and complete resolution of migraine-associated symptoms.

Disclosure of Interest: None Declared.

IHC-OR-035

Acute Actions of Caffeine in the Trigemino-cervical Complex Relevant to Headaches

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Objective: Caffeine, an adenosine receptor antagonist, is often used as an analgesic of headache attacks. Here we aimed to investigate its actions in the trigemino-cervical complex (TCC), a key relay centre in headache's pathophysiology.

Methods: The presence of A1 and A2 adenosine receptors in the trigeminal ganglia and TCC was investigated utilising qPCR and immunofluorescence. Caffeine at 10 and 60 mg/kg was injected in the trigemino-vascular migraine model and activation of second order neurons in the TCC in response to A δ - and C-fibre activation was assessed. In a different set of experiments, the actions of caffeine at 60 mg/kg were investigated on the number of Fos-positive cells in the TCC following trigemino-vascular stimulation, assessed using immunohistochemistry.

Results: The A1 but not the A2 receptor was found to be present in both trigeminal ganglia and TCC. Caffeine at 10 and 60 mg/kg induced an initial facilitation of spontaneous neuronal firing ($P < 0.05$), which was in line with a rapid drop of blood pressure within the first 5 min of administration. Caffeine at both doses significantly inhibited A δ -fibers activation in response to trigemino-vascular stimulation ($P < 0.05$), while it had little effect of C-fibre evoked activity ($P \leq 0.49$). Caffeine at 60 mg/kg reduced significantly the number of Fos-positive cells in the TCC following trigemino-vascular stimulation ($P < 0.05$).

Conclusion: Acute caffeine at high doses blocks activation of the ascending trigemino-vascular pathway, potentially by blocking the A1 receptor activity.

Disclosure of Interest: None Declared

Migraine Preventive Therapy**IHC-OR-039****Sustained efficacy and long-term safety of erenumab in patients with episodic migraine: 4+ year results of a 5-year, open-label treatment period**

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Objective: Erenumab (AMG334; Aimovig™, Amgen®, Novartis Pharma AG) is a fully human monoclonal antibody specifically designed for the prophylactic treatment of migraine. Long-term efficacy and safety data of erenumab for prevention of migraine are limited.

Methods: We conducted an efficacy and safety analyses at an interim 4+ years of a 5-year, open-label treatment period (OLTP) with erenumab in patients with episodic migraine (EM). In the OLTP, patients initially received erenumab 70 mg monthly (QM), and later (protocol amendment after ~2 years) switched to 140 mg QM.

Table. Exposure-adjusted incidence rate/100 patient-years for constipation.

	Placebo	Erenumab 70 mg	Erenumab 140 mg
During the 12 weeks of shorter-term studies*	4.3	5.6	13.3
During the 4+ years of the OLTP	–	1.3	2.6

*Pooled results across 4 placebo-controlled studies; OLTP, open-label treatment period.

Results: Of the 250 patients who switched from erenumab 70 mg to 140 mg, 221(88%) completed OLTP or remained on 140 mg at 4+ years. Mean[SD] change from baseline, in monthly migraine days (MMD; 8.7[2.7]) to end of year 4+ was –5.8[3.8], and in acute migraine-specific medication treatment days (baseline: 6.1[2.7]) was –4.6(3.3). A ≥50%/≥75%/100% reduction in MMD at 4+ years was achieved by 77%/56%/33% of patients, respectively. The median(Q1, Q3) exposure for 383 patients who received ≥1 dose of erenumab 70 mg or

140 mg was 58.5(17.0, 62.2) months. The exposure-adjusted incidence rate/100 patient-years of AEs and serious AEs was 124.9 and 3.8, respectively. AEs were less frequent vs. placebo; nasopharyngitis (10.9), upper respiratory tract infection (6.8), and influenza (4.7) were the most frequent. Rate of SAEs during OLTP was similar to that observed for erenumab and placebo during shorter term period. Compared to shorter term period, the exposure-adjusted incidence rate/100 patient-years for constipation did not increase during OLTP (**Table**) and no new safety signals or increase in incidence of AEs or SAEs were observed. 19(5.0%) patients discontinued due to an AE.

Conclusion: In a 4+ year interim analysis of the OLTP with erenumab in EM, long-term treatment demonstrated sustained reductions in migraine frequency, and was well tolerated and safe.

Disclosure of Interests: This study (NCT01952574) was supported by Amgen Inc. Erenumab is codeveloped by Amgen and Novartis.

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Neurology, American Headache Society, PeerView Institute for Medical Education, Chameleon Communications, Academy for Continued Healthcare Learning, Universal Meeting Management, Haymarket Medical Education, Global Scientific Communications, UpToDate, Meeting LogiX; Royalties from editorial or book publishing: Oxford University Press, Cambridge University Press, Wiley Blackwell, Sage, Wolters Kluwer Health; Consulting use agreement through employer: NeuroAssessment Systems, Myndshft; Equity (stock options): Aural Analytics, Healint, Theranica, Second Opinion/Mobile Health, Epien, Ontologics. Board of Directors position: King-Devick Technologies, Epien, Ontologics; Denise E. Chou – employee of and stockholder in Amgen; Shaloo Pandhi – employee of and stockholder in Novartis; Fei Xue – employee of and stockholder in Amgen; Feng Zhang – employee of and stockholder in Amgen; Sunfa Cheng – employee of and stockholder in Amgen; Daniel D. Mikol – employee of and stockholder in Amgen.

IHC-OR-042

A Randomized, Placebo-Controlled Study of Galcanezumab in Patients with Treatment-Resistant Migraine: Double-Blind Results from the CONQUER Study

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Objective: The CONQUER study assessed galcanezumab efficacy and safety in patients with episodic or chronic migraine who had multiple migraine preventive treatment failures.

Methods: In this phase 3, double-blind study, patients were aged 18–75 years, met criteria for episodic or chronic migraine, had 4–29 migraine headache days per month, and had 2–4 migraine preventive medication category failures in the past 10 years. Eligible patients were randomized 1:1 to receive galcanezumab 120 mg/month (with 240-mg loading dose; N=232) or placebo

(N=230). Headache information was captured in a daily electronic diary. Primary endpoint was overall mean change from baseline in number of monthly migraine headache days across Months 1–3. Key secondary endpoints included $\geq 50\%$, $\geq 75\%$, or 100% reduction in monthly migraine headache days and change on the Migraine-Specific Quality of Life-Role Function Restrictive domain.

Results: Galcanezumab-treated patients had significantly greater reduction in migraine headache days versus placebo. The galcanezumab group averaged 4.1 fewer monthly migraine headache days from a baseline of 13.4, and the placebo group averaged 1.0 fewer from a baseline of 13.0 (between-group difference -3.1 ; $p < 0.0001$; 95% CI: $-3.9, -2.3$; effect size = 0.72). Galcanezumab was superior to placebo on all key secondary endpoints. There were no statistically significant differences in treatment-emergent adverse events except for those reported more frequently in the placebo group. One galcanezumab-treated patient discontinued early due to an adverse event (rash).

Conclusion: Galcanezumab was superior to placebo in preventive treatment of migraine and was safe and well tolerated in patients who had previous failures to standard-of-care preventive treatments.

Disclosure of Interests: Wim M. Mulleners: Financial compensation for a Lilly European Advisory Board.

Byungkun Kim: Advisory role from Eli-Lilly, Teva, Novartis, Allergan and National Pension Service of Korea and received the honoraria for speeches from Allergan, SK chemicals, YuYu, and Sandoz Pharma.

Miguel JA Láinez: Honoraria, consultation fees and research grants from: Allergan, Amgen, ATI, Bayer, Bial, Boehringer, Chiesi, ElectroCore, Eli Lilly, Medtronic, Novartis, Otsuka, Roche, Teva and UCB.

Michel Lanteri-Minet: In the last five years, received honoraria for advisory boards, speaker panels or investigation studies from Allergan, Amgen, Astellas, ATI, BMS, Boehringer, Boston Scientific, CoLucid, Convergence, Glaxo-SmithKline, Grunenthal, Lilly, Medtronic, Menarini, MSD, Novartis, Pfizer, ReckittBenckiser, Saint-Jude, Sanofi-Aventis, Teva, UCB, Zambon.

Sheena K. Aurora: Employee and minor stockholder of Eli Lilly and Company.

Russell M. Nichols: Employee and minor stockholder of Eli Lilly and Company.

Shufang Wang: Employee and minor stockholder of Eli Lilly and Company.

Antje Tockhorn-Heidenreich: Employee and minor stockholder of Eli Lilly and Company.

Holland C. Detke: Employee and minor stockholder of Eli Lilly and Company.

IHC-OR-025**Treatment of chronic migraine with Erenumab alone or as an add on therapy; a real world prospective observational study**Guy P. Boudreau^{1,*} and Demers Catherine¹¹Neurology, Clinique des céphalées de Montréal, Montreal, Canada

Objective: We treated chronic migraineurs that have failed more than 3 preventive drugs with Erenumab alone or as an add on therapy to reduce the frequency of monthly headache days, to evaluate if the add on of Erenumab to another preventive therapy is superior to Erenumab alone, and assess all adverse events related to the use of Erenumab.

Methods: Migraineurs with 15–30 headache days per month at baseline with or without an actual preventive drug, were clustered in 3 categories. Failure of Erenumab was defined as no improvement in the frequency of monthly headache days. Group I: no preventive therapy, prior to the start of Erenumab. (No botox cohort), Group II: on Botulinum Toxin A (Botox), prior to the add on therapy with Erenumab. (Botox cohort), Group III: on an oral preventive drug, prior to the add on therapy with Erenumab. (No Botox cohort).

Results: Patients were evaluated after the 4th injection session. A total of 158 patients were involved in this study. 118 patients (75%), received Erenumab 140 mg., and 40 patients (25%) received 70 mg., In the Botox cohort, of 650 patients, 90 (13%) patients were eligible. In the no Botox cohort, 533 patients, 83 (15%) patients were eligible. From all cohorts; 53pts/158(34%) obtained no improvement. 36pts/158 (23%); obtained a reduction in intensity of headache only. 69pts/158 (43%); reduced the frequency of their monthly headache days. 57% of patients failed the primary end point. The primary objective being the reduction of monthly headache days, of these 69 patients: in group I: 16patients (26%), reduced their monthly headache days. In group II, 45 patients (65%), and group III, 11 patients (15%) reduced their monthly headache days by 5–7 days. In group II and III all patients became episodic, in group I, 25% stayed chronic, 75% became episodic. 72 adverse events were experienced during the 4 months of treatment, mostly with the 140 mg. dose. The most frequent were: constipation 34%, fatigue 19%, itching 7.5%, muscle cramps 6.3%, increased headache 4.4%, rhinitis 4.4%, injection site discomfort 3.7%, lack of energy 3.1%

Conclusion: In this study the add on of Erenumab to a preventive therapy is more effective than Erenumab alone, Botulinum toxin A with the add on of Erenumab was the most effective combination.

Disclosure of Interests: principle investigator in a Lilly clinical trial with galcanezumab

IHC-OR-026**The Aimovig “Wear-Off” Effect: A Retrospective Analysis**Rose Duncan^{1,*}, Naveen George¹ and Deborah Reed¹¹Neurology, University Hospitals Cleveland Medical Center, Cleveland, United States

Objective: Recently, the class of Anti-CGRP monoclonal antibodies has been approved for use in the treatment of migraine headaches. With the advent of this migraine specific medication class, many chronic migraine patients have started this preventative treatment. The first FDA approved in this class is Aimovig (erenumab). As demonstrated in collaborative research, a small cohort of patients on this medication have been found to have a “wear-off” effect where Aimovig was found to not be as effective by the end of the month as it was at the beginning of the month. The primary objective of this study was to identify trends in demographics, migraine characteristics, and comorbidities among patients who experienced an Aimovig “wear-off” effect.

Methods: Through retrospective chart review, we identified patients that were started on Aimovig 140 mg monthly injections that had an initial response to medication at the beginning of the month, followed by an increase in frequency and severity of headaches by the end of the month. Patient demographics, BMI, migraine type, and comorbidities were assessed to identify trends among this cohort of patients experiencing an Aimovig “wear-off” effect.

Results: Of the 190 patients started on Aimovig in this outpatient headache specialty clinic, 17 were identified as having a “wear-off” effect. Of these 17 patients, patient age range spanned 30–76 years, however 76.5% were between the ages of 45 and 65. 76.5% were female, and 100% were Caucasian. 100% suffered from chronic migraine, and 94.1% had migraines without aura. 41.2% had an overweight BMI, and 23.5% were obese. 41.2% had cardiovascular comorbidities, 52.9% had psychiatric comorbidities, and 26.3% had BPPV. 64.7% had non-headache pain syndromes, including 23.5% with cervical dystonia and 23.5% with cervical radiculopathy.

Conclusion: Among patients with Aimovig “wear-off”, the vast majority were middle-aged, Caucasian, and female, and all but one denied migraine aura. Over half of patients had psychiatric comorbidities, and an even larger portion of patients had comorbid non-headache pain syndromes. BPPV, cervical dystonia, and cervical radiculopathy were surprisingly prevalent among this cohort. While many trends were identified, additional information is still necessary in order to further predict and identify patients at risk of this Aimovig “wear-off” effect.

Disclosure of Interest: None Declared

Other Primary Headache Disorders

IHC-OR-034

Analgesic effect of intranasal oxytocin in a rat model of trigeminal neuralgia

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Objective: Trigeminal neuralgia (TN), is a chronic syndrome manifesting primarily in episodes of “lightning like”-sharp pain, usually the results of trigeminal root compression (TRC) by an adjacent artery. Current therapy often provides incomplete management.

We have shown that nasally applied oxytocin concentrates in the trigeminal nerve and ganglia, and inhibits firing of peripheral and central trigeminal nociceptive neurons. The purpose of this study was to determine whether nasally applied oxytocin would attenuate the exquisite facial mechanical hypersensitivity that is observed in a rodent model of trigeminal neuralgia.

Methods: Male rats were prepared using a trigeminal neuralgia model (Klukin and Yeomans, 2012), wherein crystals of a super absorbent polymer were stereotaxically placed between the trigeminal nerve root and the crista petrosa of the temporal bone. Over the next few days, the polymer absorbed moisture and expanded to form a compressing mass, resulting in exquisite hypersensitivity to touch with a fine artists brush in the peri-oral region, which is assessed by blinded scoring of the response to stimuli. In order to establish the pharmacologic validity of the model, the effects of 4 days of daily high dose of carbamazepine (30 mg/kg, IP), the first line drug for the treatment of trigeminal neuralgia, was tested on perioral brush sensitivity was tested. In other similarly prepared rats, the effects of a single administration of nasal oxytocin (1.0IU) was similarly tested.

Results: Behavioral Phenotype: Application of polymer crystals to the trigeminal nerve root produces a resident mass which compressed the trigeminal nerve root resulting in a behavioral phenotype highly reminiscent of human trigeminal neuralgia, including exquisite peri-oral hypersensitivity to brush.

Behavioral Pharmacology: Both daily treatment with carbamazepine for 4 days significantly and a single dose of nasal oxytocin both significantly decreased responsiveness to brush stimulation of the peri-oral face.

Conclusion: These results indicate that the trigeminal neuralgia-like behavioral phenotype consequent to chronic compression of the trigeminal nerve root of rats can be attenuated by nasal application of oxytocin, implying the potential of this treatment for patients suffering from TN.

Disclosure of Interests: Founder and shareholder Trigemina, Inc.

Post-Traumatic Headache

IHC-OR-037

CGRP dependent- and independent-mechanisms of acute and persistent post-traumatic headache following mild traumatic brain injury in mice

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Objective: The underlying physiological mechanisms of post-traumatic headache (PTH) and persistent PTH (PPTH) remain unknown, and there are no currently approved therapies for these often debilitating conditions. The aim of this study is to explore the efficacy and timing of intervention with a murine anti-calcitonin gene related peptide (CGRP) monoclonal antibody (mAb) in novel mouse models of PTH/PPTH.

Methods: Male C57Bl/6J mice received sham or mild TBI (mTBI) from a weight drop that allowed free head rotation. Periorbital and hindpaw tactile stimulation were used to assess cutaneous allodynia (CA). Mice were challenged with stress, a common aggravator of migraine and PTH, by exposure to bright lights (i.e., bright light stress, BLS) 2 weeks after mTBI; CA was again assessed. A murine anti-CGRP mAb was administered after mTBI with different dosing regimens to investigate the effect of either early and sustained CGRP sequestration or late administration on CA.

Results: mTBI-mice, but not sham-mice, displayed acute periorbital and hindpaw CA. After resolution of CA, exposure to BLS evoked CA in mTBI-mice only. Early and repeated administration of an anti-CGRP mAb attenuated the development of acute CA and prevented BLS-induced CA. A single administration of an anti-CGRP mAb, prior to BLS challenge, did not prevent BLS-induced CA.

Conclusion: In clinically-relevant, novel models, mTBI-mice demonstrated transient periorbital and hindpaw CA suggestive of PTH-related pain and central sensitization; subsequent exposure to BLS re-established CA, suggestive of PPTH-related pain. Continuous early sequestration of CGRP prevented both PTH and PPTH. A single, delayed anti-CGRP mAb treatment was ineffective in preventing PPTH-like pain. These observations suggest that CGRP-related mechanisms underlie the symptoms of PTH and

drive the development of central sensitization, increasing vulnerability to headache triggers and promoting PPTH. Early and continuous CGRP blockade following mTBI may represent a viable treatment option for PTH and for the prevention of PTH persistence.

Disclosure of Interests: This study was funded by Teva Pharmaceutical Industries Ltd.

Psychological and Behavioural Factors and Management

IHC-OR-030

Loneliness in migraine: results from a case-control study

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Objective: While there is solid evidence for a bilateral correlation between psychiatric comorbidities and migraine, loneliness has been only been examined sparsely in migraine. Increased rates of loneliness have been reported in elderly patients with migraine. Importantly, loneliness correlates also with depression, physical activity and sleep. The aim of this study was to examine the correlation between migraine and loneliness in a case-control study.

Methods: In a case-control study, 112 patients (80% females, mean age 42 years) with migraine according to the ICHD-3 treated at a tertiary referral center and 107 controls (55% females, mean age 41 years) were recruited. Loneliness was determined with the German translation of the UCLA Loneliness Scale (20 items with a 5 point Likert scale with a sum score between 20–100 with higher scores indicating greater loneliness). Additionally, depression was assessed with the PHQ-9 (9 items). To detect statistical differences, a general linear model was used.

Results: The level of loneliness was higher among participants with migraine ($M = 34.64$, $SD = 12.69$) compared to controls ($M = 29.04$, $SD = 7.18$) and differed significantly ($F(1,209) = 11.39$, $p < .001$). There was no statistically significant difference in loneliness sum scores for the different age groups ($F(2,208) = 0.48$, $p = .619$), for sex ($F(1,209) = 1.89$, $p = .171$) and for the interaction case/control*sex ($F(1,209) = 0.11$, $p = .740$) and the interaction case/control*age group ($F(2,208) = 0.39$, $p = .675$). An additional linear regression was conducted which showed that depression is a predictor of loneliness ($\beta = .42$,

$p < .001$), while a group specific effect cannot be found anymore ($\beta = -.06$, $p = .441$).

Conclusion: Loneliness is more pronounced in patients with migraine and not related to age or sex in this sample. However, depression seems to predict loneliness. These results are important as both loneliness and depression are relevant comorbidities of migraine and underline the need of proper psychiatric assessment in migraine patients and rigorous treatment. Additional analyses on the influence of social networks will reveal further insights into this potentially relevant finding.

Disclosure of Interests: None.

Big Data

IHC-LB-001

Effect of digital smartphone application “Migräne App” on therapy decisions, compliance, treatment quality and headache parameter

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Objective: Tension-type headache and migraine are among the most prevalent disorders. The use of smartphones enables “apps” for digital therapy accompaniment. In this study, the use of the “migraine app” will be examined in the treatment of migraine and headache patients in an extensive population sample.

Methods: An online survey was developed. It contains socio-demographic variables, course of headache disorders, previous treatment as well as usage of the migraine app. The app establishes compliance to recommended therapy, treatment plan, and therapeutic rules devised by the treating physician. The data was compared to pen-and-paper documentation, prior to using the migraine app.

Results: 1.464 users participated in the study. Average age was 47.19 ± 11.37 years (87.4% female). Users suffered from headaches for 27.28 ± 13.6 years. Most (76.5%)

were seen by general practitioners. 70.9% reported presentation of data from the app to their physician on consultation. 76.4% reported the app helped to adhere to treatment plan and rules designed with their physician. A significant reduction of headache days per months prior to usage ($13,30 \pm 7,45$) in comparison to the time of survey conduction ($10,03 \pm 7,30$) and significant reduction of intake of acute medication was seen (before: 7.61 ± 5.58 vs. ongoing: 6.78 ± 4.72 days). No gender/age differences were observed. A significant reduction of mean headache hours/month and headache intensity was ascertained ($p < 0.0001$)

Conclusion: The data shows that the digital treatment control for therapy decisions made by the physician is highly relevant. Therapy compliance is improved and possible complications such as medication-overuse headache are reduced. Overall, a marked improvement of treatment quality due to more easily available information and self-help tools can be observed.

Disclosure of Interest: None Declared.

IHC-LB-002

Is migraine frequency correlated with its periodicity? An annual follow-up of how migraine cycles

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Objective: To analyze the cyclic evolution of migraine patients over a 12-month period.

Methods: Prospective observational study. Patients were recruited according to completion of a digital migraine calendar, available on the midolordecabeza.org website, over a 12-month period. Basic clinical characteristics were recorded. A comparative trimestral analysis, identifying the variation coefficient (VC) and fold-change (FC) as a function of basal frequency intervals, was executed.

Results: 97 patients (83.5% female; mean age 44.0 ± 11.6 years) were analyzed: 71.1% met criteria for episodic migraine (EM) with a mean monthly frequency (MMF) of 8.1 ± 3.5 and 28.9% for chronic migraine (CM) with a MMF of 22.9 ± 4.9 . At follow up, a 20.6% of participants were using preventative treatment. Patients with EM presented increased heterogeneity (VC) as compared to those with CM (EM-28% vs. CM-16%, $p < 0.05$). There were no differences in FC in respect to diagnosis. A negative correlation between frequency and FC ($p < 0.05$) was identified, which permitted us to detect that a MMF between

6–15 days co-occurred with a higher FC ($p < 0.01$) and worse disease progression ($\leq 5d$: 11.1%, 6–15d: 46.2% $y > 15d$: 14.8%; $p < 0.01$). Factors associated with increased heterogeneous periodicity and exacerbation of symptoms include: younger age ($p < 0.01$), absence of aura ($p < 0.05$) and increased stress ($p = 0.05$).

Conclusion: EM patients with a basal frequency between 6–15 days present increased trimestral cyclical heterogeneity as compared to EM with < 6 days and CM. In addition to the basal frequency, a younger age, absence of aura and higher stress levels are correlated with increased oscillatory behavior of trimestral frequency. Increased cyclical heterogeneity would therefore appear to imply an increased risk for disease progression.

Disclosure of Interest: None Declared.

IHC-LB-049

Network Analysis of Headache Literature Citations

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Objective: Citation analyses of headache literature have usually been conducted through direct keywords or topic searches of “headache” and/or “migraine” in databases. This method systematically excludes non-headache publications and may offer an incomplete view of areas influencing headache research. We seek to resolve this shortcoming by analyzing all PubMed Central (PMC) articles discovered through citations, up to 2 degrees of separations, from known headache articles.

Methods: We obtain an initial list of PMC articles, or *seed articles*, through keyword searches for “headache” and “migraine”. We then identify all PMC articles that each of our *seed articles* references. New articles discovered through this process are documented and their citations are also identified for the purpose of discovering more articles. We identify new articles through this process for a total of 2 iterations. The set of all articles obtained are included in our study.

We generate a network model as follows: each article is considered a “node” in the model; if one article references another then an “edge” exists between the two. We obtain the 10 most important articles based on 3 measures of interconnectedness: *Degree centrality* identifies nodes with the most edges. *Between-ness centrality* identifies nodes serving as bridges between subgroups. *Closeness centrality* identifies nodes occupying the shortest distances to all other articles in the network.

Results: Our model has 79666 nodes and 143154 edges. Top 10 articles by *closeness centrality* include: 6 research articles on either migraine genetics or aura

pathophysiology, 4 review articles on migraine pathophysiology and burden of diseases. Top 10 articles by *betweenness centrality* include: 3 research articles on migraine genetics or aura pathophysiology, 3 review articles on migraine pathophysiology, 4 review article on migraine and cardiovascular diseases, pharmacology, and burden of diseases. Top 10 articles by *degree centrality* include review articles on topics of epidemiology, migraine and sleep pathophysiology, pharmacology, and molecular biology.

Conclusion: Review articles on migraine pathophysiology as well as original researches on migraine aura and migraine genetics serve as major brokers of ideas in PMC headache literature. Non-headache literature influencing headache research comprise mostly of review articles in epidemiology and pharmacology.

Disclosure of Interests: Consultant for BoardVitals Inc., Consultant for Fieve Clinical Research.

Cluster Headache and Other Trigeminal Autonomic Cephalalgias

IHC-LB-003

Clinical Evidence for Peripheral and Central Nervous System Sensitization in Hemicrania Continua

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Objective: Determine the clinical evidence for both peripheral and central nervous system (trigeminal nucleus caudalis, thalamus, and limbic system) sensitization in subjects with hemicrania continua (HC).

Methods: A total of 108 subjects (hemicrania continua [n=34], tension-type headache [n=54] and non-headache [n=20]) participated in this clinical investigation. All subjects completed an extensive medical history which included quantitative measures of headache related disability (Migraine Disability Assessment Scores [MIDAS], cutaneous allodynia (Allodynia Symptom Checklist [ASC-12]), misophonia (Misophonia Assessment Questionnaire [MAQ]), tryphobia (Tryphobia Image Score [TIS]), modified Lee, Cole and Wilkins Tryphobia Score [mLCWTS]) and TES (Emotional Response to Various Surfaces Score [ERVSS]).

Results: Average MIDAS were 0.2, 1.4, and 64 for non-headache (NH), tension-type headache (TTH) and hemicrania continua (HC) respectively. Headache days in the last ninety ranged from an average of 0.2 (NH), 1.4 (TTH) and 57 (HC). Average pain intensity also varied depending on headache type: NH (1.1), TTH (1.7) and HC (5.2).

Seventy-nine percent of HC subjects described their pain as “throbbing” and 65% claimed routine physical activity made their pain worse. Average ASC-12 scores were <0.5 in NH and TTH groups and 5.4 in HC. HC subjects reported both cephalic (54%) and extra-cephalic (18%) cutaneous allodynia. Allodynia was confined to the side of their headache 79% (cephalic) and 29% (extra-cephalic) of the time. The average MAQ scores were <0.7 in NH and TTH and 7.7 in HC. TIS and mLCWTS were lower in NH (0.3/18) and TTH (0.2/17) as compared to HC (1.4/20). ERVSS were higher in HC (1.9) versus NH (0.5) and TTH (0.6).

Conclusion: HC subjects commonly reported a “throbbing” pain exacerbated by routine physical activity which supports a capacity for peripheral sensitization. Likewise, HC subjects had average allodynia scores ~18x greater than NH subjects. Both cephalic and extra-cephalic allodynia were reported in HC subjects supporting central sensitization at the level of both the trigeminal nucleus caudalis and the thalamus. Finally, limbic system sensitization can be implicated in HC as evident by misophonia, tryphobia and TES scores that were ~19x, ~4.7x and ~3.8x (respectively) more severe compared to NH subjects.

Disclosure of Interest: None Declared.

IHC-LB-004

Evaluating the Treatment of Cluster Headache with Oxygen

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Objective: To identify the phenotypical features of patients with cluster headache that predict therapeutic response and rebound attacks with oxygen therapy.

Methods: A questionnaire study was conducted in the South Central region of the UK from a database of 489 patients receiving oxygen for the indication of cluster headache. The diagnosis of cluster headache was made using the International Classification of Headache Disorders (ICHD-3). The questionnaire was validated by telephone follow-up interview of 20% of respondents randomly selected. Oxygen therapy satisfaction, reporting of rebound attacks after oxygen therapy, patient characteristics and cluster attack characteristics were collected and tabulated. Differences were examined by Mann Whitney U, Kruskal-Wallis and χ^2 tests.

Results: From the database, 170 patients consented to receiving questionnaires, of which, 77 responded.

All respondents met the ICHD-3 criteria for cluster headache; 62% male and 28% with chronic cluster headache. Current or ex-smokers accounted for 49%. In association with cluster headache attacks, 97% reported presence of at least one cranial autonomic symptom, 93% report agitation, 55% reported photo-sensitivity, 46% reported photophobia and 41% reported nausea.

Rebound attacks after acute treatment with oxygen was reported by 67% of patients.

We identified that patients reporting 5 or more cranial autonomic symptoms ($p=0.049$), conjunctival injection ($p=0.048$) or ptosis ($p=0.047$) were more likely to be satisfied with oxygen treatment.

We did not identify a cluster headache phenotypic feature nor patient characteristic that was significantly different in patients who reported rebound attacks.

Conclusion: Cluster headache patients who report 5 or more cranial autonomic symptoms with attacks, particularly conjunctival injection or ptosis are more likely to be satisfied with treatment of oxygen. Previously reported predictors of oxygen response were not found to be significant. These findings suggests the importance of the parasympathetic pathway in oxygen response.

Disclosure of Interests: Helin Gosalia, Calvin Chan and Diana Y Wei have no conflicts of interest to disclose.

Peter J Goadsby reports, over the last 36 months, grants and personal fees from Amgen and Eli-Lilly and Company, and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Biohaven Pharmaceuticals Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Impel Neuropharma, MundiPharma, Novartis, Teva Pharmaceuticals, Trigemina Inc., WL Gore, and personal fees from MedicoLegal work, Massachusetts Medical Society, Up-to-Date, Oxford University Press, and Wolters Kluwer; and a patent magnetic stimulation for headache assigned to eNeura without fee.

IHC-LB-005

Evaluation of the Computerized Headache Assessment Tool (CHAT-III) for the Diagnosis of Cluster Headache

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Objective: The diagnosis of cluster headache is often delayed for years, leading to delay in effective therapy. The Computerized Headache Assessment Tool (CHAT) is an algorithm-based instrument that screens for primary headache disorders. CHAT was previously validated in a primary care population. The present study was designed to evaluate CHAT in a population of individuals with known cluster headache.

Methods: Phase I was an exploratory phase, to test the algorithm in individuals with known cluster headache, recruited from the website of ClusterBusters.org. Subjects whose CHAT diagnosis differed from their clinical diagnosis were asked to participate in a diagnostic interview. Self-reported diagnoses were also compared to CHAT diagnoses. Discordant results were reviewed, and led to changes in the algorithm. Phase 2 was designed to test the modified questionnaire.

Results: Phase I. 93 subjects completed the survey and 17 completed a diagnostic interview. The mean age was 43.2 years, and 65% were males. Of the 89, 57 received a CHAT diagnosis of cluster headache, 8 a trigeminal autonomic cephalgia not classified as cluster headache (TAC), and 28 a non-cluster headache diagnosis. 22 subjects reported a clinical diagnosis of cluster headache but received either a diagnosis of a non-cluster headache ($n=12$), probable cluster headache ($N=3$), or a TAC ($n=7$). 15 subjects who received other CHAT diagnoses did not participate in a diagnostic interview.

Reasons for CHAT misdiagnosis were caused by: survey responses of headache duration greater or less than ICHD-III criteria; or attack frequency greater or less than ICHD-III criteria. Responses to questions during diagnostic interview often differed from responses to the survey (eg, indicating attacks "never go away").

Modifications were made to the diagnostic algorithm of CHAT, to allow it to query for diagnostic criteria for cluster headache, even if headache duration or frequency are atypical, if headaches occur in cycles.

Phase 2 will evaluate the diagnostic accuracy of CHAT with the revised algorithm.

Conclusion: CHAT-III is highly specific for the diagnosis of cluster headache in a population of individuals with known cluster headache. Modifications to the algorithm will be studied to demonstrate increased sensitivity.

Speakers Bureau for Lilly, Teva, and Amgen/Novartis

Disclosure of Interests: Study funded by Lilly, Inc.

IHC-LB-050

Peripheral Nerve Blocks for the treatment of headache disorders in the UK: An Audit of BASH members' practice

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Objective: To obtain information about the current practice of peripheral nerve blocks-PNB's- for the treatment of headache disorders in the UK.

Methods: Cross-sectional survey (Survey Monkey®) delivered to BASH members about their clinical practice using PNB's. The survey included 11 multiple choice questions about the headache practitioner's geographical location and role, indications and technical aspects of PNB's, clinical setting, safety and outcome measures.

Results: Electronic invitations were sent to registered BASH members without financial incentives, of whom 48% provided data. Of the responders, 80% performed PNB's mostly in dedicated PNB's injection clinics. Responders were: consultant neurologists (51%) and GP's and Nurses (28%); most were from London area, Yorkshire and the south of England. The headache disorders treated were episodic/chronic cluster headache (83%), chronic migraine (80%), occipital neuralgia (60%), PH/HC (51%), status migrainosus and headaches during pregnancy (46%). Practitioners perceived that cluster headaches responded better to PNB's than any other headache disorder. The most common PNB performed was greater occipital nerve GON (98%) followed by lesser occipital nerve (48%), supraorbital (35%) and supra-trochlear (28%) nerve blocks. The most common agents used for GON blocks were lidocaine +/- bupivacaine + methylprednisolone, and for other PNB's was lidocaine only. Local pain/minor bleeding 55%, headache exacerbation 42% and dizziness/presyncopal symptoms 36% were the most frequently reported side effects. Patient satisfaction (68%), headache diaries (50%) and HIT 6 scores (38%) were used more frequently by practitioners as treatment outcome measures.

Conclusion: PNB's are frequently used by UK practitioners for the treatment of headache disorders with variability on their practices. This first collaborative BASH member's survey may serve as an initiative to provide foundations for developing a practical and evidence-based consensus for PNB's, a safe and widespread headache treatment option.

Disclosure of Interests: No Disclosures.

IHC-LB-051

Distinguishing Clinical Features Between Hemicrania Continua and High Frequency Chronic Migraine

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Objective: Determine clinical features beneficial in distinguishing between hemicrania continua (HC) and high frequency chronic migraine (HFCM)

Methods: A total of 68 subjects (HC [n = 34] and HFCM [n = 34]) completed an extensive medical history and differences were explored. HFCM was defined as experiencing over 23 days of headache per month, at least eight of which fulfilled the criteria for migraine.

Results: HC and HFCM subjects were predominantly female (85%/82%) and Caucasian (88%/85%). Average age and age of onset was 53/30 years for HC and 47/19 for HFCM. Without treatment HC subjects experienced a continuous (97%) one-sided (100%) headache compared with HFCM (38% and 74%). Migraine Disability Assessment Scores were 64 for HC and 99 for HFCM. Headache days per month and pain severity were 25/5.2 (HC) and 28/6.2 (HFCM). Allodynia Symptom Checklist scores were 5.4 (HC) and 6.5 (HFCM). Cephalic / extra-cephalic allodynia was more common in HFCM (21%/6%) than HC (15%/3%). Misophonia Assessment Questionnaire scores were 7.2 (HC) and 12.8 (HFCM). Trypophobia Image Scores were 1.4 (HC) and 0.6 (HFCM). Headache features for HC and HFCM were: pounding (79%/97%), severe (97%/100%), worse with routine physical activity (65%/91%), nausea and/or vomiting (74%/88%), photophobia (82%/94%) [worse on side of headache (74%/50%)], phonophobia (79%/100%) [worse side of headache (50%/25%)], ipsilateral "scratchy" eye (35%/21%), misophonia (50%/56%) [worse on side of headache (18%/6%), and trypophobia (20%/18%) [worse side of headache (6%/0%)].

Conclusion: Aside from an absolute response to therapeutic doses of indomethacin, it often can be difficult to clinically separate HC from HFCM. In this cohort, HFCM was associated with an earlier age of onset, more allodynia and increased misophonia. HC was characterized by its unilateral, continuous pain and predominance of ipsilateral associated features.

Disclosure of Interest: None Declared.

IHC-LB-052

Case Report: A 51-year-old Lady With Hemicrania Continua And A Swollen Tongue

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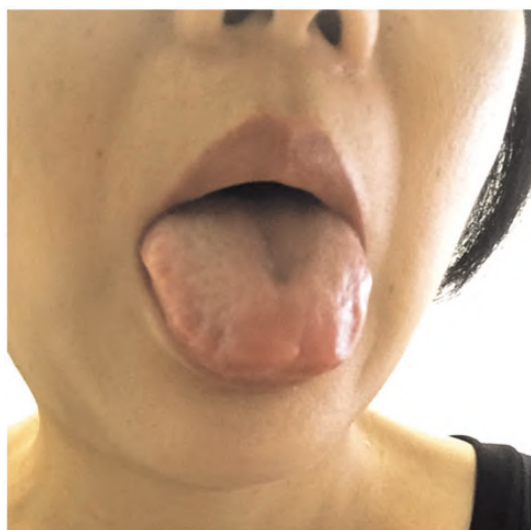
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Objective: To present a patient with hemicrania continua who has a swollen tongue during exacerbation.

Methods: The patient is a 51-year-old lady who has had persistent daily headache for seven years. She had a surgery for chronic frontal sinusitis three months prior to the onset of headache. She recalled that as the discomfort of frontal sinus gradually diminished, she started to felt pain over left neck and left upper teeth. The pain became persistent and never went away a few days later.

She described the pain as a moderate persistent aching pain with exacerbation to severe about three to four times a month. The exacerbation usually lasted hours to two days. During exacerbation, the pain would extend to left retro-orbital and whole left side head accompanied with left ptosis, left periorbital edema, and voice change. She also noticed that her tongue became swelling and even left teeth marks on it during exacerbations (Figure 1).

According to the patient, she has had many unremarkable image studies and has failed lots of medication in these years. She started to experience pain-free since the ninth day with indomethacin 75 mg three times a day. The diagnosis of hemicrania continua was established.



Results: The cranial autonomic features are very important accompanying features in hemicrania continua. To the best of our knowledge, tongue swelling has not been mentioned in the literature. Palatoglossus muscle, which is innervated by vagus nerve and inserted into lateral side of the tongue, may be involved.

Conclusion: Cranial autonomic features other than those listed in the ICHD-3, such as itching eye, aural fullness or aural swelling, had been reported in the literature. The broader symptomology we know may help us understand this unbearable pain better.

Disclosure of Interests: None.

Comorbidity of Primary Headaches

IHC-LB-006

Burden of comorbid depression and anxiety on migraine-specific health-related quality of life in adult migraine patients in the United States

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Objective: Depression and anxiety are often comorbid with migraine and are associated with reduced quality of life and increased overall disease burden. The objective of this study was to examine the impact of comorbid depression and/or anxiety on migraine-specific health-related quality of life (HRQoL) outcomes in the real world from a patient perspective.

Methods: Data were drawn from the 2017 US Adelphi Migraine Disease Specific Programme, which included primary care physicians and neurologists and their consulting migraine patients. Patients completed a questionnaire that included validated measures of migraine-specific HRQoL and general quality of life, such as the Migraine Disability Assessment (MIDAS), Migraine-Specific Questionnaire (MSQ), and the EuroQol 5-Dimension 5-Level (EQ-5D-5L). Depression/anxiety was derived from the EQ-5D domain, and patients were categorized as experiencing none, slight, or moderate-to-severe (moderate+) depression/anxiety. Linear regressions were performed on the EQ-5D visual analogue scale (VAS) and MSQ domains to assess the relationship between the severity of anxiety/depression and headache days on HRQoL outcomes. Poisson regressions were performed on the square root of MIDAS being closest to normality from a number of transformations.

Results: 873 persons with migraine from the Adelphi Migraine Disease Specific Programme provided information on depression/anxiety. More severe anxiety/depression and an increasing number of headache days were associated with poorer MSQ scores, including the overall MSQ score and all 3 MSQ domains ($P < 0.01$). Similarly, more severe anxiety/depression and an increasing number of headache days were associated with more severe disability, based on MIDAS scores ($P < 0.001$). Worse anxiety/depression was also associated with worse overall quality of life, based on EQ-5D VAS scores ($P < 0.001$).

Conclusion: In patients with migraine, higher levels of depression/anxiety were associated with significant

reductions in both migraine-specific (MSQ) and generic (EQ-5D) HRQoL and increments in disability (MIDAS).

Disclosure of Interests: R. B. Lipton is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. Dr. Lipton receives research support from the NIH: 2PO1 AG003949 (mPI), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), IRF1 AG057531 (Site PI), RFI AG054548 (Investigator), IRO1 AG048642 (Investigator), R56 AG057548 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor), IK01AG054700 (Mentor). Dr. Lipton also receives support from the Migraine Research Foundation and the National Headache Foundation. Dr. Lipton serves on the editorial board of *Neurology*, senior advisor to Headache, and associate editor to *Cephalalgia*. Dr. Lipton has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. Dr. Lipton receives royalties from Wolff's Headache 7th and 8th Edition, Oxford Press University, 2009, Wiley and Informa. R. Iyer, J. M. Cohen, and V. Ramirez-Campos are employees of Teva Pharmaceuticals. J. Jackson, S. Cotton, and G. Milligan are employees of Adelphi Real World, and worked on the current analyses, funded by Teva Pharmaceuticals. D. C. Buse has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Lilly, Promeius and Teva. D. C. Buse is on the editorial board of *Current Pain and Headache Reports*.

IHC-LB-007

Risk of Ischemic Vascular Events with DHE use in Chronic Headache

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Objective: Since 1925, ergotamines have been used in the treatment of primary headaches. Dihydroergotamine (DHE) was introduced as an adrenergic agent in 1943; inspired by the vascular theory of an initial cerebral vasoconstriction followed by extracranial vasodilation (1). However, underlying cardiovascular diseases or risk factors represent the major limitation for their use in practice. DHE induces systemic vasoconstriction that may potentially cause serious ischemic events. DHE is still prescribed worldwide and evidence concerning the risk for

serious ischaemic vascular events is scarce (2). Risk of vascular events in patients receiving DHE was explored within a tertiary Neurology Centre.

Methods: A retrospective audit was performed of all patients receiving two or more iv DHE infusions between January 2014 and June 2019 within a tertiary Neurology Centre. The case notes were examined for documentation of cardiovascular events and their risk factors including; hypertension; diabetes mellitus; ischaemic heart disease; smoking history; cerebrovascular disease; hypercholesterolaemia. Any ischemic vascular event was highlighted.

Results: 65 patients were identified; 23 of whom were identified as having risk factors for vascular events. The most prevalent risk factor in those experiencing an ischemic vascular event was a history of smoking. 7 of the 23 patients had a history of ischaemic heart disease or stroke, 4 of whom were diagnosed before commencing DHE. 20 of the 23 patients identified as having risk factors for vascular disease experienced no vascular events whilst receiving DHE. 3 patients who were identified to have had an ischemic vascular event had received DHE infusions between 2–5 years prior to the event. No patients experienced an ischemic vascular event while on treatment with DHE either during the infusion or in between regular treatment periods.

Conclusion: 23 out of 65 patients (35%) receiving DHE infusions had risk factors for vascular disease with 7 patients (10%) having had ischemic heart disease or stroke. No ischemic vascular events were experienced during DHE infusions or in between regular treatment periods. Our audit does not suggest any increased risk of ischemic vascular events with DHE treatment. However we would recommend that all patients who receive DHE treatment should be screened for cardiovascular risk factors.

Disclosure of Interests: Dr Tyagi- from Janssen Cilage, GSK, Allergan, Electrocore, Lily, AMGEN, Novartis, eNeura, Teva, Alder, Abbott, he has received:

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- funding to conduct clinical trials.
- educational grants for meetings/teaching courses.
- funding to attend medical conferences.
- hospitality in and out of hospital premises

IHC-LB-008

Are Migraine and Benign Paroxysmal Positional Vertigo (BPPV) linked?

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Objective: Repeated migraine attacks may cause vestibular dysfunction and dislodge of otoconia from utricle to semicircular canal resulting in Benign Paroxysmal Positional Vertigo (BPPV). The aim of the present study was to evaluate risk factors and linkage of migraine in patients of BPPV

Methods: This observational case-control study was conducted at an outpatient private neurology clinic of Ahmedabad, India from January 2017 to April 2019. 18 to 60 years old patients of confirmed BPPV were evaluated for past or present history of migraine (case). The control was selected from volunteer blood donors of matched demographic features. Patients suffering from severe cervical spine disease, significant carotid artery stenosis, Meniere's disease and acute ongoing strokes were excluded from the study. Latest version of SPSS software was used to analyse this data.

Results: 295 consecutive BPPV cases (250 posterior canals, 45 horizontal canals) and 300 control subjects were studied. Mean age was 42.32 ± 11.45 years in cases and 44.15 ± 12.30 years in the control group. Out of total subjects, 68% were females in cases and 66% in the control group. In the case group, 55 (18.64%) were having past or present migraine (45 migraines without aura, 8 migraines with aura and 2 migraine variants), while in control group 24 (8.0%) were having migraine (20 migraines without aura, 4 migraines with aura). Among BPPV patients, those associated with migraine were younger and more often females, with many having a history of diabetes mellitus and coronary artery disease. Migraine was 2.3 times higher in cases as compared to the control (OR 2.63, 95% C.I. 1.58–4.39, $p=0.0002$) in unadjusted analysis. These results were significant even after multidiscipline adjustment of variables (OR 2.50, 95% C.I., 1.26–4.30)

Conclusion: Migraine was more than two times associated with BPPV as compared to control. Although BPPV and migraine both can present as vertigo, the coexistence of both the diseases is more likely particularly if patients are female, have a history of diabetes mellitus or coronary artery disease. However, our study data should be validated by further large scale trials.

Disclosure of Interest: None Declared

IHC-LB-053

Incidence of constipation in patients treated with commonly used migraine medications

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Objective: Constipation has been reported with newer migraine therapies targeting the CGRP pathway; however, older commonly used migraine medications may also be associated with constipation. The objective was to estimate incidence rates of constipation in patients with migraine treated with commonly used migraine medications.

Methods: A retrospective cohort study was conducted using the MarketScan[®] Research Databases. Patients with migraine were identified from 01/2010-12/2011 using ICD-9-CM codes and claims for migraine-specific acute medications (triptans or ergots). Constipation, identified using ICD-9-CM codes, was defined as any constipation (e.g. a constipation claim in an outpatient (OP), emergency room (ER), or inpatient (IP) hospital setting) or serious constipation (e.g. a constipation claim in ER or IP). Incidence rates per 100 person-years and 95% confidence intervals (CI) of constipation were estimated in 1) all migraine patients; 2) in migraine patients newly initiating various types of acute or preventive migraine medications; and 3) in migraine patients by number of preventive treatments received in the prior 12 months.

Results: In the 584,475 patients with migraine, incidence rates were 3.41 (95% CI 3.39, 3.44) per 100 person-years for any constipation and 0.63 (95% CI 0.62, 0.64) for serious constipation. Incidence rates per 100 person years of any and serious constipation were even higher when various types of commonly used acute or preventive migraine treatments were initiated: opioids (6.13 and 1.79 for any and serious constipation); non-steroidal anti-inflammatory drugs (4.81 and 0.87); amitriptyline (6.50 and 1.08); nortriptyline (6.70 and 1.14); topiramate (5.29 and 0.85); gabapentin (8.22 and 1.81); pregabalin (9.41 and 1.95); and propranolol (4.82 and 0.84). There was a trend of increasing incidence rates with number of preventive migraine medications used in the 12 months prior.

Conclusion: In a large US administrative claims dataset, among patients with migraine, incidence rates of constipation were elevated among patients initiating commonly used types of acute or preventive migraine medications compared to all migraine patients. These data suggest that constipation occurs in patients treated with commonly used acute or preventive migraine medications.

Disclosure of Interests: All authors are employees and shareholders of Amgen Inc.

IHC-LB-054**Altered postural control in patients with migraine under visual stimulation**

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Objective: To assess the postural control of patients with migraine and controls under visual-induced movement.

Methods: Up to 27 headache-free participants and 34 migraineurs between 18 and 65 years old were recruited from the community and from the University Clinic Hamburg Eppendorf, Germany. Patients were diagnosed with migraine according to the ICHD-3 and subjects were excluded when presented concomitant headaches, BMI > 30, any neurological or vestibular disease, or also any lower limb dysfunction. A colored marker was placed on subjects' head and their balance displacement was assessed with a camera recording in HD 30fps, positioned 30 cm above the head. The subjects were instructed to gaze a screen positioned 70 cm from the body at the eye level, during three conditions: *rest*, with a fixed circle in the screen; *lift*, with a roller coaster video in constant and linear movement; and *stimuli*, with a roller coaster video in several directions and velocities. Data were processed through CVMob software (Ufba, Brazil). The total displacement length and displacement area were calculated through MATLAB2019a. Groups and conditions were contrasted using ANOVA with repeated measurements corrected by multiplicity in the SPSS 21.0 software, at $\alpha = 5\%$.

Results: Interactions between groups and conditions were verified for both total displacement ($F = 3.20$, $p = 0.04$) and area ($F = 3.04$, $p = 0.05$). The migraine group presented greater displacement length and area in all the three conditions compared to controls ($p < 0.05$) and all subjects presented greater displacement in the *stimulicondition* compared to *lift* and *rest* conditions ($p < 0.05$). Furthermore, the *lift* condition also was related to more displacement compared to the rest condition for all subjects ($p < 0.05$) (table 1).

Conclusion: Visual motion stimulation can induce greater total displacement length and greater area of displacement in subjects with and without migraine. For all conditions, migraine patients had poorer postural control compared to headache-free participants.

Disclosure of Interests: None.

IHC-LB-055**The effect of sound stimulus on the balance control of patients with different subtypes of migraine**

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Abstract number: IHC-LB-054

Table 1. Average and 95% Confidence Intervals of total displacement (cm) and area (cm²) among migraine patients and controls.*

	Control group (n = 27)	Migraine group (n = 34)
Rest		
Total displacement	20.08 (18.9 to 21.2)	24.85 (23.84 to 25.87)
Area	3.61 (2.75 to 4.48)	5.87 (5.09 to 6.64)
Lift		
Total displacement	27.35 (25.61 to 29.08)	33.90 (32.35 to 35.44)
Area	7.19 (5.69 to 8.69)	11.50 (10.17 to 12.84)
Stimuli		
Total displacement	56.69 (52.73 to 60.65)	66.92 (63.39 to 70.45)
Area	21.45 (17.49 to 25.41)	27.35 (23.82 to 30.88)

* $p < 0.05$ in the comparison among groups and all conditions.

Objective: To assess the balance of patients with migraine and controls with and without sound stimulus.

Methods: Fifty women with migraine and twenty-two non-headache women were assessed. They were aged between 18–55 years, and the migraineurs were divided into three groups according to the migraine subtype: Migraine without aura (MoA, $n = 18$), migraine with aura (MA, $n = 16$) and chronic migraine (CM, $n = 16$). All participants were instructed to keep standing posture on a force plate for 30 seconds, with closed eyes, in two conditions: in a quiet room (QR) and with a sound stimulus between 84–94dBA (SS). The center of pressure (CoP) displacement area was calculated and analyzed through groups and conditions using ANOVA two-way with repeated measures and Bonferroni *post-hoc*. Also, the prevalence ratio (PR) was calculated to assess whether the sound stimulus was associated with a greater imbalance ($p < 0.05$).

Table 1. Mean and SD of CoP displacement area (cm^2) between groups and conditions.

	Control ($n = 22$)	MoA ($n = 18$)	MA ($n = 16$)	CM ($n = 16$)
Quiet room (QR)	1.68 (0.96)	1.35 (1.09)	2.83 (2.68)	1.99 (1.24)
Sound stimulus (SS)	2.48 (2.26)	1.50 (0.76)	5.02 (4.42)*†	5.83 (6.46)†

*MA versus MoA, SS $p < 0.02$.

†SS versus QR, $p < 0.001$.

Results: We observed an interaction between group and condition ($F_{3,69} = 3.07$, $p = 0.03$). The MA group exhibited a greater CoP area than MoA group on the SS condition ($p < 0.01$). Both the MA group and the CM group presented a greater CoP area on the SS condition than QR ($p < 0.001$) (Table 1). The prevalence ratio analysis showed that the sound stimulus is associated with an increased CoP area for MA group and CM group (MA PR 2.55, CI95% 1.32 to 4.91, $p = 0.00$; CM PR 2.16, CI95% 1.07 to 4.33, $p = 0.02$).

Conclusion: In the absence of the visual system, the sound stimulus is a disturbing factor for the balance of patients with migraine with aura and chronic migraine, but not for migraineurs without aura and healthy controls.

Disclosure of Interests: The authors declare no conflicts of interest.

IHC-LB-056

Impact of insomnia on the prevalence and clinical presentation of depression: a population study

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Objective: A close association has been reported between depression and migraine. However, information concerning the impacts of migraine on the clinical presentation and prevalence of depression in a population-based study is currently limited.

Methods: Data from the Korean Headache-Sleep Study, a nationwide survey about headache and sleep for adults aged 19–69 years were used. Depression was defined when Patient Health Questionnaire-9 score ≥ 10 .

Results: Of 2,695 participants who included in this study, 116 (4.3%), 143 (5.3%), and 1130 (41.9%) had depression, migraine, and non-migraine headache, respectively. Migraine (25/116 [20.7%] vs. 118/2579 [4.6%], $p < 0.001$) and non-migraine headache (67/116 [57.8%] vs. 1063/2579 [41.2%], $p < 0.001$) was more prevalent in the group of participants with depression than among participants without depression. Among participants with depression, there was no statistically differences in total Patient Health Questionnaire-9 scores among migraine, non-migraine headache, and non-headache groups (median with interquartile range, 12.0 [10.3–17.8] vs. 13.0 [11.0–16.0] vs. 12.0 [11.0–15.5], $p = 0.514$). Among subcomponent scores of Patient Health Questionnaire-9, all subcomponent scores did not significantly differ by headache status except feeling tired or having little energy scores (non-migraine headache 2.0 [1.0–3.0] vs. non-headache 2.0 [1.0–2.0], $p = 0.019$).

Conclusion: Participants with depression exhibit an increased risk of migraine and non-migraine headache compared with participants without depression. Among participants with depression, the severity of depression did not significantly differ on the basis of headache status.

Disclosure of Interests: The authors declare that they have no conflicting interests.

Genetics and Biomarkers of Headache Disorders

IHC-LB-010

Zonulin: a possible driver of gut-brain axis in migraine

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Objective: Gut symptoms (as constipation, inflammatory and irritable bowel disorders) are very frequent among patients with migraine, however the integrity of the gastrointestinal system is not yet very well studied.

Aim of this study is to analyze the link between zonulin serum concentration (a marker of gut barrier integrity) and type and frequency of headache in a population of patients with different gastrointestinal disorders.

Methods: In a group of patients who self-referred to a gastroenterologist for various disorders, we asked them to undergo to a neurological evaluation, looking for a possible headache diagnosis. We divided 104 patients in 3 groups. Group 1: 22 patients without headache. Group 2: 32 patients with tension-type headache. Group 3: 50 patients with migraine.

We compared among groups the zonulin serum concentration and analyzed its correlation with the frequency of headache.

Results: Differences in terms of zonulin serum concentration emerged among Group 1 and 3 ($p < 0.001$).

Further, we observed a positive correlation between zonulin serum levels and the frequency of migraine attacks ($R = 0.54$; $p < 0.001$). There was no significant correlation between zonulin serum levels and tension-type-headache attacks.

Conclusion: The observed links between zonulin and migraine could be explained by the role of zonulin as marker of gut inflammation. Alterations of zonulin pathway have been associated with the leaky gut phenomenon, which could lead to the passage of potentially systemic pro-inflammatory substances in the blood circulation, leading to a migraine worsening. Another possible explanation of the observed correlation is the link between zonulin

release and the dysfunction of vagal system that is one of the principal driver in migraine pathophysiology.

Further prospective studies on patients without gastrointestinal symptoms should confirm our early observations and clarify the actual mechanism of action underpinning this link.

Disclosure of Interests: Authors declare no conflict of interests.

IHC-LB-057

Endogenous Glucocorticoids may be Potential Biomarkers for Migraine Chronification

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Objective: a) to identify difference in CSF and serum glucocorticoids among episodic and chronic migraine patients compared to controls.

b) to determine longitudinal changes in serum glucocorticoids among chronic migraine patients with remission to episodic migraine compared to those with persistent chronic migraine.

c) to determine migraine-related clinical features associated with glucocorticoid group differences.

Methods: CSF and serum cortisol and corticosterone levels were measured using liquid chromatography-mass spectrometry among age- and sex-matched adult patients with episodic migraine, chronic migraine, and healthy controls. Serum and CSF samples were collected from 26 and 4 participants in each group, respectively. Serum cortisol and corticosterone levels were measured at a second timepoint after 2 years among 10 of the chronic migraine patients – 6 of whom reverted to episodic migraine while 4 persisted as chronic migraine. Association analysis was conducted to determine link between glucocorticoid levels and clinical variables i.e. headache frequency, headache intensity, medication-overuse headache, depression, anxiety, pain catastrophizing, sleep quality, somatic symptoms, post-traumatic stress disorder, pain self-efficacy, migraine-related disability.

Results: Chronic migraine patients exhibited significantly elevated serum cortisol compared to episodic migraine patients (Holm-Sidak's $p < 0.001$; Figure 1A).

Figure 1

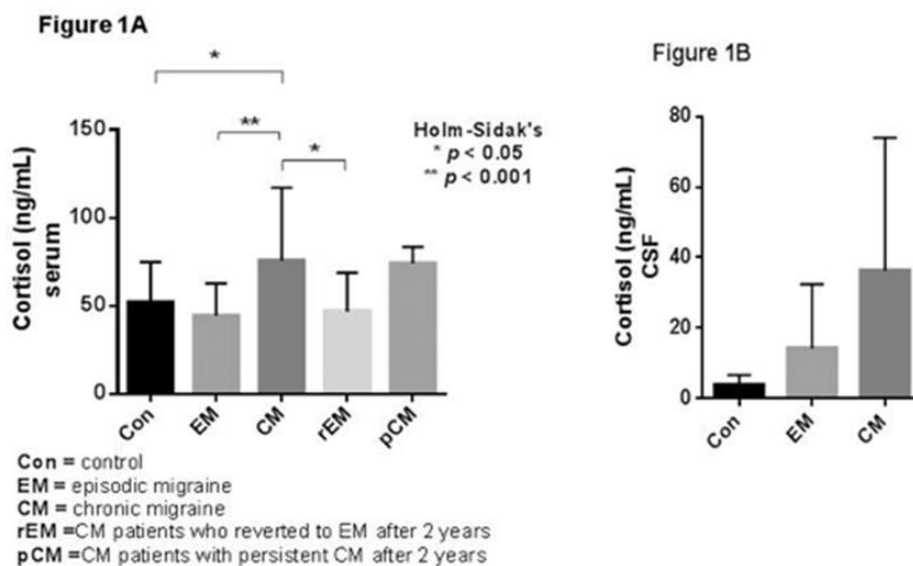


Figure 1. Chronic migraine patients (n=26) exhibited significantly elevated levels of serum cortisol compared to episodic migraine (n=26) patients (Fig. 1A). After a 2-year follow-up, chronic migraine patients who reverted to episodic migraine (n=6) showed observably lower cortisol level comparable to that in episodic migraine; while those who continued to have chronic migraine (n=4) showed persistently elevated cortisol levels (Fig. 1A). In cross-sectional study, CSF levels of cortisol were found to be highest in chronic migraine (n=4), followed by episodic migraine (n=4), and control (n=4) (Fig 1B). Bars represent mean values, error bars represent standard deviation.

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CSF cortisol and corticosterone were highest in chronic migraine, followed by episodic migraine, and control (Figure 1B). Chronic migraine patients with remission had their cortisol and corticosterone return to control or episodic migraine levels ($p < 0.05$). Chronic migraine patients with persistent chronic migraine showed continued elevated cortisol and corticosterone levels. Cortisol and corticosterone levels were directly related to headache frequency ($p = 0.002$) and migraine-related disability ($p = 0.0001$), while inversely associated to pain self-efficacy ($p = 0.008$).

Conclusion: Endogenous glucocorticoids may be used as potential biomarker for episodic to chronic migraine progression and for monitoring treatment response of chronic migraine remission. Improving socio-cognitive skills of pain self-efficacy may help optimize endogenous glucocorticoid levels which in turn may prevent migraine attacks.

Disclosure of Interests: None.

Headache Classification

IHC-LB-059

Rare migraine variants not defined in international classification of headache disorders (ICHD)-3: clinical case series

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Objective: We evaluated unique migraine variant cases which have not been classified in the international classification of headache disorders.

Methods: Patients of 14 to 60 years of age with episodic neurological symptoms diagnosed as migraine variants during January 2017- March 2019 were included in the study. These cases were not defined by ICHD 3 guidelines.

Results: Case -1: A 30 year old female presented with recurrent episodes of spontaneous vertigo lasting for about 30 minutes. They were preceded by severe weakness and photophobia for about 5 to 10 minutes and were precipitated by eating fermented food products or inadequate sleep. 12 such episodes of vertigo occurred at work in the last 3 months.

Case 2: A 28 year old female presented with recurrent episodes of true vertigo lasting for 5 to 6 hours associated with nausea and heaviness of head, but not classical migraine headache. She has experienced about episodes 6 to 8 in a month.

Case 3: A 32 year female presented with 8 episodes of syncope in last three months. All episodes occurred on the day of fasting.

Case 4: A 30 year male presented with sudden onset drooping of left side of face 10 to 15 minutes. This upper motor neuron facial weakness recovered in next 20 minutes and was followed by severe left sided throbbing headache with vomiting. He had 4–5 such episodes per month in last 6 months.

In all these cases, clinical examination in between the episodes was normal and the diagnostic work up was unrevealing. All these cases improved significantly when they were treated with prophylaxis of migraine. And when the treatment of discontinued, the symptoms recurred re-emphasising the disorder as migraine variants. First two cases were unexplained vertigo and the third case was of undetermined neuro cardio reflex syncope. All three cases were not associated with headache and were suspected due to past or family history of migraine. Fourth case is of migrainous headache associated with

upper motor neuron facial palsy with ipsilateral headache, which is a unique brainstem aura migraine variant.

Conclusion: Migraine should be suspected in any episodic neurological disorder of unexplained aetiology with normal neurological examination when investigations are undetermined.

Disclosure of Interests: Conflict of interest; Nil.

Headache Disorders in Children and Adolescents

IHC-LB-012

Comparison of the prevalence of infantile colic between pediatric migraine and other types of pediatric headache

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Objective: To examine whether the reported association of infantile colic and migraine in children pertains also to other headache types.

Methods: A cross-sectional historical study was conducted of 226 patients aged 3–18 years who presented to a tertiary pediatric headache clinic in 2016–2018. Parents were asked a series of questions to determine if their child had had infantile colic as defined in the ICHD3-beta version. Findings were compared between children diagnosed with migraine or other headache types.

Results: There were 137 girls (60.6%) and 89 boys (39.4%) of mean age 12.3 ± 3.47 years at presentation.

Abstract number: IHC-LB-012

Table 1. Demographic and clinical data of children with migraine versus other types of chronic headache (226 participants)

Parameter	Patients with migraine (N = 170)	Patients with other types of headache (N = 56)	p value
Gender (female)	104 (61.2%)	33 (58.9%)	0.874
Age (years)	12.49 ± 3.46	11.71 ± 3.48	0.147
Headache age onset (years)	9.58 ± 3.97	10.20 ± 3.90	0.311
Duration of attacks (hours)	15.96 ± 23.25	10.77 ± 24.08	0.1652
Headache frequency/month	13.70 ± 12.2	22.98 ± 11.72	0.853
Awakening pain	74 (43.5%)	13 (23.2%)	0.011
Nausea	108 (63.5%)	14 (25%)	<0.001
Dizziness	99 (58.3%)	18 (32.1%)	0.001
Attention deficit disorder	49 (28.8%)	7 (12.5%)	0.012
Organic comorbidity	57 (33.5%)	11 (19.6%)	0.064
Psychiatric comorbidity	70 (40.7%)	12 (21.4%)	0.006
History of infantile colic	45 (26.5%)	6 (10.7%)	0.016

Data are presented as n (%) or mean ± standard deviation.

Migraine headache was diagnosed in 170 patients (75.2%) and other types of headache (14 in total) in 56 (24.8%). Fifty-one patients had a history of infantile colic: 45 in the migraine group (26.5%) and 6 in the comparison group (10.7%); the difference in colic prevalence was statistically significant ($p < 0.0161$; OR 3, 95% CI 1.17–9.11). There was no association of specific migraine parameters or symptoms with infantile colic.

Conclusion: There appears to be an association of infantile colic with pediatric migraine but not with other types of pediatric headache. Our results reinforce the theory that infantile colic may have share a pathogenic pathway with migraine.

Disclosure of Interests: The authors have no conflicts of interests to disclose.

IHC-LB-013

Cephalic cutaneous allodynia in children and adolescents with migraine of short duration: a retrospective cohort study

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Objective: Allodynia is prevalent in adults with migraine and has been associated with long disease duration and severe course. Studies of the pediatric population are sparse. The aim of this study was to evaluate the rate of cephalic cutaneous allodynia in children and adolescents within the first six months of migraine onset and to identify associated clinical and migraine-related parameters.

Methods: The electronic database of a tertiary pediatric headache clinic from 2014 to 2017 was retrospectively searched for all children and adolescents diagnosed with migraine headache within 6 months or less of symptom onset. Cephalic cutaneous allodynia was identified by validated questionnaire. Demographics, symptoms, and headache-related parameters were compared between patients with and without allodynia.

Results: The cohort included 119 patients, 69 girls (58.0%) and 50 (42.0%) boys, of mean age 11.6 ± 3.6 years. Mean time since onset of migraine attacks was 3.6 ± 1.8 months. Cephalic cutaneous allodynia was reported by 31.1% of patients. It was significantly associated with female gender ($p = 0.03$), older age at admission ($p = 0.037$), older age at onset ($p = 0.042$) migraine with aura ($p = 0.002$) and higher rate of awakening pain ($p = 0.017$).

Conclusion: Cephalic cutaneous allodynia may occur in children and adolescents already in the first 6 months of migraine onset. Contrary to adult studies, we found no association of allodynia with migraine frequency or long disease duration. Allodynia was significantly associated with migraine with aura, female gender, and awakening pain. A genetic tendency may contribute to the appearance of allodynia in the pediatric age group.

Disclosure of Interests: The Authors have no interests to disclose.

Abstract number: IHC-LB-013

Parameter	Patients without allodynia (N = 82)	Patients with allodynia (N = 37)	p value
Gender (female)	42 (51.2)	27 (73.0%)	0.030
Age (years)	11.2 ± 3.5	12.7 ± 3.5	0.037
Migraine age onset (years)	10.9 ± 3.5	12.4 ± 3.5	0.042
Duration of attacks (hours)	10.9 ± 15.1	6.7 ± 5.4	0.393
Headache frequency/month	20.9 ± 12.0	18.6 ± 11.9	0.272
Chronic migraine (≥ 15 episodes/month)	28 (34.6%)	16 (45.7%)	0.300
Duration of disease before admission (months)	3.5 ± 1.7	3.8 ± 1.9	0.631
Migraine with aura	18 (22%)	19 (51.4%)	0.002
Unilateral pain	29 (38.2%)	11 (32.4%)	0.669
Phonophobia	62 (76.5%)	27 (79.4%)	0.811
Photophobia	43 (54.4%)	25 (71.4%)	0.101
Osmophobia	12 (27.9%)	7 (41.2%)	0.365
Awakening pain	29 (35.4%)	22 (59.5%)	0.017

IHC-LB-060

Ramosetron as a treatment for cyclic vomiting syndrome: A clinical trialToshiyuki Hikita^{1,2,*}¹Hikita Pediatric Clinic, Kiryu, Gunma²Department of Pediatrics, Teikyo University School of Medicine, Tokyo, Japan

Objective: Cyclic vomiting syndrome (CVS) is characterized by severe, recurrent episodes of vomiting in otherwise healthy subjects, and is classified within the subgroup of episodic syndromes that may be associated with migraine. Ramosetron, a selective serotonin 5-HT₃ receptor antagonist, has been applied clinically for treatment of irritable bowel syndrome (IBS). In this clinical trial, we evaluated the potential efficacy of ramosetron for treatment of CVS.

Methods: Six patients referred to Hikita Pediatric Clinic or Teikyo University Hospital and diagnosed with CVS and IBS were enrolled in this trial after obtaining informed consent. Treatment consisted of oral administration of 2.5–10 µg ramosetron. Patient responses to treatment for subsequent attacks were classified as: (i) complete (no vomiting following treatment), (ii) effective (frequency of vomiting reduced $\geq 50\%$ relative to previous attack prior to initiation of treatment), or (iii) noneffective (frequency of vomiting not notably affected by treatment).

Results: One of the 6 patients had been experiencing abdominal pain every morning, and diarrhea prior to vomiting. She took ramosetron every morning for 3 months. She did not vomit during that 3-month period, but did suffer occasional constipation. Following a constipation episode, she temporarily stopped taking ramosetron daily, but did take it at prodrome phase if she experienced abdominal pain and headache. She did not start vomiting after taking ramosetron.

All 6 patients experienced prodrome symptoms such as abdominal pain and/or diarrhea, nausea, appetite loss, headache, or menstruation-associated headache or vomiting. Following ramosetron treatment during prodrome phase, 5 of the 6 patients showed essentially “complete” response (out of 39 attacks, there were 32 complete, 1 effective, and 5 noneffective responses), and 1 showed effective response (for 1 attack). Overall, 34 of the 39 responses (87.2%) were classified as complete or effective.

For 3 of the patients, ramosetron treatment was initiated after vomiting had started, in a total of 10 attacks. One of these 3 patients showed effective response (in 1 attack), while the other 2 showed noneffective responses (in 9 attacks).

Conclusion: Ramosetron, a serotonin receptor antagonist, is potentially effective for treatment of patients with CVS.

Disclosure of Interest: None Declared.

Headache Education for Clinicians and Patients

IHC-LB-014

A novel CTP-based quantitative tool for assessment of perfusional alteration in migrainous aura stroke mimicAntonio Granato^{1,*}, Laura D’Acunto¹, Miloš Ajčević¹, Giovanni Furlanis¹ and Paolo Manganotti¹¹Department of Medical Sciences, University Hospital and Health Services, Clinical Unit of Neurology, Trieste, Italy

Objective: Diagnosis of migrainous aura (MA) represents the third most common stroke mimic (SM) in Emergency Department (ED). The studies on computed tomography perfusion (CTP) in SM differential diagnosis are based only on qualitative data and highlights controversial perfusion patterns. Aim of the study was to investigate brain perfusion abnormalities in MA using a novel CTP-based quantitative approach in order to improve differential diagnosis.

Methods: A two-year retrospective analysis of the patients who accessed the ED of the Hospitals of Trieste with acute focal neurological symptoms was performed. All the patients performed in ED general and neurological examination, hematological tests, brain non-enhanced CT, CT angiography of the supra-aortic and intracranial arteries, and CTP within 4.5 hours from symptom onset. Patients with normal qualitative CTP and with a final diagnosis of migraine with aura were included. ROIs were delineated on CTP source image anatomical area compatible with MA symptoms, while control ROIs were automatically delineated symmetrically on the contralateral side. The differences between ROI on the MA side and contralateral in terms of asymmetry index (AI%) were automatically estimated by the newly developed tool for each of CTP parameters (MTT, CBF and CBV). The AI% $\geq 10\%$ was considered significant.

Results: Fourteen patients (8 F, 6 M, mean age 47 years) were included. In 13 patients a significant hypoperfusion was observed by quantitative analysis in at least one of the CTP parameters. In 7 patients all three CTP parameters showed significant hypoperfusion. MMT AI% increase was observed in 11 (79%) patients (median MTT AI% = 13.9), while CBF AI% and CBV AI% decrease were observed in 12 (86%) (median CBF AI% = -21.4) and in 9 (64%) (median CBV AI% = -17.9) cases respectively. All CTP values were outside ischemic stroke core or penumbra range.

Conclusion: The quantitative analysis of CTP images during MA detects a slight hypoperfusion pattern in the cerebral regions compatible with MA. It could be helpful in differential diagnosis between MA and acute cerebrovascular disease.

Disclosure of Interest: None Declared.

IHC-LB-061

Experiences of a motivational focused patient education – A qualitative study

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Objective: Patient education is recommended as part of the treatment for medication-overuse headache (MOH), however, knowledge of patients' experiences when participating in an educational programme is sparse. The objective of this study was to explore how patients with MOH experienced participation in a patient educational programme (PEP) focusing on coping strategies and motivation for behavioural changes.

Methods: A qualitative interview study based on a phenomenological-hermeneutical approach was conducted. Semi-structured interviews (n=8) were conducted among patients with MOH who had attended a PEP in a randomised controlled trial. The PEP had Motivational Interviewing (MI) as the communicative approach and focused at behavioural changes and empowering coping strategies. The interviews explored how the patients experienced participation in the PEP and possible changes in their perceived coping strategies and/or any behavioural changes associated with headache.

Results: Three overall themes emerged from the analyses; *Changing coping strategies after participation*, *Self-perception and feeling of stigmatization*, *Experience of motivation during the PEP*. Generally, patients with MOH found the PEP relevant with respect to coping with headache. Patients shifted from focusing on medication only to include other ways of managing their headache. Ambivalent feelings of changing behaviour and involvement of relatives were of particular interest to the patients.

Conclusion: Participation in the PEP helped the patients cope with headache in new ways, relevant to their everyday lives and challenges. The individualized approach enabled by the MI was experienced as useful by the patients, as it actively involved them in the treatment. Knowledge regarding the patients' perspectives is paramount in planning future educational interventions.

Disclosure of Interests: The authors declare no conflicts of interests.

Headache Epidemiology, Outcomes and Burdens

IHC-LB-015

Impact of an employer-provided migraine coaching program on burden and patient engagement: results from interim analysis

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Objective: This study aimed to assess the impact of Migraine Care support program offered by a healthcare company as a complimentary service to medical care for its Swiss based employees and their family members living with migraine.

Methods: Of 320 participants with a diagnosis or high probability of migraine who registered to the program till mid-June 2019, 120 enrolled into the study for retrospective analysis of their data collected in the program. All participants received personalized telecoaching by a specialized nurse for up to 6 months supported by an advanced version of the Migraine Buddy smartphone application. The study participants were evaluated through a series of questionnaires including Migraine Disability Assessment (MIDAS), Patient Activation Measure (PAM), and the more commonly used coaching lessons and implemented action plans.

Results: The interim results are presented for 70 participants who completed both baseline and 3-month follow-up assessment, of which 41 reached 6 months. The mean age (standard deviation, SD) at baseline were 38 (8) years with 67% females, 69% had a confirmed diagnosis of migraine, and 51% were not treated by a physician despite 73% having MIDAS grade 2 or higher. The total mean (SD) MIDAS score improved from 15.2 (14.3) at baseline to 13.7 (16.9) (p=0.342) at 3 months and to 6.5 (8.1) (p=0.001) at 6 months. The mean (SD) PAM scores also improved from 63.7 (11.0) at baseline to 67.5 (11.6) (p=0.012) at 3 months and to 70.8 (12.1) (p=0.0009) at 6 months. The most used coaching lessons focused on progressive muscle relaxation (75.7%), sleep (57.1%), general disease understanding (50.0%), stress (45.7%), and diet (38.6%). Similarly, the top action plans concentrated on drinking enough (80.0%), sleep (78.6%), diet (52.9%), daily routine (52.9%), and sports (41.4%).

Conclusion: The study results demonstrate that employer-initiated educational and counseling support

can significantly decrease migraine-related disability and promote disease self-management among employees.

Disclosure of Interest: None Declared.

IHC-LB-016

Polish omnibus online survey on migraine conducted in a population of 2000 adults

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Objective: The objective of the survey was to assess the prevalence of migraine in the adult population in Poland, the percentage of people who experience symptoms that may be indicative of migraine attacks and the extent to which patients seek treatment and medical advice.

Methods: An online, quantitative survey involving a representative sample of 2000 adults aged 18–69 years residing in Poland, conducted in January 2019. The participants completed an online questionnaire (CAWI). The study group was representative for adults in terms of age, region and the size of place of living. The participants declared that within the past 12 months they experienced headache or headaches lasting 4 – 72 hours (or shorter if treated), and that these headaches were accompanied by symptoms corresponding to diagnostic symptoms of migraine without aura and/or with aura.

Results: Twenty five % of the respondents reported the presence of symptoms indicative of migraine within the past 12 months, in particular: 2.5% of people experienced only attacks of migraine with aura, 6.4% only without aura, 16.2% experienced both. In total, 18.7% of adults experienced aura symptoms. The results obtained that 1% of the adult population suffer from chronic migraine. Thirty seven % of migraineurs declare that they had migraine diagnosed by a physician in the past. The following symptoms are reported most frequently: pulsating headaches – 85%, photophobia and phonophobia – 82%, headaches that are aggravated by routine physical activity – 80%. Forty three % of people suffering from migraine attacks received medical advice for their condition, in the majority of cases – from a primary care physician / general practitioner (71%), and rarer – from a neurologist (48%). Ninety six % of people with migraine attack/attacks declared taking acute analgesics. Considering the last 30 days, half of these people took analgesics for a total of several days, 22%—several days per week, and 3%—everyday. Twenty five % of people with migraine take medications for migraine prophylaxis.

Conclusion: The omnibus study conducted in the group of 2000 adults in Poland indicates the need to improve

awareness of migraine and its modern methods of treatment, especially prophylactic treatment.

Disclosure of Interests: ID, JR, AS – Teva ad boards. JR, AS – Teva studies investigators. AL – Teva employee.

IHC-LB-017

Forecasting Migraine Using Weather: A Retrospective Study

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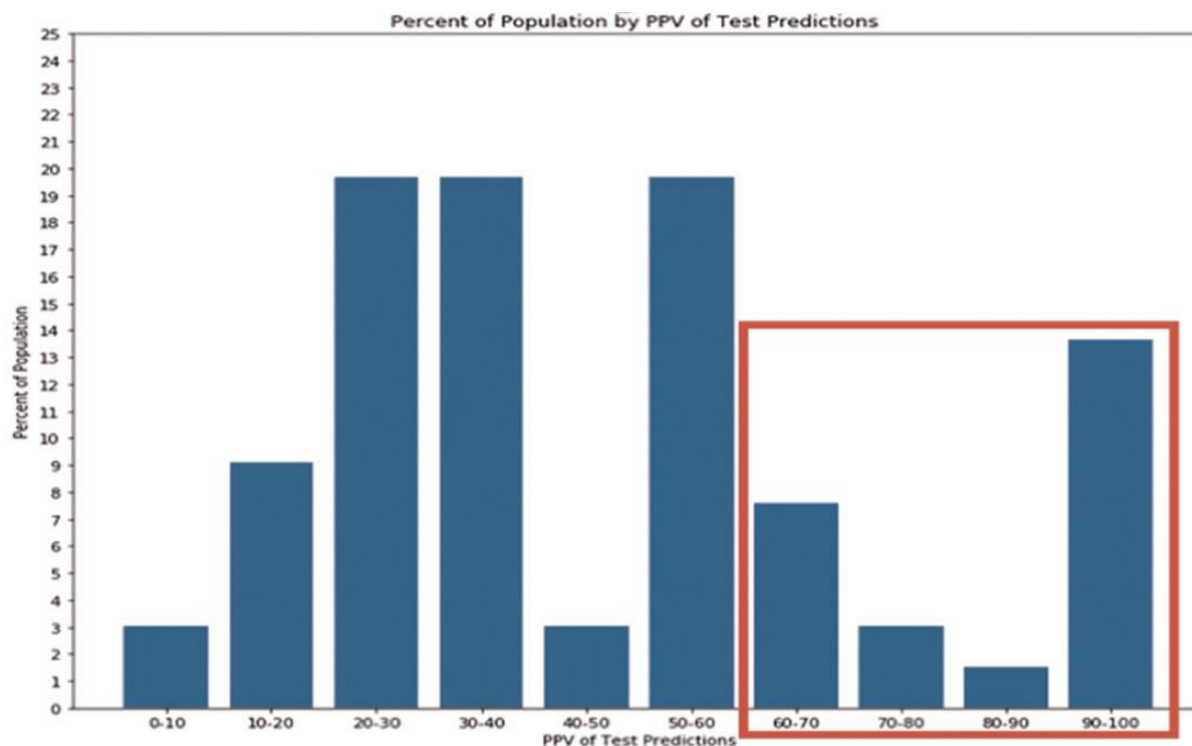
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Objective: Migraine weather triggers were derived from 11,712 migraines paired with weather data. Weather-based neural network migraine forecasts are reported. The association between migraine and weather triggers is controversial. Using the smartphone app MigrnX, migraine weather triggers and migraine forecasting are explored.

Methods: Sample N=89 met ICHD-3 criteria for migraine diagnosed by a Neurologist. A longitudinal study was conducted using de-identified patient data of MigrnX users from Atrium Health. The cohort reported headaches using MigrnX over 12 months. Records included GPS-based weather data. Analysis of migraine weather triggers used a Random Forest algorithm with relative risk >4. Baseline weather data for the algorithm used patients' non-headache days. To forecast migraines, a training set with an average of 100 episodes/pt was compiled. Each model compares predicted headache days with observed headache days to calculate Positive Predictive Values (PPV).

Results: Analysis used an average of 130 migraines per pt, average <8 per month. Patients were aged 24–62 yrs; 80% White, 76% Female. Over 1 yr, MigrnX clinical data with subsequent improved diagnosis and treatment, monthly headaches per pt declined ca 40%. Weather triggers strongly correlate with migraine frequency in the following order: wind speed > humidity, barometric pressure > temperature. The results are multifactorial, and demonstrate varied, multiple weather factors contributing to migraine, and cautions against using any single trigger as a forecasting measure. **Weather-based Migraine Forecast** The prediction of migraine PPV for individual patients from the neural network is shown in Figure 1A. 28% of the population has high PPV values (70–90%) where prophylaxis based on such predictions could be medically recommended, as for menstrual migraine prediction. For patients with PPV values 50–70%, additional information might make a prediction medically actionable.

Conclusion: Real-time headache reports coupled to passive weather collection can identify weather triggers, and allow weather-based migraine forecasting. Advances in



Abstract number: IHC-LB-017

real-time data collection combined with machine learning methods could provide a new paradigm for prediction-based prophylaxis.

Disclosure of Interests: Officer of SensorRx Inc.

IHC-LB-018

Predictors of urgency in headache patients looking for assistance in low complexity emergency units in Brazil: An analysis of 163,207 emergency visits

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Objective: In the last decade, hundreds of low complexity Emergency Care Units (UPA 24 h) were launched in Brazil. Distributed throughout the city, the UPA 24 h, are designed to provide care for patients with acute diseases. Headache is one of the most common symptom that lead patients to UPA 24 h. The Manchester protocol is the tool used in UPA 24 h to detect patients who will need urgent or critical care. This study aimed to evaluate predictors of urgency in patients seeking medical care for headache in UPA 24 h.

Methods: We evaluated the ED charts of 163,207 visits motivated by headache to nine UPA 24 h in the city of Fortaleza, Ceará, from April 13, 2013 to June 31, 2017.

Results: The 163,207 consultations represented 3% of all the UPA 24 h visits and were made by 118,623 patients (mean age of 37.2 ± 15.7 ; 69,4% women). On average, patients had the Manchester Risk Classification in 01 minute and 22 seconds and 1,276 (0,8%) were classified as blue, 84,443 (51.7%) as green, 60,844 (37.3%) as yellow, 16,640 (10.2%) as orange and only 4 cases were classified as red. Older patients (>40 years) (OR 1.563; 95% CI, 1.532–1.595; $P < 0,0001$), female sex (OR 1.474; 95% CI, 1.442–1.507; $P < 0,0001$), off hours (from 19 to 07) (OR 1.825; 95% CI, 1.789–1.863; $P < 0,0001$) and on weekends (OR 1,047; 95% CI, 1.024–1.070; $P < 0,0001$) were predictors of urgency. Those classified as yellow, orange and red received medical evaluation in a mean time of 16 minutes versus 01 hour and 17 minutes for the patients classified as blue and green.

Conclusion: In Brazil, low complexity Emergency Care Units (UPA 24 h) represent an important channel of care for patients with acute headache. While about half of the patients have pains that could be treated in primary care, the other half have emergency and urgency characteristics captured in the Manchester Classification. Older age, female sex, arrival time and weekend days are strong predictors of urgency in patients seeking UPA 2 h for headache.

Disclosure of Interest: None Declared.

IHC-LB-062

Clinical audit of premonitory and postdromal symptomatology in patients with migraine

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Objective: To compare the range and duration of premonitory and postdromal symptoms in patients with migraine attending headache centre on a year by year basis.

Methods: We carried out an audit of migraine patients who attended a tertiary headache referral centre between 2014 and 2018 using clinical documentation.

Results: Of patients ($n = 340$), 78% ($n = 264$) had chronic migraine. The median age of the cohort was 44 years with an interquartile range (IQR) of 31–53. The median age of headache onset was 14 (10–20) years. Medication overuse was present in 39% of patients.

There was an increase in the total number of premonitory symptoms recorded in 2018 with respect to 2014 (median and IQR: 5 and 3–5 vs 2 and 0–4; $p < 0.001$). The five most common were concentration difficulty (66%), mood changes (56%), fatigue (42%), neck stiffness (42%) and yawning (31%). There was an increase in the total number of postdromal symptoms recorded in 2018 with respect to 2014 (median and IQR: 2 and 1–3 vs 0 and 0–1; $p < 0.001$). The five most common were lethargy (32%), tiredness (29%), feeling drained (29%), cognitive impairment (24%) and irritability (14%). The number and duration of premonitory and postdromal symptoms did not correlate with the frequency of headache days (Pearsons correlation) or presence of MOH (chi square test). There was a correlation between the number of premonitory and postdromal symptoms and number of both associated migrainous symptoms and cranial autonomic symptoms (CAS; Pearsons correlation – $r = 0.32$, $p < 0.001$)

Conclusion: The data shows an increase in the total number of premonitory and postdromal symptoms recorded over the course of four years. This difference may be due to increased awareness among patients and medical personnel. We also found a significant correlation between the number of premonitory and postdromal symptoms and associated migrainous symptoms and CAS. This is consistent with the underlying biological basis of the premonitory and postdromal symptomatology.

Disclosure of Interests: The authors have no conflicts of interest to declare for this study.

IHC-LB-063

Clinical characteristics, comorbidities and functional impact in patients with migraine treated in a headache center at Buenos Aires, Argentina

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Objective: This study describes clinical characteristics of patients with migraine in a headache center at Buenos Aires, Argentina.

Methods: Transversal study, patients +18 years were asked to complete an auto administered questionnaire about clinical characteristics, quality of life, allodynia, hospital anxiety and depression (HAD) and Oviedo questionnaire of sleep (COS). Patients classified as migraine according to the IHC-III by a headache specialist were included.

Transversal study, +18y/o patients with migraine according IHC-III answered a questionnaire about clinical characteristics, quality of life, and comorbidities.

Results: 183 patients were included, 94% women, average age 40 years ($\pm 27,5$). Frequency headaches was 10 days/month and intensity was 7/10 in average. 78% had episodic migraine, 55% referred aura with a predominance of visual symptoms. HIT-6 score was 59,5 ($\pm 13,3$); impact was substantial in 21,9% and severe in 61.7%.

Pain localization: temporal (56,8%), frontal 48,1% and neck 48,1%. Unilateral pain was present in 78% of the patients. Characteristic of pain: oppressive (71%) and pulsatile (56,3%). Accompanying symptoms: Photophobia (71%) and phonophobia (62,8%). Triggers: stress (66,7%) and anxiety (60,7%). Comorbidities: anxiety (48%), depression (30,6%) and insomnia (23%) among the patients. Table I shows the differences between episodic and chronic migraine.

183 patients, 94% women, age 40($\pm 27,5$) years. Frequency headache: 10 days/month. Intensity 7/10. Episodic migraine: 78%, 55% referred aura. HIT-6 score was 59,5 ($\pm 13,3$); impact was severe in 61.7%. Characteristics: Localization: temporal (56,8%) and frontal (48,1%). Unilateral pain: 78%. Accompanying symptoms: Photophobia (71%) and phonophobia (62,8%). Triggers: stress (66,7%) and anxiety (60,7%). Comorbidities: anxiety

(48%), depression (30,6%) and insomnia (23%). Table 1 shows differences between episodic and chronic migraine.

Conclusion: Our population reflects similar results reported by other specialized centres in migraines. The majority of our patients with migraine present a severe functional impact and it is necessary to have more resources and studies.

Disclosure of Interest: None Declared.

IHC-LB-064

Knowledge about migraine headache prevention and disability among migraine patients

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Objective: Headache is the most disabling phase of migraine and after this phase patients feel drained-out. Prevention of migraine headache and reducing the severity of migraine attack can be achieved if patients know exactly what are the common semiology migraine shows and the triggers of migraine headache. This study also aims to identify knowledge regarding migraine headache prevention and disability due to migraine among migraineurs.

Methods: A total of 155 migraineurs were assessed regarding the prodromal symptoms, the triggers and the preventive strategies. The migraineurs were also assessed about the level of disability and the impact of migraine on work productivity using the Migraine Disability Assessment Scale and Headache Impact Test.

Results: The study findings showed moderate to severe disability was experienced by migraineurs in doing their daily activities and work productivity was also severely affected. 43% of migraineurs have poor knowledge regarding migraine headache prevention, especially regarding triggers.

Conclusion: This study reveals the knowledge level of migraineurs was poor among the rural population and the newly diagnosed patient who had a severe disability due to migraine which insists on the importance of patient teaching and education for prevention of disability among migraine patients.

Disclosure of Interests: There is no conflict of interest.

Headache Pathophysiology – Basic Science

IHC-LB-019

Potential Clinical Evidence for Limbic System Sensitization in Migraine

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Objective: Determine the clinical evidence for limbic system sensitivity (LSS) in migraine subjects as indicated by the incidence and severity of misophonia, tryphobia and tactile-emotional synesthesia (TES).

Methods: A total of 290 subjects (migraine [n=195], tension-type headache [n=54], probable migraine [n=21] and non-headache [n=20]) participated in this clinical investigation. All subjects completed a medical history including quantitative measures of misophonia (Misophonia Assessment Questionnaire [MAQ]), tryphobia (Tryphobia Image Score [TIS], modified Lee, Cole and Wilkins Tryphobia Score [mLCWTS]) and TES (Emotional Response to Various Surfaces Score [ERVSS]). These measures were explored in relation to headache type, frequency, severity, associated disability (Migraine Disability Assessment Scores [MIDAS] and cutaneous allodynia (Allodynia Symptom Checklist [ASC-12]).

Results: Average MIDAS were 0.2, 1.4, 5.1, 2.3 and 7.7 for non-headache (NH), tension-type headache (TTH), all migraine (M), episodic migraine (EM) and chronic migraine (CM) respectively. Average headache days in the last ninety were 0.2 (NH) to as high as 58 (CM). Average pain intensity was: TTH (1.7), M (5.7), EM (4.9) and CM (6.4). Average ASC-12 scores were <0.5 in NH and TTH groups and 5.7 (M), 5.3 (EM) and 6.0 (CM). MAQ showed average scores <0.7 in NH and TTH. Elevated average MAQ scores of 7.7, 6.2 and 9.1 were seen in M, EM and CM respectively. Tryphobia indicators (average TIS and mLCWTS) were lower in NH (0.3/1.8) and TTH (0.2/1.7) versus M (1.2/2.1), EM (1.2/2.0) and CM (1.3/2.1). Average ERVSS, a measure of TES, were higher in M (2.3), EM (2.4) and CM (2.3) versus NH (0.5) and TTH (0.6).

Conclusion: The clinical measures for LSS were elevated in subjects with M when compared to those with NH or TTH, and CM subjects were more affected than their EM counterparts. Misophonia, tryphobia and TES scores were ~23 ×, ~4.3 × and ~4.6 × (respectively) more severe in the CM group compared to NH subjects. In addition, these scores increased with headache frequency, severity, associated disability and cutaneous allodynia. These findings suggest that not only is the limbic system hyperexcitable in migraineurs, but that dynamic changes may lead to limbic network sensitization within the

migraine matrix like known to occur in trigeminal and thalamic structures.

Disclosure of Interest: None Declared.

IHC-LB-021

Increased phase-synchronization and power oscillatory activity in patients with episodic migraine during the interictal period

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Objective: To analyze Phase-Synchronization and Power of oscillatory activity in migraine during the presentation of auditory stimuli.

Methods: In this case-control exploratory study, we recorded 20-channel Event Related Brain Potentials (ERPs) during an Active Novelty Oddball Paradigm in women with episodic migraine (EM) without aura (ICHD-3), and healthy matched controls (HC) without family history of migraine. We collected sociodemographic and clinical data, disability, quality of life, anxiety and depression (HIT-6, MIDAS, MSQ, MIG-SCOG, STAI, BDI-II, BSI, ASRS). We calculated behavioural data including reaction times (RTs), hit rates, false alarms, and d-primes. Phase-Synchronization (Inter-Trial phase Coherence, ITC) and Power of oscillatory activity were separately obtained for standard, target and novelty stimuli, from Current Source Density Transformed ERPs (CSD-ERPs).

Results: We studied 21 – EM (22.0 ± 2.2 years) and 21-HC (23.0 ± 2.0 years). There were no significant differences at a behavioural level ($p > 0.1$). We found an increased Phase-synchronization in response to standard trials, in migraine with respect to controls, in several frequency ranges: theta (3-9 Hz; 100–400 ms; $F(1,40) = 4.106$, $p = 0.049$), alpha (9-12 Hz; 50–250 ms; $F(1,40) = 4.137$, $p = 0.049$) and low-beta (12-15 Hz; 50–250 ms; $F(1,40) = 4.186$, $p = 0.047$). Similarly, compared to controls, migraineurs showed increased theta (at Fz: $t(40) = -2.206$, $p = 0.033$), alpha (Cz at Block 1: $t(40) = -2.379$, $p = 0.016$) and low-beta power (Cz at Block 1: $t(40) = -2.345$, $p = 0.024$). However, in alpha and low-beta, the significant effect was observed only on the first blocks. No evidences of lack of habituation were encountered in the migraine group ($p > 0.1$).

Conclusion: Hypersensitivity to auditory stimuli during the interictal period in young female patients with episodic migraine might be defined by a higher Synchronization of neural activity together with a higher Power activity.

Disclosure of Interest: None Declared.

IHC-LB-065

Anti-CGRP Monoclonal Antibody Eptinezumab Does Not Engage Fc γ Receptors Involved in ADCC and ADCP, Nor Does It Activate the Complement Cascade

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Objective: Eptinezumab is a therapeutic monoclonal antibody targeting CGRP peptide developed for the preventive treatment of migraine. It contains the Fc region of human IgG1 with a modification of amino acid Asn297 to prevent the canonical N-linked glycosylation that is normally present at this site. This glycosylation is essential for antibody interactions of wild-type IgG1 with Fc γ receptors (Fc γ R) to induce ADCC (antibody-dependent cellular cytotoxicity) or ADCP (antibody-dependent cellular phagocytosis). It is also important for interactions with complement proteins to activate CDC (complement-dependent cytotoxicity). Eptinezumab was specifically designed to avoid these interactions. A series of assays were conducted to test the hypothesis that eptinezumab does not support these immune-related processes.

Methods: Binding of eptinezumab to Fc γ R was assessed using surface plasmon resonance technology. Fc γ R-dependent cell-based assays were also used to evaluate the engagement of eptinezumab with Fc γ R *in vitro*. A cell viability assay was used to evaluate complement activation by eptinezumab.

Results: The collective results of binding and Fc γ R-dependent cell-based assays demonstrated the absence of engagement of eptinezumab with Fc γ R *in vitro*. In addition, there was no activation of complement-mediated cytotoxicity by eptinezumab.

Conclusion: These results confirm that eptinezumab does not induce ADCC, ADCP, or CDC.

Disclosure of Interests: All authors are full-time employees of Alder BioPharmaceuticals.

IHC-LB-066**Entrainment of neural band oscillations in patients with migraine**

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Objective: To study, using electrophysiology, the entrainment of neural band oscillations to repetitive, visual stimuli in migraine.

Methods: This is an exploratory case-control study. We studied women with episodic migraine (EM) without aura (ICHD-3) and healthy matched controls (HC) with no family history of migraine. We collected sociodemographic, psychometric and clinical data (HIT-6, MIDAS, MSQ, MIG-SCOG, STAI, BDI-II, BSI, ASRS). EEGs were recorded using 64-channels during the realization of a visual entrainment paradigm with rhythmic and arrhythmic targets. We obtained behavioral data (reaction times, hit rates, d-primes, false alarms). Separate measures of alpha band activity (range 7–14 Hz) and entrainment (peak 12 Hz) were calculated at the Oz electrode: phase synchronization (inter-trial coherence), phase concentration (kappa and mean vector length) and the mean angular difference between rhythmic-arrhythmic time-points.

Results: We included 19-EM (23.85 ± 3.36 years) and 22-HC (22.09 ± 2.04 years). Despite a lack of group differences on behavioural measures and phase synchronization ($p > 0.1$), phase trended to be more concentrated in EMs than in HCs on catch trials (kappa concentration, $p = 0.06$; mean vector length, $p = 0.068$). In addition, the difference

in phase mean angle ($p = 0.039$) between rhythmic and arrhythmic catch trials was closer to 180° in EMs than in HCs.

Conclusion: Enhanced oscillatory alpha synchronization and entrainment (phase-angle and concentration) indicates that migraineurs display an increased tendency to synchronize and predict external rhythms present in their natural environment, even when these stimuli are not present. This hyper-vigilance, linked to an augmented capacity for stimulus prediction, could in part explain the hyper-sensibility to sensory stimuli seen in migraine.

Disclosure of Interest: None Declared.

IHC-LB-067**Only 3.8% (19/464) of papers on migraine and headache published in Cephalalgia 2014–2018 concerned actual spontaneous or provoked migraine/headache attacks**

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Objective: Ideally, the mechanisms of migraine and other headaches should be investigated during actual attacks; but it is the impression that most scientific headache experts rarely, if ever, investigate spontaneous or provoked migraine/headache attacks. This bibliographic review was performed in order to document this problem.

Methods: The 494 original reports published in 5 volumes of Cephalalgia (from 2014 to 2018) were screened by reading the abstracts, and if necessary, the whole paper; and classified as: (1) spontaneous acute migraine/headache; (2) provoked acute migraine/headache; and (3) reports on other aspects of migraine/headache. For each report in (1) and (2) the number of patients or volunteers were noted.

Results: As shown in Table 1 only 7/494 (1.4%) of papers reported on investigations of spontaneous and only 12/494 (2.4%) on provoked migraine/headache.

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Table. Number of original reports in Cephalalgia from 2014 to 2018 on spontaneous acute headaches, provoked experimental headaches, and papers on other subjects. Number of patients or volunteers are presented in brackets.

Type of paper	Year and (volume)					
	2014 (Vol. 34)	2015 (Vol. 35)	2016 (Vol. 36)	2017 (Vol. 37)	2018 (Vol. 88)	2014–18 (Vol. 34–38)
Spontaneous acute migraine/headache	1 [17]	1 [96]	1 [17]	2 [46]	2 [30]	7
Provoked acute migraine/headache	1 [24]		1 [30]	6 [324]*	4 [78]	12
Other papers	73	91	85	96	132	475
Total papers	75	92	87	102	138	494

Note: *In one study 163 males ascended by plane in two hours to 3700 m, and high altitude headache was studied.

Conclusion: This mini-review confirms that investigations of patients during spontaneous or provoked migraine/headache attacks are rarely performed.

If the pathophysiology of migraine and other headaches are to be fully elucidated there is an urgent need for investigations during actual attacks. Relevant imaging and functional methods have been developed and can be used in our patients. What is needed now is that headache experts prioritize the establishment of facilities at their headache centers for receiving acutely patients in migraine or other headache attacks; alternatively, provoked attacks can be investigated in these headache centers.

Disclosure of Interests: None.

Headache Pathophysiology – Imaging and Neurophysiology

IHC-LB-022

Cerebrovascular reactivity in patients with Migraine using Transcranial Doppler

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Objective: To assess cerebrovascular reactivity in interictal phase of migraine patients.

Methods: • This study was conducted over three months in institute of neurology, madras medical college. • 30 patients who satisfied the criteria for migraine as per IHS criteria were selected from headache outpatient clinic of our institute. • 30 controls were selected who were age and sex matched with patients. • Inclusion criteria: 1) age 20–70 years 2) Migraine as per IHS criteria 3) Willing to participate.

Exclusion criteria: • Arterial hypertension and brain disease • Pregnancy • Metabolic and pulmonary disease • Alcohol abuse • Migraine preventive drugs beta blockers, calcium channel blockers.

• All patients complete history was included, Complete clinical examination, routine investigations, imaging was done. • Transcranial doppler using 2 Hz probe was done in all patients in supine position. • The baseline Peak systolic velocity(PSV),Pulsatility index(PI) was measured in Middle cerebral artery (MCA) and posterior Cerebral artery(PCA) in all patients. Photic stimulation using a flickering light was done for 100 seconds from a distance 1 m.

• After photic stimulation, PSV in MCA and PCA was measured, the highest PSV value was averaged.

Results: Demographic data: We included 30 patients, 25 female and 5 male patients. The average duration of headache

was 2.3 years in patients. Of 30 patients 12 had history of aura and all were visual aura and 18 were without any aura. The systolic velocities in MCA, in patient and control group was compared. There was no significant difference between PSV MCA between patient and the control group at baseline. After photic stimulation there was increase in peak velocities, however it was not statistically significant with p value (0.08). The systolic velocities in PCA were compared between the patient and the control group. The baseline velocities in patients was comparatively higher in patient group. After photic stimulation the increase in PSV in patient group was higher and statistically significant (p=0.001) but the PSV changes in control group was not significant. The velocities were also compared in between two subgroups that is aura and without aura, the baseline PCA PSV in patients with aura was higher compared to those without aura. After photic stimulation the velocities in patient with aura was higher and statistically significant. The PSV in MCA however was not significant before and after photic stimulation in between the two subgroups.

Conclusion: There was increased cerebrovascular reactivity in patients with migraine. There was further increase in Cerebrovascular reactivity in patients with aura. There was maladaptation of cerebrovascular reactivity in migraineurs, more so in patients with aura causing activation of the trigeminovascular system causing change in neurovascular homeostasis thereby inducing migraine attacks. Transcranial doppler can be useful tool to assess the cerebrovascular reactivity in migraineurs. This study demonstrates increased cerebrovascular reactivity in patients of migraine with aura using photic PSV. Photic PSV along with other indices can be valuable tool to assess CVR in patients with migraine.

Disclosure of Interests: Nil.

IHC-LB-068

Cyclic fluctuations of sensorimotor cortex sensory processing in migraine may be important for attack initiation: observations from event related EEG changes

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Objective: Migraineurs experience altered sensory perception throughout migraine phases. For the first time, we mapped cyclic changes of cortical responsivity with “event

related synchronization and desynchronization" (ERS/ERD).

Methods: We recorded ERS/ERD changes during a motor test (M) and a sensorimotor test (SM) in 41 migraineurs. Longitudinal analyses compared the interictal phase to the preictal (<36 h before headache, $n = 11$) and ictal ($n = 13$) phase. We studied low beta (12–19 Hz) ERD, representing cortical excitability during sensory processing, and post movement beta synchronization (PMBS) which represents post-stimulation cortical inhibition.

Results: In the preictal phase, baseline beta power and beta-ERD in contralateral sensorimotor cortex were significantly increased ($p < 0,049$). PMBS on the other hand, tended to be increased at the ipsilateral side (SM $p = 0,058$), while post-hoc test of cortical PMBS-side difference was highly significant ($p = 0,001$). In the ictal phase the baseline beta activity was significantly increased, and PMBS was significantly decreased in the ipsilateral sensorimotor cortex ($p < 0,045$). Beta-ERD was not altered during the ictal phase.

Conclusion: Preictal findings indicate lower contralateral sensorimotor cortical pre-activation and increased responsivity during sensory processing, followed by increased inhibition of the ipsilateral sensorimotor cortex. The results support the theory of underlying cortical hyperresponsivity in migraine, interictally contained by inhibitory control. Decrease in preictal cortical pre-activation may cause higher thresholds for inhibitory control and consequent release of the underlying hyperresponsivity seen as increased beta-ERD. Meanwhile, ipsilateral sensorimotor cortex may compensate with increased post-stimulation inhibitory control.

During the ictal phase, cortical pre-activation and post stimuli inhibition ipsilateral to stimuli decrease, with contralateral normalization. We postulate that decreasing cortical activation with compensatory inhibitory thresholds culminating in ictal escalation may trigger headache attacks.

Disclosure of Interests: All authors declare no conflict of interest regarding this study and article.

IHC-LB-069

Aberrant Structural Network Architecture in Chronic Migraine

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Objective: The goal of the current study was to assess structural interconnections in patients with CM and

healthy controls (HC) using MRI measures of cortical thickness and subcortical volume combined with graph theoretical network analyses.

Methods: 100 participants (52 CM and 48 HC) were included in the study. Cortical thickness and subcortical volumes of 83 regions were extracted and included as nodes in the network analysis. Edges were computed as Pearson correlations setting the negative correlations to zero. Analyses were carried out on binary undirected graphs, controlling for densities from 5% to 40% in steps of 0.5. To assess differences between groups in network architecture, we examined both local (nodal) and global measures of centrality, segregation, and integration. Significant between-group differences in network measures were examined using non-parametric permutation tests with 1000 replications in combination with two-tailed p -values based on 95% confidence intervals.

Results: Several significant differences in both local and global network topology were evident between the CM and HC groups. Patients with CM had disrupted global network properties characterized by lower global and local efficiency and higher transitivity. Additionally, patients with CM demonstrated aberrant local network topology characterized by higher path length, lower closeness centrality, lower clustering, and lower local efficiency. These differences were most prominent in the limbic and insular cortices but also occurred in frontal, temporal, and brain-stem regions.

Conclusion: Structural MRI measures of gray matter combined with graph theoretical network analysis revealed multiple significant network topology differences in patients with CM compared to HC. Our results suggest that aberrant structural brain networks in CM are less central, less efficient, more segregated, and less integrated. These findings contribute to an increased understanding of structural connectivity in CM and provide a novel approach to potentially track and predict the progression of migraine disorders.

Disclosure of Interests: None.

Migraine Acute Therapy**IHC-LB-023****Acute Migraine Treatment with Rimegepant 75 mg and Health Related Quality of Life in Migraine: Results from a Long-Term, Open-Label Safety Study (BHV-3000-201)**

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Objective: Migraine is a painful and disabling condition, with substantive patient burden on health related quality of life (HRQoL). This study assessed the effects of rimegepant 75 mg oral tablet on migraine-specific quality of life over 52 weeks of use as an acute treatment.

Methods: This ongoing, multicenter, long-term, open-label safety study (Study 201) of rimegepant 75 mg oral tablet included adults with ≥ 1 year history of migraine defined by ICHD-3 beta criteria. Subjects treated attacks of any pain intensity with rimegepant 75 mg up to once daily as-needed for up to 52 weeks. A validated 14-item Migraine-Specific Quality of Life Scale (MSQoL) was administered at baseline and Weeks 12, 24, 36, and 52. The MsQoL is designed to measure how migraine affects and/or limits daily functioning across three domains: Role-Restrictive [RR]: 7 items assessing how migraine limits daily social and work-related activities; Role Preventative [RP]: 4 items assessing how migraine prevents activities; Emotional Role [ER]: 3 items assessing the emotional impact of migraine. Raw total scores were computed and rescaled from 0 to 100 with higher scores indicating better HRQoL.

Results: The analyses included 1795 subjects at baseline, 1634 at Week 12, 1215 at Week 24, 1087 at Week 36, and 920 at Week 52. Mean MSQoL scores at baseline were 52.7 for RR, 67.9 for RP and 60.9 for ER. By Wk 12, rimegepant-treated subjects showed clinically and statistically significant improvements: mean Δ from baseline of +14.5, +11.5, and +15.4, for RR, RP, and ER respectively, ($p < 0.0001$). These benefits were sustained at Wk 24: +15.4, +12.8, +15.8 ($p < 0.0001$), Wk 36: +17.4, +13.7+17.0, ($p < 0.0001$), and Wk 52: +17.6, +14.4, +17.2, ($p < 0.0001$) for RR, RP, and ER

Conclusion: Effective Acute Migraine Treatment with Rimegepant 75 mg is associated with clinically meaningful improvements in HRQoL when dosed as needed up to once daily. These improvements demonstrate that treated patients would achieve better overall function and reduced impediments to social and work related activities.

Disclosure of Interests: GL, RC, ES, ML, CJ, VC are employees and shareholders of Biohaven Inc. RL is a consultant and shareholder of Biohaven Inc.

IHC-LB-024**Concomitant Use of Serotonergic Drugs with Zolmitriptan in a One-year Safety Trial**

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Objective: In the United States, all triptans carry a warning against concomitant use with serotonergic medications – specifically SSRIs and SNRIs – in the Warnings and Precautions section of the package insert. Similarly, many serotonergic drugs carry a warning against concomitant use with triptans. Despite these warnings, some believe that the risk of serotonin syndrome is not supported by reliable data (e.g. Orlova, Rizzoli and Loder, 2018).

Zosano is currently studying intracutaneous zolmitriptan (Qtrypta) for the acute treatment of migraine and completed a 1-year open-label safety trial in which subjects dosed with the Qtrypta 3.8 mg system an average of twice per month over the course of twelve months. Though some serotonergic medications were not allowed during the trial, several subjects initiated one of these drugs at some point in the trial. Thus, we sought to analyze whether concomitant use of these medications affected the safety of the study drug with regard to serotonin syndrome.

Methods: We analyzed the medication database for known serotonergic drugs. Using the Hunter Criteria for the diagnosis of serotonin syndrome, the adverse event database was queried for the following terms: clonus, agitation, diaphoresis, tremor, hyperreflexia, hypertonia or fever (MedDRA version 20.0); and the frequency of these terms was compared between the two groups.

Medication	N
TRAZODONE	8
TRAMADOL	6
NORTRIPTYLINE	3
AMITRIPTYLINE HYDROCHLORIDE	1
VENLAFAXINE HYDROCHLORIDE	1
SERTRALINE HYDROCHLORIDE	1
ESCITALOPRAM OXALATE	1
MIRTAZAPINE	1
VILAZODONE HYDROCHLORIDE	1

Results: The safety population of the trial totaled 335. Twenty-two subjects reported being on serotonergic drugs while in the study (6.6%). One subject was on two serotonergic medications.

None of the serotonin syndrome diagnostic terms were reported in either group, nor were there any reports of serotonin syndrome.

Conclusion: The results of this analysis suggest that a certain proportion of migraine patients will use triptans and serotonergic drugs concurrently, despite the warnings in the respective package inserts. However, in this limited sample there were no reported cases of serotonin syndrome, presumably the most serious complication of concomitant use. These findings lend further support to the argument that the risk of serotonin syndrome with concomitant use of triptans and serotonergic medications may be overstated.

Disclosure of Interests: PS, JE and DK are employees of Zosano.

IHC-LB-025

Efficacy of Qtrypta (zolmitriptan intracutaneous system) Before and After the Initiation of CGRP Antibody Therapy in Subjects with Migraine – a Preliminary Assessment

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Objective: With the recent introduction of the highly effective CGRP antibodies for migraine prevention, it is important to evaluate their effect on the efficacy of abortive migraine therapy.

A 1-year open-label safety study of Qtrypta was ongoing in 2018 and 2019 at the time of market introduction in the U.S. of erenumab, galcanezumab, and fremenumab. Several subjects participating in the long-term safety trial requested one of these injectable CGRP antibodies and as there were no safety concerns, the sponsor granted permission for the subjects to receive this treatment and continue to participate in the long-term safety trial.

Methods: To assess the potential impact of CGRP antibodies on the efficacy of Qtrypta 3.8 mg, we evaluated the standard co-primary endpoints for acute treatment of migraine trials (pain freedom and most bothersome symptom freedom, both at 2 hours from subject-recorded eDiary symptom scores) for all migraine attacks treated prior to and after CGRP antibody therapy initiation.

Results: Ten subjects started CGRP antibody therapy during the trial: 9 erenumab, and 1 galcanezumab. Six of 10 subjects treated migraine attacks with Qtrypta after initiating erenumab. These subjects treated 72 attacks prior to initiating anti-CGRP treatment and 37 attacks post initiation. Results for pain and most bothersome symptom freedom at 2 hours pre-and post-initiation of CGRP antibodies for all attacks treated are shown in the table.

Conclusion: From limited data, it appears that Qtrypta remained highly effective in relieving acute migraine symptoms in subjects receiving prophylactic treatment with CGRP antibodies. Further studies are needed, but these data suggest that attacks are more successfully treated with rapidly absorbed triptans when subjects are being treated prophylactically with a CGRP antibody.

Disclosure of Interests: NH is on the advisory board of Zosano, PS, JE, WH and DK are employees of Zosano.

IHC-LB-026

The 200 mg dose, the highest dose of 3 doses of lasmiditan investigated in phase 3, has a pain-free effect after 2 h, comparable to sumatriptan 50 mg

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Objective: Lasmiditan has not been compared with oral triptans in randomized, controlled trials (RCTs). The aim was therefore to evaluate the 3 doses of lasmiditan (50 mg, 100 mg, and 200 mg) relative to the triptans by comparing results from meta-analyses.

Methods: Lasmiditan results were obtained from 2 large phase 3 RCTs. Triptans results were obtained from meta-analyses. For pain-free (PF) after 2 h the therapeutic gain (effect after active drug minus effect after placebo) (TG) with 95% CI was calculated.

Results: As shown in Table 1 the TG of lasmiditan 200 mg (17%) was comparable to the TG for sumatriptan 50 mg (17%), but this dose of lasmiditan has a TG less than the TGs of sumatriptan 100 mg (21%), zolmitriptan 2.5 mg (20%), and rizatriptan 10 mg (32%). Any adverse events (placebo-subtracted) was 27% for lasmiditan 200 mg and this incidence of adverse events was higher than the incidences for rizatriptan 10 mg (10%), zolmitriptan 2.5 mg (15%), and sumatriptan 100 mg (19%).

Table

Treatment Status	Pain Freedom at 2 hours (%)	MBS Freedom at 2 hours
Pre CGRP Ab Initiation	63%	74%
Post CGRP Ab Initiation	76%	88%

Abstract number: IHC-LB-025

Abstract number: IHC-LB-026**Table 1.** Efficacy and tolerability of oral lasmiditan and 3 oral triptans.

Drug and dose	PF after 2 h.			Adverse events (AEs)
	Active drug	Placebo	Therapeutic gain	Any AE placebo subtracted
Lasmiditan 200 mg	36%	18% ^a	17% (95% CI: 13–21%)	27% (95% CI: 23–30%)
Lasmiditan 100 mg	30%	18% ^a	12% (95% CI: 8–15%)	22% (95% CI: 19–26%)
Lasmiditan 50 mg	29%	21% ^a	7% (95% CI: 2–12%)	6% (95% CI: 2–10%)
Rizatriptan 10 mg	42%	10%	32% (95% CI: 29–34%)	10% (95% CI: 6–14%)
Zolmitriptan 2.5 mg	30%	10%	20% (95% CI: 18–21%)	15% (95% CI: 13–17%)
Sumatriptan 100 mg	32%	11%	21% (95% CI: 19–23%)	19% (95% CI: 16–23%)
Sumatriptan 50 mg	28%	11%	17% (95% CI: 15–19%)	7% (95% CI: 5–10%)

Note: a, this high placebo effect remains unexplained.

Conclusion: The comparison of lasmiditan with 3 triptans indicates that only lasmiditan 200 mg has a clinically relevant effect on migraine pain. One possible problem is the high incidence of AEs of lasmiditan 200 mg. Comparative RCTs of lasmiditan and triptans are needed.

Disclosure of Interests: No conflict of interests.

IHC-LB-070

Oral Rimegepant Produces No Significant Effect on Blood Pressure When Administered Concomitantly with SC Sumatriptan

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Objective: To evaluate the effects of rimegepant, a small molecule calcitonin gene-related peptide receptor antagonist with efficacy in migraine, on resting blood pressure (BP) when administered concomitantly with sumatriptan in healthy volunteers.

Methods: This was a single center, Phase I, randomized, partially-blinded, placebo-controlled study in adult non-smokers aged ≥ 18 and ≤ 40 years (males) or ≥ 18 and ≤ 50 years (females) with BMI > 18.5 and < 30.0 kg/m² and weight ≥ 50.0 kg (males) or ≥ 45.0 kg (females). On Days 1 and 5, subjects received 12 mg of sumatriptan as 2 SC 6 mg injections separated by 1 h; Day 5 injections were administered 2 and 3 h after oral rimegepant 75 mg or matching placebo tablet. From Days 2 to 5, subjects received rimegepant or placebo once daily (randomized 6 to 1, rimegepant to placebo). Parameters for BP were the time-weighted average (TWA) of mean arterial pressure (MAP), diastolic BP (DBP), and systolic BP (SBP). Similar TWA of MAP was concluded if the upper bound of the 90% CI of the difference between rimegepant +

sumatriptan on Day 5 and sumatriptan on Day 1 was < 5 mmHg. Plasma concentrations of rimegepant (Days 4 and 5) and sumatriptan (Days 1 and 5) were used to calculate PK parameters (AUC, C_{max}, T_{max}, T_{1/2 el}) by standard noncompartmental methods.

Results: All 42 subjects who enrolled were treated and analyzed. There were no significant differences in the TWA of MAP, SBP, or DBP and no clinically meaningful PK interactions between rimegepant and sumatriptan. Overall, 39 (92.9%) subjects experienced ≥ 1 AE; all but 3 (related to sumatriptan) were mild. The most common AE was injection site reaction (59.5%). Two subjects experienced mild increases in heart rate and BP. No other clinically meaningful changes from baseline in laboratory values, vital signs, or ECGs were identified.

Conclusion: No significant difference in BP parameters was detected between treatments with rimegepant + sumatriptan on Day 5 and sumatriptan on Day 1, and the TWA of MAP was similar. No clinically meaningful PK interactions were observed. Coadministration of rimegepant with sumatriptan was safe and well tolerated.

Disclosure of Interests: Robert Croop, MD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Joseph Stringfellow, MS, receives compensation from Biohaven Pharmaceuticals.

Michael Hanna, MD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Christopher M. Jensen, PharmD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Andrea Ivans, MHS, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

Vladimir Coric, MD, is employed by and holds stock/stock options in Biohaven Pharmaceuticals.

IHC-LB-071**Nasal cavity evaporative cooling for the symptomatic relief of withdrawal headache during triptan detoxification, a randomized, double-blind, sham-controlled pilot-study**

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Objective: Medication overuse, especially the overuse of triptans, is an important problem in a share of (chronic) migraine patients as it maintains their headaches. With intranasal evaporative cooling (RhinoChill by BrainCool) a beneficial effect on migraine-attacks was shown in an open label study previously. The aim of study was to evaluate the efficacy of intranasal evaporative cooling compared to sham treatment in reducing withdrawal headache during triptan detoxification.

Methods: 14 patients with both migraine (mean age 56, 64% female, 50% migraine with aura) and triptan-overuse headache according to the ICHD III criteria were admitted for inpatient detoxification for the first week of their 8 week triptan detoxification period and randomized to either intranasal cooling or sham treatment with the same device with normal temperature air. Both patients and all personnel were blinded for treatment status. Patients could use the RhinoChill device up to 4 times per 24 hours for up to 10 minutes during this first week of detoxification. Admission was on forehand limited to at most 7 days. The pain-scores (predefined as none, mild, moderate, severe) were recorded by patients on 3 time-points each use (before treatment, directly following 10 minute treatment and 60 minutes after treatment). Treatment success was defined as going from baseline moderate or severe pain to mild headache or no headache. Of the secondary endpoints only side effects are presented here.

Results: Baseline characteristics did not differ between active and sham-group. Triptans were used on average 21 days during the 4 week baseline period. Subjects in active group remained 3.3 (SD 2.5) days in hospital vs 3.7 (SD 2.1) in sham-group. Subjects in active arm treated a total of 4.5 (SD 3.1) headaches vs. 5.1 (SD 2.1) in sham-group. Most of these headaches were rated as severe.

Primary outcome: At least one attack with acute good effect (from moderate or severe to mild or less, 10 minutes after start of treatment) was reported by 50% in active group vs. 33% in sham group ($p=0.6$). Only 38% of active treatment group reported this effect in at least 50% of treatments vs. 17% in sham group ($p=0.6$). At least one attack with good effect at one hour timepoint (from moderate or severe to mild or less) was reported by 29% in active group vs. 33% in sham group ($p=1.0$).

Only 14% of active treatment group reported this effect at one hour in >50% of treatments vs. 17% in sham group ($p=1.0$).

Side effects were reported by 38% in active treatment group and 50% in sham-group and generally mild. One subject receiving coolant reported epistaxis, two subjects (one in active group and one in sham-group) experienced nasal drip. Painful stabs were reported by two subjects in sham group and one in active-group.

Conclusion: We could not demonstrate a therapeutic effect (at both $t=10$ and $t=60$ minutes) of intranasal cooling using RhinoChill device, compared to sham-treatment for migraine patients during in-hospital detoxification. We acknowledge the fact that this study was underpowered to detect a imaginable small therapeutic effect, as number of subjects was limited in this study. Intranasal cooling did not cause important side-effects limiting its use.

IHC-LB-072**Is the early therapeutic action of 75 mg orally disintegrating tablet of rimegepant clinically relevant? A comparison of rimegepant with oral triptans**

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Objective: In a recent paper in The Lancet (July 13, 2019) on a large randomized, controlled trial (RCT) on rimegepant (75 mg orally disintegrating tablet [ODT]), T_{max} is 1.5 h, it is stated: "With early and sustained therapeutic action, the 75 mg ODT formulation of rimegepant should be clinically useful for the acute treatment of migraine" [1]. In order to evaluate the clinical relevance of the early effect of rimegepant was compared with the early (0.5 to 2 h) effect of sumatriptan 100 mg [2], and rizatriptan 10 mg [3].

Methods: The results (0.5–2 h), pain free (PF) and headache relief (HR) (decrease of headache from moderate or severe to none or mild) of the rimegepant paper [1] were compared with a Cochrane review of oral sumatriptan [2], and a meta-analysis of rizatriptan [3]. For each time point the therapeutic gain (effect for active drug minus effect for placebo) (TG) with 95% confidence intervals (95%CI) were calculated.

Results: An overview of the time-effect curves (from 0.5 h and 2 h) for the three drugs are shown in Table 1.

In a review of 4 RCTs with almotriptan 12.5 mg (T_{max} 2.6 h) only detailed results after 0.5 and 2 h are presented.[4]: The TGs for HR after 0.5 and 2 h are 7% (95%CI: 3–10%) and 26% (95%CI: 26–32%). The TGs for

Abstract number: IHC-LB-072

Table 1. Pain freedom (PF) and headache relief (decrease of headache from moderate or severe to none or mild) (HR) after ODT rimegepant 75 mg [1] ($T_{max} = 1.5$ h), sumatriptan 100 mg [2] ($T_{max} = 1.5-2$ h), and rizatriptan 10 mg [3] ($T_{max} = 1$ h) from 0.5 h to 2 h. TG (effect for active drug minus effect for placebo) is presented in bold. In parentheses: 95% CI for TG.

	0.5 h	1 h	1.5 h	2 h
Pain-free				
Rimegepant 75 mg PF			8% (4–11%)	10% (7–14%)
Sumatriptan 100 mg PF		6% (4–7%)		20% (18–22%)
Rizatriptan 10 mg PF	1% (0.2–1.8%) ^a	9% (7–11%)	19% (17–21%)	31% (28–34%)
Headache relief				
Rimegepant 75 mg HR		6% (0.5–11%)	12% (7–18%)	16% (11–21%)
Sumatriptan 100 mg HR		15% (12–17%)		29% (27%–31%)
Rizatriptan 10 mg HR	6% (3–9%)	20% (17–23%)	29% (26–32%)	33% (30–36%)

Note: a, should be disregarded due to the small, not relevant magnitude, of the PF.

PF after 0.5 and 2 h are 2% (95%CI: 0.2–3%) and 21% (95%CI: 16–26%), respectively.

Conclusion: When judging time-effect curves for early effects of 2 acute drugs for migraine 2 factors should be evaluated: 1. When does a clinical relevant effect occur? 2. What are the TGs for PF (most relevant for patients) or HR at the same early time-points?

It can be questioned whether a TG of 6–7% for HR is clinically relevant effect, but the fact that this result was obtained 1 h after ODT rimegepant vs. 0.5 h after rizatriptan and almotriptan, strongly indicates an earlier effect for these 2 triptans. In addition, the TG ratios for HR for rimegepant/triptan at the same time-points (1, 1.5, and 2 h) varied from 0.3 to 0.5 (ratios in the same range was also observed for PF).

In summary, the onset of effect for ODT rimegepant is slower than the onset for the 2 triptans tested at 0.5 h postdose. The effect from 1 to 2 h for rimegepant is considerably lower for both HR and PF for sumatriptan and rizatriptan, see Table 1.

Disclosure of Interests: No interests of conflict.

IHC-LB-073**The Next Frontiers in Digital Therapeutics for Headache**

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Objective: Neuromodulation is a rapidly developing therapeutic approach for migraine. In addition to providing an alternative to pharmacological treatment that is inadequate for many migraine sufferers, non-invasive adaptive multi-channel brain neuromodulation (MCBN) eco-system

is pushing the frontier in the realm of digital health. In the context of neuromodulation, the next frontiers for digital health are prediction of migraine attacks, multichannel therapeutic electrical stimulation, and AI in the cloud.

Methods: Machine learning (ML) is emerging in the management of acute medical situations. In contrast with the classic scientific approach in which a hypothesis is formulated regarding possible associations between a disease attack and a triggering situation, ML systems can take a data mining approach. Utilizing data that come from sensors on the patient, from devices used by the patient, from the social media posts the patient and others, from electronic medical records, and from online descriptions of similar cases, ML systems potentially can “discover” associations that were not hypothesized in advance. To be sure, such an approach entails the risk of shining a spotlight to what is not really an association, but merely a coincidence due to the fact that if enough tests are performed, or enough test results checked, that a certain fraction of the results will be false positives.

Results: The MCBN eco-system is on the forefront in the realm of predicting attacks of medical conditions, in this case migraine attacks. Current understanding of migraine disorder suggests that the triggering of migraine attacks is linked with numerous subjective and objective events experienced by affected individuals. Many migraine sufferers experience an aura consisting of various sensorial disturbances, such as flashing of lights. These auras, as well as bodily changes of which the affected individual may not be aware, are linked to some overt physiological changes, but also numerous subtle changes.

Conclusion: Advancing data science in neurological and neuropsychiatric disorders, such as migraine, depression, ADHD and insomnia. AI, and ML technologies can enable advances that push the limit, in term of providing precise, personalized therapy, applied to migraine disorder.

Disclosure of Interests: Working with Neuroliet LTD in the last two years building strategic partnership.

Migraine Preventive Therapy

IHC-LB-027

Anti-migraine CGRP receptor antagonists (gepants) worsen cerebral ischemic outcome in mice

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Objective: Migraine is a risk factor for cerebral and myocardial infarction. CGRP pathway inhibitors are emerging treatments for migraine. CGRP-mediated vasodilation is, however, a critical rescue mechanism in brain and cardiac ischemia. We, therefore, investigated whether gepants, small molecule CGRP receptor antagonists, worsen cerebral ischemia.

Methods: Middle cerebral artery was occluded by an endovascular filament for periods ranging 12–60 minutes in wild type and familial hemiplegic migraine type I (FHMI) mice. We compared infarct rates and volumes, collateral flow, and neurological outcomes after pretreatment with olcegepant (single or 10 daily doses of 0.1 or 1 mg/kg) or rimegepant (single doses of 10 or 100 mg/kg) versus vehicle.

Results: Olcegepant (1 mg/kg) increased infarct rates after 12–20-minute occlusions mimicking transient ischemic attacks (odds ratio 5.6, 95%CI: 1.4–26.1, $p=0.022$), and infarct volumes ($p=0.031$) and neurological deficits ($p=0.001$) after 60-minute occlusions. Ten daily doses of 0.1 or 1 mg/kg olcegepant yielded similar results. Rimegepant 10 mg/kg increased infarct volumes after 20 minutes of ischemia ($p=0.03$); 100 mg/kg caused 75% mortality after 60-minute occlusion versus none with vehicle. In FHMI mice, olcegepant (0.1 or 1 mg/kg) dose-dependently increased infarct size after 30 min occlusion. Both gepants consistently diminished collateral flow during occlusion and reduced reperfusion success.

Conclusion: Gepants worsened experimental ischemic stroke in mice by inhibiting CGRP-mediated collateral

vasodilation. CGRP pathway blockers might thus aggravate coincidental cerebral ischemic events. The cerebrovascular safety of these agents must therefore be better delineated, especially in patients with comorbid vascular disease and long-term CGRP inhibition for migraine prevention.

Disclosure of Interests: None.

IHC-LB-028

High Frequency Episodic Migraine Shift to Low Frequency Episodic Migraine in Patients Treated with Galcanezumab

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Objective: To assess the proportion of patients with episodic migraine (EM) who shift from high-frequency EM (HFEM) to low-frequency EM (LFEM) or very low-frequency EM (VLFEM) status after doses of galcanezumab.

Methods: EVOLVE-1 and EVOLVE-2 were double-blind, placebo-controlled, Phase 3 studies that enrolled 1773 patients with EM. Patients 18–65 years of age were randomized 2:1:1 to subcutaneous monthly injections of placebo, galcanezumab 120 mg (240 mg loading dose) or 240 mg, respectively, for up to 6 months. Data were pooled and endpoints were change from baseline in number of monthly migraine headache days (MHD) and patients who shifted from HFEM (8–14 MHD) to LFEM (≤ 7 MHD) or VLFEM (≤ 3 MHD).

Results: At baseline, patients with HFEM (66% of 1773 patients) had mean monthly migraine headache days of 11 days and Migraine Disability Assessment Score of 37 (severe disability). During the treatment phase, more galcanezumab-treated patients shifted to LFEM for 3 or more consecutive months and maintained LFEM until study end (68.4% and 69.2% for 120 and 240 mg/month, respectively; $p < 0.001$) vs placebo-treated patients (50.7%). Furthermore, significantly more galcanezumab-treated patients maintained LFEM for 3 or more consecutive months (75.2% and 77.1% for 120 and 240 mg/month, respectively; $p < 0.001$) vs placebo (58.3%).

Similarly, significantly more galcanezumab-treated patients shifted to VLFEM for 3 or more consecutive months during the treatment phase (47.7% and 47.7% for 120 and 240 mg/month, respectively; $p < 0.001$) vs placebo-treated patients (25.5%). Furthermore, more galcanezumab-treated patients shifted to VLFEM for 3 or more consecutive months and maintained VLFEM until study end (39.9% and 38.6% for 120 and 240 mg/month, respectively; $p < 0.001$) vs placebo (19.5%).

Abstract number: IHC-LB-028

Table. Frequency of Shifts from High-Frequency Episodic Migraine to Low-Frequency Episodic Migraine or from High-Frequency Episodic Migraine to Very Low-Frequency Episodic Migraine Following Subcutaneous Injections of Placebo, Galcanezumab 120 mg or Galcanezumab 240 mg for ≥ 3 Consecutive Months to the End of the Study.

Sustained Response and Treatment	N	n	Percentage	Odds Ratio	95% CIs for Odds Ratio ^a
Shift from HFEM to maintenance of LFEM					
Placebo	875	444	50.7%		
Galcanezumab 120 mg/month	436	298	68.4%	2.21	(1.72, 2.84)
Galcanezumab 240 mg/month	428	296	69.2%	2.28	(1.77, 2.94)
Shift to maintenance of VLFEM					
Placebo	875	171	19.5%		
Galcanezumab 120 mg/month	436	174	39.9%	2.88	(2.21, 3.74)
Galcanezumab 240 mg/month	428	165	38.6%	2.69	(2.06, 3.50)

Abbreviations: CI = confidence interval; HFEM = high-frequency episodic migraine; LFEM = low-frequency episodic migraine; N = number of patients who had at least one non-missing post-baseline value; n = number of patients meeting sustained response definition among the number of patients; VLFEM = very low-frequency episodic migraine.

^aAll p-values from logistic regression were <0.001 , confirming the statistical significance of the results.

Conclusion: Both doses of galcanezumab were superior to placebo in the reduction of monthly migraine headache days, with significantly more patients shifting from HFEM to LFEM or VLFEM postdose. Results were similar between the galcanezumab doses.

Studies were registered as NCT02614183 and NCT02614196 at ClinicalTrials.gov.

Disclosure of Interests: V. Stauffer and J. Jedyak are employees of Eli Lilly and Company; A. Gendolla is an employee of Praxis Gendolla; E. Eross is an employee of Phoenix Headache Institute, Consultant with: Allergan, Amgen, Teva, Novartis, Speaker for: Amgen, Teva, Novartis, Founder and President of Glia Sciences, Inc.; L. Jin is an employee of Covance, Inc.

IHC-LB-029**Safety and tolerability of erenumab in older migraine patients: A subgroup analysis of randomised trials**

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Objective: Erenumab (AMG334; AimovigTM, Amgen[®], Novartis Pharma AG) is a fully human monoclonal antibody specifically designed for the preventive treatment of migraine, and has been used by over 250,000 patients since it was first made available. Migraine is a disabling neurological disease in all age groups, including older adults.

Treatment of migraine in older patients requires further consideration due to possible comorbid medical conditions and concomitant medications. Here, we present a subgroup analysis of data including older patients (aged > 50 years) with chronic migraine (CM) or episodic migraine (EM).

Methods: Safety and tolerability of erenumab (70 mg or 140 mg) versus placebo was evaluated in subgroups of patients from two studies with CM (NCT02066415) or EM (NCT02456740, STRIVE). Subgroup analysis of patients in age groups 18–40, >40 –50, >50 –55 and >55 years was used to assess the safety and tolerability of erenumab during the 12-week double-blind period.

Results: Overall, the safety in the erenumab treatment groups was comparable to placebo across the age groups. Exposure-adjusted subject incidence rates were comparable between older (>50 –55 and >55 years) and younger (18–40, >40 –50) age groups. No notable imbalance was observed in the subject incidence of treatment-emergent adverse events (AEs), serious AEs or in the severity of AEs by age group. Safety and tolerability assessments for cardiovascular, cerebrovascular and peripheral vascular events were comparable across age groups. Common AEs such as sedation, cognitive dysfunction or anticholinergic syndromes associated with older patients were not seen in patients treated with erenumab.

Conclusion: Erenumab is safe and well-tolerated in older patients with CM and EM. Safety and tolerability in the erenumab treatment groups is comparable across different age groups.

Disclosure of Interests: Christian Lampl has received honoraria for planning and conducting clinical trials, participating in advisory board meetings and speaking for: Allergan, Eli Lilly, Janssen-Cilag, MSD, Novartis, Pfizer,

Sanofi-Aventi and Teva. Josefin Snellman, Shannon Ritter, and Jan Klatt are employees and stockholders of Novartis.

IHC-LB-030

10-year cost-effectiveness analyses of response-based fremanezumab use in migraine patients with inadequate response to prior preventive treatments

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Objective: Cost-effectiveness (C-E) of fremanezumab for preventive treatment of chronic (CM) and episodic migraine (EM) in patients (pts) with inadequate response to 2–4 prior preventive treatment classes was examined, accounting for cessation of fremanezumab treatment for non-responders.

Methods: A semi-Markov C-E model (CEM) was developed with a 4-week (wk) cycle and 10-year (yr) analysis time horizon. Costs and benefits were discounted at 3.0% annual rates. Treatment efficacy was incorporated as reduction in mean migraine days (MDs)/28 days vs placebo (PBO). Pt cohorts were distributed among MD categories (0–28 MDs/28 days) based on mean MD levels. The CEM estimated costs (fremanezumab acquisition and MD-related costs) and health-related-quality-of-life (MD- and treatment status-based utilities) for fremanezumab and no-treatment arms. Only background mortality was modeled. Analyses were performed on a combined CM(67%)/EM(33%) population. CM/EM patients not achieving 30%/50% reductions, respectively, in MDs/28 days at 12 wks (non-responders) stopped treatment. The incremental C-E ratio (ICER) was reported as cost/quality-adjusted life-year (QALY) gained between fremanezumab and no treatment. Fremanezumab MDs/28 day reductions vs PBO and 12-wk non-response rates were sourced from a network meta-analysis. In base-case analysis, fremanezumab was compared with constant no-treatment MD profiles. Fremanezumab was also compared with randomized-controlled trial (RCT)-sourced PBO-arm MD profiles.

Results: In base-case, 10-yr analysis time horizon, fremanezumab dominates no treatment (less costly, more effective): average cost savings, \$3,492/pt; incremental QALYs, 0.22; reduction in MDs, 161.5 MDs. Excluding indirect costs, fremanezumab resulted in a cost/QALY ICER of \$13,606; average incremental costs, \$2,998/pt. When PBO effects were included, fremanezumab dominates no treatment: average cost savings, \$13,905/pt; incremental QALYs, 0.412; reduction in MDs, 353.9 MDs.

Conclusion: Based on current pricing and RCT results, fremanezumab treatment is cost-effective versus no

treatment, especially if discontinued at 12 wks for non-responders.

Disclosure of Interests: L. Smolen and T. Klein are employees of Medical Decision Modeling Inc., Indianapolis, Indiana, USA, which received payment for their work on these analyses from Teva Pharmaceuticals. S.K. Gandhi, S. Thompson, and J.M. Cohen are employees of Teva Pharmaceuticals.

IHC-LB-031

A Phase 2 Study of Galcanezumab in Japanese Patients with Episodic Migraine

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Objective: Galcanezumab (GMB), a humanized monoclonal antibody that selectively binds to the calcitonin gene-related peptide, was investigated to determine superiority to placebo in the prevention of migraine headache in Japanese patients.

Methods: This study was a double-blind, 6 month (M) study in patients with episodic migraine (4–14 monthly migraine headache days [MHD]). Patients were randomized 1:1:2 to monthly subcutaneous injections of GMB 120 mg (N = 115), GMB 240 mg (N = 114), or placebo (N = 230). Primary endpoint was overall (M1–6) mean change from baseline in the number of monthly MHD (Mixed Models Repeated Measures analysis). Key secondary endpoints included overall rates of $\geq 50\%$, $\geq 75\%$ and 100% reduction in monthly MHD and overall mean change from baseline in monthly MHD with acute migraine treatment, and mean change from baseline over M4–6 on the Migraine-Specific Quality of Life Questionnaire–Role Function-Restrictive domain (MSQ-RFR) and Patient Global Impression of Severity (PGI-S).

Results: Baseline mean of monthly MHD was 8.7 and was similar across treatment groups. Both GMB doses demonstrated a statistically significant improvement compared to placebo ($p < .05$) for overall mean change in monthly MHD (placebo = -0.59 , GMB 120 mg = -3.60 , GMB 240 mg = -3.36). Percentage of patients with MHD reductions of $\geq 50\%$, $\geq 75\%$ or 100%, and reduction of monthly MHD with acute migraine treatment were significantly higher for each GMB dose relative to placebo. Mean change in MSQ-RFR was greater for each GMB dose versus placebo and in PGI-S for GMB 240 mg. There were no statistically significant differences between GMB and placebo on treatment-emergent adverse events except for a greater incidence of injection site-erythema, -pruritus, -swelling, -pain, influenza, and urticaria.

Conclusion: Both doses of GMB met the primary objectives and all key secondary objectives except for PGI-S. Efficacy and safety outcomes were similar across GMB doses. A very low placebo effect was observed. This study demonstrated that GMB provided clinical benefit, improved function, and was safe in Japanese patients with episodic migraine.

Disclosure of Interests: FS is an advisor of Eli Lilly Japan K.K.; AK and AO are full-time employees of Eli Lilly Japan K.K.; VS is a full-time employee of Eli Lilly and Company.

IHC-LB-032

User Acceptance of a Prefilled Auto-injector Device for Erenumab in Patients with Migraine

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Objective: Erenumab (AMG334; AimovigTM, Amgen[®], Novartis Pharma AG) is a fully human monoclonal antibody specifically designed for the preventive treatment of migraine. Erenumab is approved for the preventive treatment of migraine in adults. Erenumab is available at doses of 70 mg and 140 mg as an auto-injector device for subcutaneous administration. The objective of this study was to evaluate the perceived ease-of-use of the device, the ability to learn self-injection, and the ergonomics of the single-dose, prefilled SureClick[®] auto-injector device for erenumab among patients with migraine.

Methods: Patients (aged 21–85 years old, inclusive) with migraine who were naïve to auto-injector or therapies targeting the CGRP pathway were recruited from 3 headache centers in the USA between March 04, 2019 and March 29, 2019. During a 30-minute 1:1 session, researchers demonstrated the SureClick[®] auto-injector device using a standard protocol-driven script under the supervision of research managers. Participants then practiced a simulated injection using a prototype device and were then asked to rate their agreement with 19 statements on the usability of the SureClick[®] auto-injector device on a 5-point Likert scale (1 = completely disagree, 2 = somewhat disagree, 3 = neutral, 4 = somewhat agree, 5 = completely agree).

Table. Patients' rating on the usability of the SureClick[®] device

Statement	Average rating*	% of Patients (N = 204) agreed (somewhat agree or completely agree)
Overall, the device is easy to use	4.75	96%
Overall, the device is simple to use	4.79	98%

(continued)

Table. Continued.

Statement	Average rating*	% of Patients (N = 204) agreed (somewhat agree or completely agree)
It's easy to inject by pressing the start button	4.79	96%
I feel confident in my ability to use the device	4.77	98%
I am confident in my ability to inject without the help of a caregiver	4.78	97%
The device is stable in my hand during administration	4.75	96%

*Out of 5 on a Likert scale (1 = completely disagree, 2 = somewhat disagree, 3 = neutral, 4 = somewhat agree, 5 = completely agree).

Results: A total of 204 patients (73% female, 27% male) participated in the study. Over 90% of the participants agreed (somewhat agree or completely agree) on 17/19 statements on ease-of-use of the device, ability to self-inject, and size of the device with an average rating of >4.5 on a 5-point Likert scale (**Table**). Two statements relating to the size of device, "I like the size of the device," and "The device is compact," were rated 4.23 and 4.26, respectively.

Conclusion: The pre-filled SureClick[®] auto-injector device for erenumab, was well-received by patients with migraine. Following a 1:1 instructional session, participants with no prior experience of using an auto-injector device felt confident in their ability to self-inject with SureClick[®] auto-injector device.

Disclosure of Interests: Erenumab is co-developed by Amgen and Novartis.

The study was supported by Amgen Inc., Thousand Oaks, CA, USA, and Novartis Pharma AG, Basel, Switzerland.

Ryan Dammerman – used to provide services to Amgen during the conduct of the study;

Jennifer Mead – is an employee of Amgen.

IHC-LB-033

Consistency of Galcanezumab Efficacy Throughout a Month Over Time

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Abstract number: IHC-LB-033**Table.** Mean Change from Baseline in Biweekly Number of Migraine Headache Days for the First and Last Two Weeks of the Last Month of the Study in Patients with Chronic or Episodic Migraine Following Injections of Galcanezumab or Placebo.

Chronic Migraine (Month 3 of REGAIN)					Episodic Migraine (Month 6 of EVOLVE-1 AND EVOLVE-2)				
Period	Treatment	N	LS Means Change from Baseline (SE)	95% CI	Period	Treatment	N	LS Means Change from Baseline (SE)	95% CI
First Two Weeks	Placebo	509	-1.64 (0.20)	(-2.03, -1.25)*	First Two Weeks	Placebo	745	-1.46 (0.10)	(-1.65, -1.26)*
	GMB 120 mg/month	262	-2.54 (0.25)	(-3.03, -2.04)*		GMB 120 mg/month	381	-2.28 (0.13)	(-2.53, -2.03)*
Last Two Weeks	Placebo	508	-1.79 (0.20)	(-2.19, -1.40)*	Last Two Weeks	Placebo	741	-1.49 (0.10)	(-1.68, -1.30)*
	GMB 120 mg/month	263	-2.66 (0.26)	(-3.16, -2.15)*		GMB 120 mg/month	378	-2.34 (0.13)	(-2.59, -2.09)*

Abbreviations: CI = confidence interval; GMB = galcanezumab; LS = least squares; N = number of intent-to-treat subjects who have non-missing baseline value and at least one post-baseline value; SE = standard error.

*Indicates statistical significance

Estimates were obtained using unstructured covariance structure. The Kenward-Roger approximation was used to estimate denominator degrees of freedom.

Objective: To determine if galcanezumab 120 mg once-monthly dosing maintains efficacy throughout the dosing interval.

Methods: This was a post-hoc analysis of 3 double-blind, placebo-controlled Phase 3 studies, in adult patients with chronic or episodic migraine. Patients received monthly subcutaneous galcanezumab 120 mg (initial loading dose of 240 mg) or placebo for 3 months (REGAIN; N = 835) or 6 months (EVOLVE-1 and -2; N = 1335). Endpoints for this study were the mean change from baseline in migraine headache days (MHDs), comparing the first 2 weeks and last 2 weeks in each month of the studies. Least squared mean changes were estimated using a mixed model for repeated measures analysis.

Results: Overall, reduction in MHDs observed in the first two weeks of the month was maintained during the last two weeks for chronic and episodic migraine. In patients with chronic migraine, mean MHDs were reduced by 1.84, 2.31, and 2.54 days with galcanezumab versus 0.73, 1.34, and 1.64 days with placebo in the first 2 weeks of Months 1, 2, and 3, respectively ($p < 0.001$; baseline monthly MHDs = 19.4). Similarly, in the last 2 weeks, mean MHDs were reduced by 1.98, 2.35, and 2.66 days with galcanezumab versus 1.15, 1.65, and 1.79 days with placebo, respectively, in Months 1, 2 and 3 ($p < 0.001$).

In patients with episodic migraine, mean MHDs were reduced by 1.80 and 2.28 days with galcanezumab versus 0.51 and 1.46 days for placebo in the first 2 weeks of Months 1 and 6, respectively ($p < 0.001$; baseline monthly MHDs = 9.1). Comparably, in the last 2 weeks, mean MHDs were reduced by 1.77 and 2.34 days with galcanezumab versus 0.86 and 1.49 days with placebo, respectively, in Months 1 and 6 ($p < 0.001$). The same pattern was seen across Months 2 to 5 ($p < 0.001$).

Conclusion: Galcanezumab 120-mg once monthly consistently maintains efficacy throughout each monthly dosing interval across months for chronic and episodic migraine. There is no difference in efficacy comparing the first and last halves of the month.

Studies were registered as NCT02614261, NCT02614183, and NCT02614196 at ClinicalTrials.gov.

Disclosure of Interests: K. Samaan, R. Nicholson, S. Rathmann, and E. Pearlman are employees of Eli Lilly and Company; P. Poso Rosich (PP-R) is an employee of Vall d'Hebron University Hospital and Vall d'Hebron Institute of Research (Spain), PP-R has received honoraria as a consultant and speaker for: Allergan, Almirall, Chiesi, Eli Lilly, Novartis and Teva. Her research group has received research grants from Allergan and has received funding for clinical trials from Alder, Electrocore, Eli Lilly, Novartis and Teva. PP-R does not own stocks from any pharmaceutical company.

IHC-LB-034**First-Hand impressions of the new monoclonal antibody erenumab from patients in Germany**

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Objective: The growing importance of real-world evidence (RWE) data in the healthcare sector has been acknowledged for some years now. However, the value of capturing the patients' benefit of a new therapeutic option is still largely underestimated. Therapy outcome in migraine treatment cannot solely be measured based on the reduction of migraine days. The quality of life including daily activity and time with the family, also the wellbeing of the patient are decisive factors driving migraine management. Thus, it is imperative to understand the patients' perspective on treatment with the newly available fully human monoclonal antibody erenumab (Aimovig®), the first-in-class calcitonin gene-related peptide (CGRP) receptor inhibitor available since November 2018. This data collection aims to characterize the perception of erenumab from the patient's point of view.

Methods: An online survey will collect data from about 200–300 erenumab patients in Germany. Patients diagnosed with migraine will be questioned about their disease in general and their experience with pharmacological and non-pharmacological prophylactic therapies. Patients who have already been on therapy with erenumab for at least three months will be specifically surveyed.

Results: By September, data of the first interim analysis will be available. The use of erenumab will be characterized from the point of view of migraine patients with regard to therapy satisfaction, daily functioning, quality of life, changes in frequency and intensity of migraine and use of acute medication.

Conclusion: PERISCOPE will provide us the first real-world evidence data of German patients treated with erenumab and will provide insight into patient perspective regarding their experience controlling their migraine with the new prophylaxis erenumab, therapy satisfaction, therapy adherence and possible effects on the quality of life.

Disclosure of Interests: K. Schuh and M. Koch are employees of Novartis Pharma GmbH, Germany.

C. Gaul received honoraria for consulting and lectures within the past 3 years from Allergan Pharma, Ratiopharm, BoehringerIngelheimPharma, Eli Lilly, Novartis Pharma, DesitinArzneimittel, Cerbotec, Bayer Vital, HormosanPharma, electroCore, Grünenthal, Reckitt Benckiser, and Teva. He does not hold any stocks of pharmaceutical companies or medical device companies.

IHC-LB-035

Non-headache benefits of onabotulinumtoxinA in chronic migraine patients: PREEMPT pooled analysis

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Objective: To evaluate the effect of onabotulinumtoxinA on clinically meaningful changes in headache severity, headache-related impact, and quality of life.

Methods: A post-hoc analysis was conducted of pooled, 24-week data from the placebo-controlled, randomized, double-blind treatment phases of the PREEMPT clinical trials. The percentages of patients meeting responder status at 24 weeks for the change in headache days ($\geq 50\%$ reduction in headache-day frequency), the Headache Impact Test (HIT-6; ≥ 5 -point improvement), MSQ Role Function-Restrictive (MSQ-RFR; ≥ 10.9 -point improvement), and Average Daily Headache Severity (ADHS; ≥ 1 -point improvement on a 4-point ordinal scale where 0 = no pain and 3 = severe pain) were calculated. Percentages of patients meeting responder status in ≥ 1 , ≥ 2 , ≥ 3 , and all 4 categories were calculated. Missing scores were estimated using modified last observation carried forward techniques.

Results: Patients (N = 1384) were randomized to onabotulinumtoxinA (n = 688) or placebo (n = 696) groups. Significantly more patients treated with onabotulinumtoxinA compared with placebo were responders with regard to change in headache days (44.8% vs 34.2%), HIT-6 (40.8% vs 25.3%), MSQ-RFR (59.0% vs 40.2%), and ADHS (35.5% vs 22.4%) at 24 weeks (all $P < 0.001$). At least 1 responder criteria was met by 72.1% and 56.6% of onabotulinumtoxinA and placebo patients, respectively ($P < 0.001$). All 4 criteria were met by 20.4% and 8.6% of onabotulinumtoxinA and placebo patients, respectively ($P < 0.001$). Linear regression analysis found approximately 20% of the variance in HIT-6 and MSQ-RFR improvement could be explained by improvement in headache days.

Conclusion: Change in headache days did not fully capture the benefit associated with 24 weeks of onabotulinumtoxinA treatment. While 45% of patients met responder criteria for monthly headache days,

>70% of patients had clinically meaningful improvements on at least 1 outcome measure.

Disclosure of Interests: Support: Allergan plc, Dublin, Ireland.

Hans-Christoph Diener, MD, has received honoraria for participation in clinical trials and for contribution to advisory boards or oral presentations from Addex Pharma, Allergan, Almirall, Autonomic Technology, AstraZeneca, Bayer Vital, Berlin Chemie, Boehringer Ingelheim, Bristol-Myers Squibb, Coherex, CoLucid, GlaxoSmithKline, Grunenthal, Janssen-Cilag, Lilly, La Roche, 3 M Medica, Medtronic, Menerini, Minster, MSD, Neuroscore, Novartis, Johnson & Johnson, Pierre Fabre, Pfizer, Schaper and Brümmer, Sanofi, St. Jude, and Weber & Weber. He has received financial support for research projects from Allergan, Almirall, AstraZeneca, Bayer, GSK, Janssen-Cilag, MSD, and Pfizer. Headache research at the Department of Neurology in Essen is supported by the German Research Council (DFG), the German Ministry of Education and Research (BMBF), and the European Union. Dr. Diener has no ownership interest and does not own stock in any pharmaceutical company.

Richard B. Lipton, MD, serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy's, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta.

David W. Dodick, MD, reports personal fees from Acorda, Amgen, Alder, Allergan, Autonomic Technologies, Biohaven, Colucid, Eli Lilly, eNeura, Foresight Capital, Neuro Relief, Zosano, WL Gore, Vedanta Associates, Promius Pharma, Magellan Healthcare, CC West Ford Group, Nocira, Novartis, NuPathe, Supernus, Electrocore, Tonix, Teva, Alcobra, Insys, Ipsen, Charleston Laboratories, Biocentric, Theranica, Xenon, ZP Opco. Travel expense reimbursement and speaking fee from Sun Pharma. Anticipated income from consulting within next 3 weeks not previously reported: Impel Pharmaceuticals (currently under review by Mayo Clinic Medical Industry Relations Committee). Compensation for activities related to data safety monitoring committee from Axsome. Speaking fees, or fees related to CME content development: Healthlogix, Medicom Worldwide, Medlogix Communications, MedNet, Miller Medical Communications, PeerView Operation Services America, Web MD/Medscape, American Academy of Neurology, American Headache Society, PeerView Institute for Medical Education, Chameleon Communications, Academy for Continued Healthcare Learning, Universal Meeting Management, Haymarket Medical Education, Global Scientific Communications, UpToDate, Meeting

LogiX. Consulting use agreement through employer: NeuroAssessment Systems, Myndshft.

Ronald E. DeGryse, MS, MA, and Aubrey Manack Adams, PhD, are full-time employees of Allergan plc and own stock in the company.

Stephen D. Silberstein, MD, is a consultant and/or advisory panel member for and has received honoraria from Alder Biopharmaceuticals, Allergan, Amgen, Avanir, eNeura, ElectroCore Medical, Labrys Biologics, Medscape, Medtronic, Neuralie, NINDS, Pfizer, and Teva. His employer receives research support from Allergan, Amgen, Cumberland Pharmaceuticals, ElectroCore Medical, Labrys Biologics, Eli Lilly, Merz, and Troy Healthcare.

IHC-LB-036

Galcanezumab shows efficacy as early as Day 1 after initial treatment v. placebo for the prevention of episodic and chronic migraine

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Objective: To evaluate onset of efficacy of galcanezumab (GMB) in patients with episodic or chronic migraine.

Methods: Migraine headache occurrence during the first 7 days including and following initial study treatment was analyzed for patients from 3 double-blind, Phase 3 studies. EVOLVE-1 (N=858) and EVOLVE-2 (N=915) were 6-month studies in patients with episodic migraine; REGAIN (N=1,113) was a 3-month study in patients with chronic migraine. Patients were randomized 2:1:1 to monthly injections with placebo (PBO), GMB 120 mg with a 240 mg loading dose, or GMB 240 mg. Onset of efficacy was defined as the earliest time point at which GMB became superior to PBO and maintained that superiority for the primary outcome (change in migraine headache days [MHD]). Monthly and weekly analyses were based on mean change from baseline in MHD; daily analyses were based on the percent of patients with migraine headache on day of injection through 6 days post-injection. Percentages were modeled to control for baseline differences.

Results: As GMB was superior to PBO in reducing MHD starting at the first month and even as early as the first week of treatment, daily analyses were also conducted. In the baseline periods, a daily average of 30% of patients in the EVOLVE-1 and EVOLVE-2 trials, and 65% of patients with chronic migraine in REGAIN trial experienced migraine headache. At Day 1 post-injection, significantly

fewer GMB-treated patients experienced MHD versus PBO-treated patients (EVOLVE-1: 14% in GMB vs 22% in PBO, $p = .002$; EVOLVE-2: 18% in GMB vs 24% in PBO, $p = .038$; REGAIN: 49% in GMB vs 58% in PBO, $p = .004$). GMB-treated patients continued to have significantly lower MHD rates for each remaining day during the first week of treatment compared with placebo-treated patients in all 3 studies (all p -values < 0.05).

Conclusion: GMB showed statistically superior efficacy to placebo starting at Day 1 after injection and the effect was sustained throughout the trials in both episodic and chronic migraine patients.

Disclosure of Interests: These studies were funded by Eli Lilly and Company.

PW, HCD, and DR are employees and minor stockholders of Eli Lilly and Company.

UR has received support from Eli Lilly, Amgen, Novartis, Alder, Allergan, TEVA, and Medscape for participation in clinical trials and speaking.

IHC-LB-037

10-year cost-effectiveness analyses of fremanezumab compared to erenumab as preventive treatment in episodic migraine for patients with inadequate response to prior preventive treatments

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Objective: Fremanezumab, a fully humanized monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide, is approved for the preventive treatment of episodic migraine in adults. Cost-effectiveness of fremanezumab versus erenumab for the prevention of episodic migraine (EM) in patients who had responded inadequately to 2 to 4 classes of prior preventive treatments was examined.

Methods: A semi-Markov cost-effectiveness model (CEM) was developed with a 4-week cycle and 10-year analysis time horizon. Costs and benefits were discounted at 3.0% annual rates. Treatment efficacies were incorporated as reductions in mean migraine days (MDs)/28 days versus placebo. Patient cohorts were distributed among MD categories (0–28 MDs/28 days) based on mean MD levels. For this study, EM was defined as patients with 4 to 14 MDs per 28 days at the start of the study. The CEM estimated costs (fremanezumab and erenumab acquisition costs, MD-related costs [direct and indirect]) and health-related-quality-of-life (MD- and treatment status-based utilities) for fremanezumab and erenumab. Outcome measures were costs, reduction in MDs, and quality-

adjusted life-years (QALYs). Only background mortality was modeled. Analyses were performed on an EM population with 2–4 prior treatment failures. The incremental cost-effectiveness ratios (ICERs) were reported as cost/QALY gained between fremanezumab and erenumab. Fremanezumab and erenumab (140 mg dosing) MDs/28-day reductions versus placebo were sourced from a Network Meta-Analysis (NMA). The analysis assumed the same discontinuation rate for fremanezumab and erenumab.

Results: In the base-case 10-year analysis time horizon, fremanezumab dominates erenumab (less costly, more effective), with an average incremental cost savings of \$1,795/patient, incremental QALYs of 0.037/patient, and a reduction in MDs of 33.3 MDs/patient. Excluding indirect costs, fremanezumab still dominates erenumab, with an average incremental cost savings of \$936.96/patient.

Conclusion: Based on current pricing and RCT results, fremanezumab treatment is cost effective versus erenumab.

Disclosure of Interests: L. Smolen and T. Klein are employees of Medical Decision Modeling Inc., Indianapolis, Indiana, USA, which received payment for their work on these analyses from Teva Pharmaceuticals. S.K. Gandhi, S. Thompson, and J.M. Cohen are employees of Teva Pharmaceuticals.

IHC-LB-038

Repeated peripheral nerve blocks reduce cutaneous allodynia symptoms, headache-related disability, depression, and anxiety in chronic migraine

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Objective: Up to date, there is a lack of evidence whether the combination of trigeminal nerve branch blocks and occipital nerve blocks is more effective than greater occipital nerve blocks (GON) alone, or if the injections should only be inserted to the localization of the migraine pain. In this study, the effects of repeated trigeminal nerve branch and GON blocks on cutaneous allodynia (CA), migraine-related disability, depression and anxiety symptoms in chronic migraine were assessed.

Methods: Twenty patients with chronic migraine who failed adequate trials of at least 3 preventive drug classes were enrolled. Six months of results following repeated bilateral supraorbital nerve, auriculotemporal nerve, and

GON blocks were evaluated. A total of 10 mL of 2 lidocaine HCL was injected each month. Change in the Numeric Pain Rating Scale (NPRS), Allodynia Symptom Checklist (ASC), Beck Depression and Anxiety Inventory, and MIDAS were used to assess the response to blocks.

Results: The mean age of patients was 46.25 ± 9.92 , 95% were female. The mean number of headaches days/month was 21.10 ± 5.07 and following the 6th injection, mean headache days reduced to 6.1 ± 2.11 ($p = 0.012$). For analysing the mid-term effect of injections on ASC, NPRS, depression, anxiety, and MIDAS scores, Anova with repeated measures test was used. These differences were noted to be statistically significant (all p values < 0.05). Medication overuse headache and localization of migraine pain were not associated with ASC scores' decline over time ($p = 0.461$).

Conclusion: This study demonstrates that repeated occipital plus trigeminal branch nerve blocks with local anaesthetics may be an effective option for management of chronic migraine, contribute to treatment of allodynia and prevent migraine chronification.

Disclosure of Interests: None.

IHC-LB-039

Cortical excitability in chronic migraine patients after preventive treatment measured by TMS

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Objective: OnabotulinumtoxinA (OnabotA) and topiramate are regulatory approved effective medications for chronic migraine (CM) preventive treatment, however, the exact mechanisms of their antinociceptive action in CM are not fully understood.

Methods: 85 patients with CM (mean age 44, women 97%, diagnosis according to ICHD-III beta, 2013) were included in the open-label prospective study. We assessed motor cortex thresholds (MT r/l, % of maximal stimulator output), cortical silent period duration (CSP r/l, ms) by motor cortex stimulation with recording responses from abductor digiti minimi muscles r/l and phosphene threshold (PT, % of maximal stimulator output) by visual cortex stimulation. Clinical data were collected from headache diaries: number of headache days per month. TMS was performed twice: before and 3 months after OnabotA injections (according to the PREEMPT paradigm; $n = 43$) and Topiramate (100 mg/day; $n = 42$).

Results: After OnabotA, MT r/l and CSP r/l significantly increased compared to baseline; after Topiramate, MT r/l and PT significantly increased compared to baseline (Table 1).

Abstract number: IHC-LB-039

Table 1. TMS parameters in CM patients before/after OnabotA ($n = 43$) and Topiramate ($n = 42$)

Parameter	OnabotA		Topiramate	
	Before	After	Before	After
MT, % Me (min-max) (25; 75%)				
Right	40 (26–60) (37; 49)	45 (32–63) (38; 52)*	41 (27–56) (35; 47)	45 (28–57) (38; 48)*
Left	42 (26–61) (38; 51)	45 (33–62) (37; 52)*	40 (27–57) (33; 44)	45 (28–55) (37; 48)*
CSP duration, ms Me (min-max) (25; 75%)				
Right	96 (47–161) (78; 114)	117 (73–167) (96; 138)*	94 (52–165) (80; 111)	92 (57–147) (83; 116)
Left	96 (47–170) (72; 120)	117 (75–170) (94; 141)*	85 (56–165) (70; 110)	87 (55–158) (72; 126)
PT				
% Me (min-max) (25; 75%)	63 (40–95) (52; 74)	63 (46–93) (52; 77)	64 (40–94) (51; 73)	72 (49–95) (62; 84)*

*- statistically significant difference between parameters before and after treatment in each group of CM patients.

The number of headache per month decreased significantly in both groups: OnabotA (before 29 days, after 12 days; $p < 0,01$) and Topiramate (before 25 days, after 12 days; $p < 0,01$).

Conclusion: The results of our study showed a combination of significant clinical parameters improvement with TMS parameters changes, reflecting cortical excitability and intracortical inhibition. This suggests that cortical mechanisms in CM “de-chronification” are obligatory involved, independently of primary peripheral (like OnabotA) or central (like Topiramate) action mechanism.

Disclosure of Interest: None Declared.

IHC-LB-074

CGRP Monoclonal Antibodies: First Year Results, Controversies, and Management Issues

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Objective: This is a retrospective review of the first year’s use of fremanezumab and galcanezumab for the prevention of chronic migraine. Efficacy and side effects are reviewed. In addition, results from switching from one monoclonal antibody(mAb) to another will be presented. controversies and management issues will be discusse.

Methods: This is a retrospective, office based review of results after 3 months for 79 fremanezumab patients and 70 emgality patients. The results of 121 patients who had switched from one mAb to another were evaluated. IRB approval was obtained. Improvement was determined primarily by the number of headache days per month.

Results: 51% of patients achieved at least a 30% improvement in the number of headache days with the use of fremanezumab, and 60% with the use of galcanezumab. Side effects were frequent, with the most common ones being constipation, nausea, depression, and increased headache. When the patients were swtiched from one mAb to another, 27% did well if the switch was due to poor efficacy. 33% improved if the switch was because of side effects, while 58% did well if it was secondary to financial or insurance reasons.

Various management issues will be discussed, such as the use of onabotulinumtoxinA with the mAb, long-term efficacy, serious side effects, and others.

Conclusion: The efficacy of the mAbs is reasonably good, but the side effects are commonly enounered. There are a number of management issues and controversies that need to be addressed.

Disclosure of Interests: Speaker for Lilly, Teva, and Amgen.

IHC-LB-075

In Vivo Antagonistic Activity and Endogenous Target Engagement of an Anti-PACAP Monoclonal Antibody in Cynomolgus Monkeys

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Objective: Pituitary adenylate cyclase-activating peptide (PACAP) is a neuropeptide that has been implicated in migraine pathophysiology. A role for PACAP in migraine is supported by clinical observations including human provocation studies that have demonstrated that PACAP triggers migraines and migraine-associated symptoms, such as photophobia, phonophobia, and nausea. In addition, clinical studies have reported increased ictal PACAP levels in the plasma of patients with migraine. We have discovered and engineered ALD1910, a humanized anti-PACAP monoclonal antibody for the preventive treatment of migraine. The amino acid sequence of PACAP is identical in human, cynomolgus monkey, rabbit, rat, and mouse; therefore, it is expected for ALD1910 to cross-react with PACAP across these species. Cynomolgus monkeys were chosen as a relevant pharmacology model to characterize the in vivo antagonistic effects of ALD1910 on PACAP-mediated biology. The objectives of this study were to determine the *in vivo* antagonistic activity and the target engagement ability of ALD1910 in cynomolgus monkeys.

Methods: The *in vivo* ability of ALD1910 to inhibit PACAP38-mediated dermal vasodilation in cynomolgus monkeys was determined via laser Doppler technology. The ability of ALD1910 to interact with cynomolgus monkey endogenous PACAP was determined via a sandwich ELISA.

Results: Our results show that ALD1910, administered by intravenous bolus injection in male cynomolgus monkeys, effectively inhibits PACAP38-induced dermal vasodilation as measured by laser Doppler technology. Target engagement of ALD1910 with endogenous cynomolgus monkey PACAP *in vivo* was confirmed through the detection of the [ALD1910:PACAP] complex.

Conclusion: Collectively, the data demonstrate that ALD1910 exhibits antagonistic *in vivo* activity and engages native endogenous PACAP when administered intravenously to cynomolgus monkeys.

Disclosure of Interests: All authors are full-time employees of Alder BioPharmaceuticals.

IHC-LB-076

Real-life management of chronic migraine with Erenumab: correlation of clinical improvement with biomolecular and neurophysiological parameters

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Objective: The aim of this study is the correlation of the clinical effectiveness of Erenumab, administered in a real-life setting, with changes in the expression of micro-RNA that are relevant for migraine and spinal central sensitization in subjects with chronic migraine (CM) with or without medication overuse (MO).

Methods: We enrolled 23 CM patients (19 female, age 48.1 ± 10.0 years), 19 of whom had MO. All patients were treated with 3 doses of Erenumab (every 28 days). The study protocol included: V1: baseline; V2: 28 days after V1; V3: end of study, 56 days after V2.

At V1, V2 and V3 we recorded headache days (HDs) and days of drug intake (DDs) using an ad hoc headache diary.

At V1 and V3 all subjects underwent neurophysiological recording of the Nociceptive Withdrawal Reflex (RTh: Reflex threshold, TST: Temporal Summation) and blood essays for the expression of micro-RNAs (using rtPCR): miR382-5p, implicated in the modulation of inflammation and miR34-5p implicated in the expression of GABA receptors.

Results: HDs markedly and progressively decreased over time (V1: 23.6 ± 5.4 ; V2: 16.1 ± 8.2 ; V3: 12.0 ± 8.1 ; $p = 0.001$), reaching the statistical level of significance already at V2. A similar pattern was observed for DDs, which significantly decreased over time (V1: 18.0 ± 8.0 ; V2: 8.1 ± 6.3 ; V3: 4.0 ± 2.5 ; $F_{20,110}$, $p = 0.001$) with a reduction that was already significant at V2.

At V3, we recorded a significant increase in both R-Th (V1: 15.9 ± 7.9 , V3: 19.37 ± 8.9 ; $p = 0.001$) and TST (V1: 11.4 ± 5.7 , V3: 12.8 ± 5.5 ; $p = 0.003$), with a parallel reduction in the expression of miR382-5p (V1: 7.8 ± 6.7 , V3: 2.2 ± 2.9) and miR-34a-5p (V1: 25.8 ± 19.4 , V3: 4.7 ± 4.0), $p = 0.001$ for both.

Conclusion: This study provides the first report of the positive effects of Erenumab on biomolecular and neurophysiological alterations related to CM.

Disclosure of Interests: RDI, GF, RG, AZ, ET, SB, EG, MA, VG, and GS have no conflicts of interest to declare. CT received honoraria for the participation in advisory boards or for oral presentations from: Allergan, Electrocore, Eli-Lilly, Novartis and Teva. CT has no ownership interest and does not own stocks of any pharmaceutical company. CT serves as Chief Section Editor of *Frontiers in Neurology – Section Headache Medicine and Facial Pain* and on the editorial board of *The Journal of Headache and Pain*.

IHC-LB-077

Erenumab and galcanezumab in chronic migraine prevention: effects after treatment termination

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Objective: Monoclonal antibodies (mAbs) targeting the CGRP pathway are safe and efficacious therapies for the prevention of migraine. In this study we assessed the effects of discontinuation of preventive erenumab and galcanezumab treatment in patients with chronic migraine.

Methods: This retrospective pooled analysis included completers of the open-label extension study phase for the preventive treatment of chronic migraine with galcanezumab (NCT02614261; 9 months) and erenumab (NCT02174861; 12 months) in a single headache center. We compare migraine data until week 12 after open-label treatment completion, when patients did not have any pharmacological preventive medication, to study baseline values of the double-blind trial period, and to the last 4 weeks of the open-label extension. The assessment included changes in monthly migraine days, headache hours, days with severe headache and acute headache medication use.

Results: Data from 16 patients after galcanezumab ($n = 9$) and erenumab ($n = 7$) open-label treatment completion were analyzed. The mean number of monthly migraine days was 18.38 ± 3.74 at baseline, and 12.19 ± 4.53 in the last 4 weeks of the open-label extension ($p < 0.001$). Monthly migraine days remained significantly reduced compared to baseline during the entire 12-week observation period after open-label termination ($p = 0.002$), with a reduction of 5.38 ± 4.92 in weeks 1–4 ($p = 0.001$), 4.75 ± 4.15 in weeks 5–8 ($p = 0.001$), and 3.93 ± 5.45 in weeks 9–12 ($p = 0.014$). There was no significant difference in monthly migraine days between the 12 weeks after open-label termination and the last 4 weeks of the

open-label phase ($p = 0.228$). All other analyses revealed numerical improvement through week 12 in comparison to baseline.

Conclusion: In this small, self-selected cohort, the results indicate a therapeutic effect of monoclonal antibodies targeting the CGRP pathway in chronic migraine prevention after treatment termination up to 12 weeks.

Disclosure of Interests: BR has received honoraria for consulting from Novartis Pharma. VM reports no disclosures. HI has received honoraria for consulting from Pharm Allergan and Autonomic Technologies. LN has received honoraria for consulting from Eli Lilly and Novartis Pharma, and for scientific presentations by Pharm Allergan, Desitin, Hormosan, Eli Lilly, Novartis Pharma and TEVA. UR has received honoraria for consulting from Amgen, Pharm Allergan, Autonomic Technologies, Co-Lucid, Eli Lilly, Medscape; StreaMedUp, Novartis Pharma and TEVA, and for scientific presentations by Amgen, Allergan, Eli Lilly, Co-Lucid, Medscape, Novartis Pharma and TEVA. BR, HI, LN and UR are involved as investigators in clinical trials with monoclonal antibodies from Amgen, Alder, Eli Lilly, Novartis, and TEVA without personal remuneration.

IHC-LB-078

Erenumab for Migraine Treatment – First Real World Data from Germany

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Objective: Erenumab is the only approved antibody against the CGRP receptor, and in Germany is used for the treatment of refractory migraine. Previously clinical trials showed that the substance is well tolerated and has a good efficacy. Data reflecting real world conditions are still scarce. This is especially relevant as clinical trials have not looked for these severely refractory patients in particular which are currently being treated due to reimbursement regulations. We here present real-world therapy response regarding headache and migraine days and intake of acute medication after 3-month Erenumab therapy.

Methods: 79 therapy refractory patients (non-response, side effects or contraindications of 4 or, in chronic migraine 5 prophylactic medication groups; 52 with chronic migraine, 27 with episodic migraine) were evaluated regarding their migraine before and after 3-month Erenumab therapy. The majority of patients started with a starting dose of 70 mg ($N = 75$ patients), the rest with 140 mg. Headache days, migraine days and the use of acute

therapies were documented in the follow-up using headache diaries. Retrospective nonparametric analysis was performed on non-normally distributed data using the Wilcoxon-Mann-Whitney test.

Results: The analysis of all patients revealed a reduction in headache days (17.862 ± 7.072 vs. 12.914 ± 9.031 ; $p < 0.001$), migraine days (14.1692 ± 6.343 vs. 9.24 ± 7.684 ; $p < 0.001$), and days on which acute medication was taken (11.243 ± 6.094 vs. 7.018 ± 5.832 , $p < 0.001$). 58% of patients with chronic migraine under therapy converted to episodic migraine within the three months follow up. The 50% response rate regarding headache days was 35.5%. The rate of patients who did not achieve any improvement under therapy or who increased the number of headache days was 27.6%.

Conclusion: As in clinical trials, under real conditions, a significant response to Erenumab therapy was demonstrated in our cohort. In particular, the conversion rate from chronic to episodic migraine is clinically relevant. However, almost one third of the patients did not respond to the therapy. The extent to which these patients could benefit from an increased dose, a longer therapy or a change of preparation to a CGRP ligand antibody is still unclear. The long-term course of therapy response needs to be investigated in more detail.

Disclosure of Interests: SN and DHL have received honorariums for advisory board and presentations from Novartis, Lilly and Teva Pharma.

IHC-LB-079

Single-pulse transcranial magnetic stimulation (sTMS) for the treatment of migraine: A prospective real world single-centre experience

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Objective: The Headache Centre at Guy's and St Thomas' NHS Foundation Trust is currently the only National Health System (NHS) service commissioned to offer sTMS to migraine patients in the United Kingdom (UK). The aim of this audit is to evaluate the effectiveness of sTMS (eNeura) as a non-pharmacological treatment modality in adults with chronic/high frequency episodic migraine in a real-world setting.

Methods: This is an open-label prospective ongoing single centre clinical audit. Patients with a diagnosis of episodic high frequency (≥ 8 migraine days/month) or chronic migraine were offered the therapy. A standard titration protocol for prevention and acute migraine treatment

was given to patients in clinic. Data were collected prospectively using a headache diary and HIT-6 scale. Change in headache days (HD), migraine days (MD) and HIT-6 at 3 and 12 months of treatment compared to baseline were analysed. Adverse events and treatment compliance were collected.

Results: A total of 128 patients were treated with sTMS. Hundred-one patients completed the 3-month trial period and were analysed. Forty-three patients (43%) received sTMS after failing at least 3 oral preventives and Botox therapy, hence were considered refractory to medical treatments. At baseline, patients displayed an average of 18.3 HD/month, of which 14.7 were MD with a average HIT-6 score of 66. Following a 3-month trial, 22 patients achieved at least a 30% reduction in HD, while a total of 49 patients (49%) obtained a clinically meaningful benefit (-6.4 HD/month, -6.7 MD/month and -8.8 points on HIT-6 score), hence continued the treatment. Fifty-two (51%) patients stopped the treatment due to lack of efficacy. Of those, the majority were refractory to medical treatments. ($N=34$; 64%). Currently, 18 patients continue sTMS treatment for over 12 months. Treatment compliance was satisfactory with sTMS used up to eight pulses three times a day. Side effects were minor and include: worsening of the headache ($N=3$), transient mild dizziness during the treatment ($N=1$), scalp tenderness ($N=2$) and nausea ($N=1$).

Conclusion: sTMS constitutes an effective and well tolerated preventive treatment option for high frequency/chronic migraine patients in a real world setting.

Disclosure of Interests: APA received sponsorship and equipment grant from eNeura. BH received sponsorship from eNeura.

IHC-LB-080

Evaluation of the efficacy of Topiramate in the treatment of vestibular migraine

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Objective: to evaluate the efficacy of a therapeutic pathway for VM with Topiramate.

Methods: 152 patients with migraine with aura and without aura, average age 39.5 ± 13.1 years, females 122 were recruited. Their medical history and neurological status was analyzed. All patients filled up Dizziness Handicap Inventory (DHI) scale and headache (HA) diary. VM was diagnosed according to ICHD-3 beta version. Patients with VM had otoneurological examination to exclude peripheral vestibulopathy.

Table. Results of treatment with topiramate of patients with VM.

	Pretreatment n = 16	Posttreatment n = 16	p
Number of days with HA	$11,63 \pm 8,5$	$2,8 \pm 1,04$	$p < 0,01$
Number of days with V	$14,88 \pm 8,4$	$2,3 \pm 2,4$	$p < 0,01$
DHI F	$17,23 \pm 6,8$	$2,63 \pm 0,8$	$p < 0,01$
DHI E	$11,88 \pm 7,7$	$2,81 \pm 0,8$	$p < 0,01$
DHI P	$15,5 \pm 5,1$	$3,75 \pm 2,2$	$p < 0,01$
Σ DHI	$45 \pm 17,03$	$9,3 \pm 2,5$	$p < 0,01$

Results: The main group consisted of patients with VM – 13,8% ($n=21$), and controls were patients with dizziness (D) – 42,2% ($n=64$); 2,6% ($n=4$) of patients had peripheral vestibulopathy and 41,45% ($n=63$) of patients had no vertigo (V) or D. Less patients with episodic migraine (EM) suffered from V than patients with chronic migraine (CM) (23 people (31.9%) vs 40 people (51.9%), $p=0.01$). In VM group CM was observed more often than in the group with EM (15 people (20.8%) vs 6 people (7.7%), $p=0.01$). 16 of 21 patients with VM passed treatment with topiramate during 6 months: during the first month, the dose was gradually increased from 25 to 100 mg/day.

100% ($n=16$) VM patients who got topiramate showed a significant decrease in the number of days with headache and vertigo per month and severity of dizziness by DHI.

Conclusion: Our data confirm high comorbidity of M and V. V in VM occurs during chronification. High efficacy of topiramate, in reducing both the frequency of migraine attacks and vertigo indirectly confirm the role of central sensitization in the pathogenesis of the VM.

Disclosure of Interest: None Declared.

IHC-LB-081

Long term safety profile of DHE use in chronic headaches

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Objective: Dihydroergotamine (DHE) has been used since 1943 in the treatment of migraine. Since the advent of triptans, its use has mainly been for medically refractory primary headaches. In 2013, the European Medicines Agency released a statement recommending restricting the use of ergot derivatives due to increasing concern over the risk of fibrosis. However it is an effective treatment for resistant primary headache. There is little published data on its safety profile to guide its use.

By examining current practice within our tertiary Neurology Centre, we hope to explore this.

Methods: We performed a retrospective audit on all patients receiving IV DHE infusions between January 2014 and June 2019 in our tertiary Neurology Centre. We examined case notes to look at number of infusions received. For those who received 5 or more infusions (time equivalent of 2 years) we noted whether patients underwent an echocardiogram or CT chest/abdo/pelvis (CT CAP) to look for valvular, retroperitoneal or pulmonary fibrosis. Any fibrosis found was highlighted.

Results: Of 65 patients identified, 38 patients received 5 or more DHE infusions. 13 underwent an echo and a CT CAP (or US as per radiology). These patients had been on treatment for 121 to 373 weeks (mean 224 weeks/4.3 years) prior to surveillance scans and received on average 9.5 infusions. 3 patients had subsequent imaging 91, 96 and 107 weeks later. These patients received 12, 13 and 16 infusions respectively. 4 patients had an echo and chest xray. 4 patients had CT CAP only. A echo and CT CAP were performed for unrelated indications. No patients were found to have valvular or retroperitoneal fibrosis. One patient with pre-existing bronchiectasis was found to have pulmonary fibrosis, but after Respiratory Review, this was felt to be unrelated to DHE use. This patient, however received no further DHE treatment. 15 patients have undergone no surveillance scans, of which 6 remain on treatment.

Conclusion: None of our patients receiving DHE have had a fibrotic reaction directly attributed to their DHE treatment, however data is incomplete for 66%. It would be our recommendation that all patients should be screened for fibrotic reactions, however there is no clear guidance on mode of imaging or frequency. This would be an appropriate area for further research.

Disclosure of Interests: Dr Tyagi, from Janssen Cilage, GSK, Allergan, Electrocore, Lily, AMGEN, Novartis, eNeura, Teva, Alder, Abbott, has received: research grants, funding to conduct clinical trials, educational grants for meetings/teaching courses, funding to attend medical conferences, hospitality in and out of hospital premises.

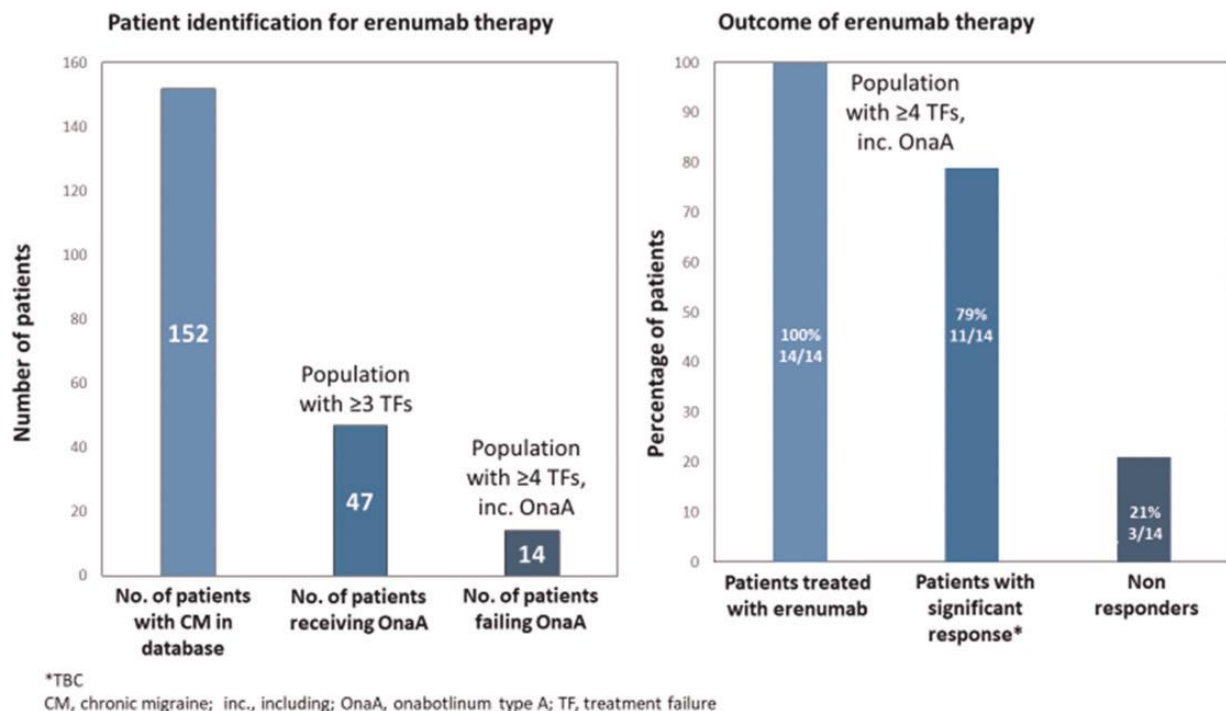
IHC-LB-082

How effective is erenumab for patients with chronic migraine who failed onabotulinum toxin type A as prophylactic treatment?

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Objective: In this single-center, retrospective database study, the efficacy and safety of erenumab was assessed in patients with chronic migraine (CM) who had failed



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prophylactic onabotulinum toxin type A and at least three other previous prophylactic treatments.

In the Netherlands, national guidelines recommend topiramate as the first-line prophylactic therapy for CM (ICHD-III), with onabotulinum toxin type A recommended as second-line therapy. However, reimbursement for onabotulinum toxin type A requires failure of at least three prior prophylactic treatments. Since November 2018, CM patients in the Netherlands failing at least four prophylactic treatments (beta-blockers, candesartan, topiramate, valproic acid and onabotulinum toxin type A) have had access to erenumab through a Managed Access Program (MAP).

Following both national guidelines and reimbursement requirements means that patients eligible for erenumab under the MAP have failed onabotulinum toxin type A and at least three other prophylactic treatments.

Methods: Of 152 (100%) patients with CM identified in our database, 47 (31 %) were treated with approved and reimbursed onabotulinum toxin type A. Of this group, 33 (70%) were successfully treated (i.e. satisfying criteria relating to reduction in the number of headache days, Headache Impact Test (HIT)/Migraine Disability Assessment (MIDAS) score, and anamnestic wellbeing). Fourteen patients (30%) did not improve. Diagnosis of CM was reconfirmed in this group of 14 patients prior to initiation of treatment with erenumab.

Results: At the end of 3 months follow up, there was a significant improvement in 11 of the 14 (79%) erenumab-treated patients, while 3 (21%) discontinued through lack of efficacy. There were no discontinuations due to adverse events.

Conclusion: Erenumab is a therapeutic option for migraine prophylaxis even in patients with CM who have failed multiple lines of prophylactic therapy, including onabotulinum toxin type A. Between November 2018 and the end of June 2019 this center has successfully treated 44 of 47 (94%) patients with CM who fulfilled the inclusion criteria for this new prophylactic treatment.

Disclosure of Interests: Consulting, boards and presentations for Allergan, Lilly, Novartis.

IHC-LB-083

Erenumab in chronic migraine: a conventional scheme versus erenumab + short dechronification – Pilot data

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Objective: Background In 1990s we detected increase of sensory neuropeptides like-immunoreactivity (LI), including CGRP-LI in trigeminal area fluids during headache attacks. We also evidenced a role of N-methyl-D-aspartate (NMDA) in migraine chronification. Since prevention with erenumab is known to carry a great variability and a not a dramatic significativity it seems interesting to improve this headache-specific therapy.

Aim To compare erenumab to CGRP-R-antibody after 5 days dechronification using 5Glu antagonists versus erenumab following 7 days wash-out in chronic refractory migraineurs. Focus: Migraine relief, side-effects.

Methods: Population: participation claim was made by using social media. Entry/exclusion criteria allowed to enroll 213 out of 587 chronic migraineurs refractory to conventional prophylactic treatments. Thus, 106 males, 107 females (age $31.8 \pm 5.2SD$) volunteered single blind 2 parallel-branches randomization: 104 assigned to 70-mg erenumab after 7 days wash-out (A), 109 to erenumab after fixed pre-treatment with NMDA antagonist (B). Treatments were administered twice. Informed consent was obtained, statements WMA Helsinki Declaration 2000 were followed.

Results: June 2019, 30 volunteers of both groups completed the observation.

Pain-Relief mean migraine-days/month.

Baseline vs. 1 month post-treatment.

$20.8 \pm 1.4SD$ vs $17.3 \pm 1.6SD$ Group A $p > 0.00001$

$22.4 \pm 2.1 SD$ vs $8.9 \pm 2.2SD$ Group B $p > 0.000001$

By month 2 (2nd treatment), migraine/days/month.

$16.4 \pm 1.9SD$ Group A $p > 0.00001$

$1.1 \pm 1.8SD$ Group B $p > 0.000001$

Scores Migraine Physical Function Impact Diary: Group A = 30%, Group B = 100% ($p > 0.00001$)

Preference Index–Group B: sustained pain-free; 0–1 rescue/2months (ibuprofen mesylate 200 mg) $p > 0.00001$ vs baseline.

Group A rescue $p > 0.004$ ($23.4 \pm 4SD$ vs $16.9 \pm 4.8SD$)

Side-effects

Nausea $n = 1$ Group A

Constipation $n = 2$ Group A, B

Menometrorrhagia n = 2 Group A, n = 1 Group B
 Anxiety n = 2 Group A
 Vital Parameters, Electrocardiogram = 0 abnormalities.
 Discontinuation due to adverse events/side-effects = 0

Conclusion: Negative NMDA modulation likely increase erenumab-induced relief.

Disclosure of Interests: No conflict of interest.

IHC-LB-084

Guideline on the preventive treatment of chronic migraine, chronic tension type headache, hemicrania continua and new daily persistent headache on behalf of the Colombian Association of Neurology

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Objective: To recommend therapeutical options for the preventive treatment of chronic migraine, tension type headache, hemicrania continua and new daily persistent headache.

Methods: The Colombian association of neurology identified an expert group in order to develop

Fig 1. GRADE evaluation for therapeutical options in chronic migraine.

Outcome	Study	Comparison	Evidence Grade	Direction	Strength	Comentario
Headache days	RCT	Placebo	● ● ● ●	For	Strong	1
Migraine days	RCT	Placebo	● ● ○ ○	For	Strong	1,2,3

GRADE Onabotulinum Toxina A,

Desenlace	Study type	Comparison	Evidence Grade	Direction	Strength	Comentario
Migraine days	RCT	Placebo	● ● ● ●	For	Strong	1,4

GRADE Erenumab

Outcome	Study type	Comparison	Evidence Grade	Direction	Strenght	Comentario
Migraine days	RCT	Placebo	● ○ ○ ○	For	Weak	1,6,7,8

GRADE Topiramate

Outcome	Study type	Comparison	Evidence Grade	Direction	Strenght	Comentario
5 days rescue	RCT	Placebo, Celecoxib	● ● ● ○	Against	Weak	4, 9
Mild HA days – No HA Days	RCT	Placebo, Celecoxib	● ● ○ ○	Against	Weak	4, 9

GRADE Prednisone

Abstract number: IHC-LB-084

recommendations. Alternatives with evidence-based information were analyzed through systematic review and GRADE methodology. In the case of options with clinical efficacy but without support based on well-designed clinical trials, the expert group performed the recommendations using delphi methodology.

Results: For chronic migraine we recommend topiramate, onabotulinum toxin and erenumab, Prednisone was not recommended in detoxification therapy (GRADE evaluation) Fig 1. Other alternatives are divalproate/valproic acid, amitriptyline, flunarizine and naratriptan (Consensus). Tension type headache could be treated with amitriptyline, imipramine and venlafaxine (Consensus). Indomethacine, topiramate and celecoxib are the pharmaceutical choices recommended to treat patients with hemicrania continua (Consensus). For new daily persistent headache we recommend gabapentin and doxycycline. According to clinical judgment cranial nerve blocks could be indicated in all the cases. Education and a comprehensive approach is essential in order to achieve better results.

Conclusion: The experts of the Colombian Association of Neurology present the therapeutic alternatives for the preventive treatment of primary chronic daily headache, although most of the information is based on expert recommendations, this approach could improve the use of resources in the treatment of this condition. Further studies are needed in order to generate evidence which strengthens these recommendations.

Disclosure of Interests: None.

IHC-LB-085

Perampanel as prophylaxis treatment in refractory chronic migraine

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Objective: Chronic migraine is a disabling disease, with high impact in their quality of life. Current prophylactic treatments are often not effective or badly tolerated. Glutamate is elevated in chronic migraine, and AMPA receptor is implicated in the maintenance of the pain. Perampanel, an antagonist of the AMPA receptor could have a preventive effect in chronic migraine.

Methods: We review the records of patients with refractory chronic migraine treated with Perampanel, and the results at third month.

Results: There were 35 patients (25 females), mean age 46.5 years (SD 11.8). All of them were not responders to, at least, Propranolol, Flunarizine, Topiramate, Amitriptyline and Onabotulinumtoxin. The mean monthly migraine days

(MMD), were 25.8 (SD 4.76). The dose was 4 mg/24 h but one patient who tolerated 6 mg/24 h. Five patients (14%), could not complete it due to adverse events (AEs). Only 10 (14%), did not complain of AEs. The AEs were drowsiness, dizziness and irritability.

After 3 months, 2 patients (6%), were slightly worse; one (3%), had reduced MMD by 30%; 5 (14%), by 50–74%; 9 (26%), $\geq 75\%$. Fifteen patients (43%), had converted to episodic migraine.

Conclusion: Even though the tolerance issue, 40% of the patients reduced MMD $> 50\%$. Perampanel might be an option in refractory chronic migraine. More studies are needed.

Disclosure of Interests: None.

IHC-LB-086

The role of botulinum toxin and anesthetic block in refractory neuralgias to medical therapy – Characterization of a sample

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Objective: Botulinum toxin administration and anesthetic block are minimally invasive interventions used for refractory pain when preventive drugs fail. Benefits of these administrations have been reported as temporary pain relief. This study's aim is to characterize the patients who underwent botulinum toxin and anesthetic block in neuralgic and cervicogenic headache in Headache outpatient clinic and verify the efficacy of these treatments.

Methods: Cohort study including patients with trigeminal and occipital neuralgia and cervicogenic headache over a 30 months period, who underwent botulinum toxin and anesthetic block. Data was obtained through the consultation records and contacting patients by telephone.

Results: 12 patients were included, mean age of 65.83 years, being 58.3% female. 50% were diagnosed with trigeminal neuralgia, 33.3% cervicogenic headache and 16.7% occipital neuralgia. 50% performed block with bupivacaine, 16.7% with botulinum toxin (follow the pain) and 33.3% did both. Patients who underwent anesthetic nerve block were back to the Clinic earlier (mean of 2 months).

33.3% didn't need to take prophylactic pills anymore. 75% had prior drug abuse. The difference between the length of the pain during a week decreased from 5.5 days to 1.8 and need to use pills decreased from 5.5 days/week to 2.99. 91.7% reported no side effects, 8.3% reported pain worsening.

Conclusion: Botulinum toxin appears to be effective in cases of neuralgia, as anesthetic nerve block in cervicogenic headache. Although the effect of blockage with bupivacaine is transitory.

The neuralgia pain relief is partial with botulinum toxin, but allow a better life quality.

We need more patients treated with these new methods to achieve new guidelines like what drugs should we use, how long and in what doses it can be effective.

Disclosure of Interest: None Declared.

Neuromodulation for Headaches

IHC-LB-040

Temporal migraine surgery: auriculotemporal and zygomaticotemporal nerves decompression under endoscopic guidance with preserving superficial temporal artery

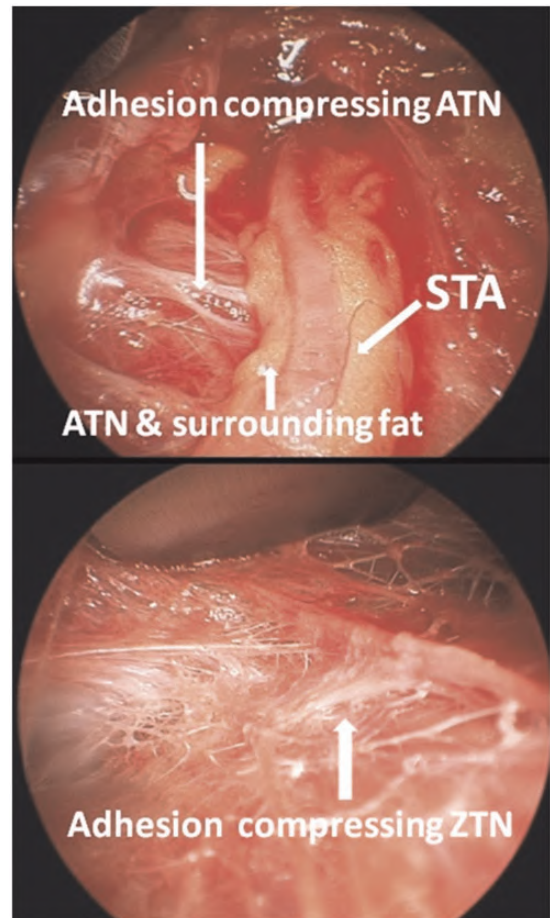
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Objective: Temporal region is the most common site in patients with migraine headache. However in a relatively large number of patients, treatment outcome remains insufficient and a drug intolerance of adverse effects further can limit the use of medication. For these patients, relatively simple decompression surgery with minimal complication can be considered as alternative and effective treatment.

Methods: The auriculotemporal and zygomaticotemporal nerves entrapment are the two primary pathology and the main surgical focus in the temporal area of migraine headache. We described and delineated the surgical procedure in eighteen patients with temporal migraine who were medically intractable and uncontrolled. All procedures were combined open decompression in auriculotemporal nerves and endoscopic decompression in zygomaticotemporal nerves with preserving superficial temporal artery under local anesthesia.

Results: Fourteen patients (77%) reported a successful surgery (>50 percent improvement of headache index) at least 6 months after surgery (mean follow-up, 8 months). Eight patients (44%) reported complete elimination of temporal migraine headache. There were no significant surgical complication or wound problem.



Conclusion: Decompression surgery of auriculotemporal and zygomaticotemporal nerve-triggered migraine headache should be considered in patients with medically uncontrolled migraine. In addition, superficial temporal artery preserving surgery showed nearly similar results compared with previous reports that coagulate or sacrifice superficial temporal artery.

Disclosure of Interest: None Declared.

IHC-LB-087**Neuromodulation with eTNS in migraine – the first Romanian experience**Bogdan I. Pana^{1,*}, Andra Iosif¹ and Adina Roceanu²¹*Emerald Medical Center, Bucharest, Romania*²*Emergency University Hospital, Bucharest, Romania*

Objective: Neurostimulation is emerging as a credible alternative in migraine therapy and is considered to have a very favorable efficacy/safety ratio. Our goal was to examine the safety and preventive effect of eTNS (external trigeminal nerve stimulation) for migraine in Romanian patients. The end points of the study where: the percentage of responder patients (more than 50% reduction) in migraine hours, medium pain intensity, migraine attacks and rescue medication.

Methods: Patients were prospectively enrolled between January to July 2019, previously or “de novo” diagnosed with migraine, with or without aura, including patients with prophylaxis prescribed at least three months before the initiation of the study. All subjects were asked to use the device for 20 minutes every day in prevention mode and for 60 minutes in acute mode for a minimum period of 3 months. The patients were asked to complete a journal with the number of migraine hours each day, the intensity of the pain (from 1 to 10) and if they used the device and/or rescue medication. The baseline parameters were recorded anamnestically.

Results: From the 32 patients that fulfilled the inclusion criteria, 6.25% dropped out because of the pain during the sessions. Nine patients fully completed the migraine diary. 44% were observed for 3 months, 22% for 4, 11% for 5 and 22% for 7 months. The total number of migraine hours was significantly reduced in 55% at 3 months, but at 5, respectively 7 months 50% of the non-responders became responders. The medium pain intensity was significantly reduced in 22% at 3 months, 14% of the others becoming responders at 4 months and 28% at 7 months. None had a significantly reduced number of migraine attacks at 3 months, but 11% had at 5 months and 22% at 7 months. At baseline 66% used triptans as rescue medication, 66% of them did not use triptans at all after 3 months and the others achieved a reduction of 40%, respectively 45%.

Conclusion: The majority of the previously migraine prevention studies with eTNS (Cefaly) were conducted for a period of three months, using the device only on prevention mode. This study raises the question if the patients should be observed for longer periods using eTNS for both prevention and acute mode. The study was not externally funded.

Disclosure of Interests: None.

Other**IHC-LB-041****Efforts to accelerate the discovery and clinical development of non-addictive therapeutics for pain within the nih heal initiative**Smriti Iyengar^{1,*}, Sarah A. Woller¹, Clinton B. Wright¹, Amir P. Tamiz¹ and Barbara I. Karp¹¹*National Institute of Neurological Disorders and Stroke, National Institutes of Health, Rockville, United States*

Objective: The NIH HEAL (Helping to End Addiction Long-term) Initiative is an aggressive, trans-NIH effort to speed scientific solutions to stem the national opioid public health crisis. Launched in April 2018, the Initiative is focused on improving prevention and treatment strategies for opioid misuse and addiction and enhancing pain management. The trans-agency, multi-institute HEAL Initiative is being led by the National Institute of Drug Abuse (NIDA) and the National Institute of Neurological Disorders and Stroke (NINDS). Within HEAL, NIDA is focused on understanding, preventing, and treating addiction. NINDS is focused on understanding pain mechanisms and developing effective, non-addictive treatments for pain, including headache. Together, programs within the HEAL Initiative will reduce the burden of illness due to addiction and pain.

Methods: NINDS was tasked with the goal of enhancing pain management through identification of non-addictive pharmacologic and non-pharmacologic interventions. As a result, NINDS, along with multiple institutes across the NIH, built a collaborative infrastructure of therapeutic development programs designed to enhance our understanding of the development and prevention of chronic pain, including headache. These programs span the discovery process from target validation through clinical trials.

Results: Programs in the infrastructure include: (1) A Preclinical Screening Platform for Pain (PSPP) focused on the identification and profiling of non-addictive/non-opioid therapeutics for pain, and (2) an Early Phase Pain Investigation Clinical Network (EPPIC-Net), to test new therapeutics for pain conditions in adults and children. These programs will evaluate small molecules, biologics, devices, and natural products across a range of pain conditions including headache.

Conclusion: This presentation will describe the two NINDS/NIH HEAL Initiative programs and efforts to test new therapies for pain, including headache.

Disclosure of Interest: None Declared.

IHC-LB-042**Identifying self-management research needs through an exploration of the views of migraine patients and their carers about their role and the roles of others**

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Objective: To explore what headache management roles migraine patients and carers identify as present, important or missing in order to identify future self-management research needs.

Methods: Patients were approached consecutively in two phases; those attending a secondary care headache service in phase one and those attending a third sector migraine primary care service in phase two. The discussion guide was developed by the author with patients and responses recorded by hand. Those who agreed to take part were asked if their responses could be used anonymously for dissemination by presentation/publication. Ethics approval was not needed as the work aimed to identify areas of research needs.

The first phase responses were analysed thematically using an inductive approach to group similar codes into themes. The results were reviewed with the patient advisor and the discussion guide was then adapted. The process was repeated in the second phase.

Results: Discussions were held with thirteen secondary care and 8 third sector patients. Patients spoke of the importance of their role. The reasons given for their role were “doing the GP’s job”, “the GP tried” or “most motivated person”, “the only solution”.

Discussions about treatment showed a power imbalance between the patient, GP and neurologist. Patients’ roles rarely mentioned treatment whereas GPs “should be able to give treatment” “alter medicines” but “do as they are told by the consultant”. It was thought that treatment “should be with the GP, not the consultant” however the neurologist was “guru” and was the one with a “range of treatment”.

The patient’s role related instead to lifestyle adaptations through awareness. “Day to day awareness”, “can I do this, can I go out?” linked to “leading the right lifestyle”.

Finally collaboration, “have to use medical side and your side together” was important in developing a “partnership”.

Conclusion: Patients were clear on their important role and a wish for active partnership with clinicians. They saw treatment access through neurologists but their roles concentrated on adaptation. There is a clear research need to

identify ways to develop active partnerships between GPs and patients to enhance treatment in primary care.

Disclosure of Interest: None Declared.

IHC-LB-043**World Brain Day; Migraine Painful Truth WFN-IHS successful collaboration with a global impact**

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Objective: Annually, the World Federation of Neurology (WFN) celebrates World Brain Day (WBD) on July 22 (the official anniversary of WFN) with each year focusing on a different theme. 2019 the theme is “Migraine, The Painful Truth”. Migraine is the leading cause of disability affecting people under the age of fifty years (the group with the highest contribution to the worldwide workforce). This makes migraine one of the highest negative economic impacts globally. The latest analysis from the Global Burden of Disease study, 3 billion people had a headache disorder in 2016, including 1.04 billion with migraine. The painful truth is despite the very high prevalence and public health burden, research in migraine remains the most underfunded area in neurology. People with migraine and other headache disorders experience substantial stigma. Migraine continues to be under-diagnosed and poorly managed, developed and especially in developing countries.

Methods: 2019 WBD campaign was organised by the IHS and WFN. This ambitious joint project between the IHS and WFN went on to develop the key messages, social media feeds, press releases, global webinar that was freely accessible to the member countries of both IHS and WFN.

WORLD BRAIN DAY | July 22, 2019



Results: Local societies were provided with material and also suggestions for press mailings.

Together, we can ensure that those affected by migraine receive the help they need.

The 2019 World Brain Day campaign had been a resounding success]. Over 100 countries took part in this well-coordinated campaign, culminating in a worldwide Webinar <https://www.wfneurology.org/world-brain-day-2019> addressing the five key messages, as above. The webinar received very positive feedback from all over the world.

The social media impressions on world brain post surpassed the three million impression mark. Just over 100 national radio, TV, print, web-based presentations cut across the world, sharing the painful truth about migraine. Several national migraine walks were launched for the first time.

The successful campaign created an unprecedented opportunity of global advocacy program with huge potential for grassroots impact. The WBD committee expect continue the momentum throughout 2019.

Conclusion: 2019 IHS-WFN World Brain Day Campaign is a tremendous success. We hope to continue the momentum throughout the year with a view to tackle this pervasive disorder and find solution to the five key themes we raised.

Disclosure of Interests: TW, WC, WG nothing to disclose.

IHC-LB-088

Zolpidem-Induced Headache: A Case Series

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Objective: The body of evidence and adverse effect reports of zolpidem is rapidly growing. The aim of presenting the current report is to discuss the possible causes of different types of headache observed in seven adults following the consumption of different doses of zolpidem with different patterns of use.

Methods: Two pharmacists have evaluated seven adults - age range 22–47 years- who self-reported different types of headache associated with zolpidem use. Every important and practical information obtained from the cases has been kept as confidential. Five electronic databases were searched to find and identify all available, accessible and relevant case reports and case series.

Results: The mean standard age of the cases was 31 years. Headache symptoms were observed in all the cases. 45 % of the affected cases had at least one type of primary headache before starting to use zolpidem. All of cases got better following zolpidem tapering down or withdrawal. The development of headache seemed to be

associated with zolpidem consumption, especially when the used dose was exceeded than recommended.

Conclusion: Given that the occurrence of such complication was 100% of all cases, it let us conclude that headache should be counted as a significant adverse effect of zolpidem. Clinicians should be aware of this risk and advise their patients accordingly.

Disclosure of Interests: The Authors haven't anything to disclose.

IHC-LB-089

Neck pain associated with migraine attacks investigated in the interictal state – a search for the origin of pain

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Objective: To investigate phenotypical differences between migraine patients with and without neck pain associated with migraine attacks in the interictal phase.

Methods: One-hundred migraine patients and 46 controls went through a semi-structured interview and sensory testing interictally. Pericranial muscle tenderness was determined using total tenderness score and local tenderness score. The occurrence of migraine attacks was prospectively recorded for the following seven days.

Results: Patients with neck pain associated with migraine attacks had increased tenderness of pericranial neck muscles compared to migraine patients without ($P = 0.023$). Neck pain associated with migraine attacks was not associated with migraine localization, tension-type headache or markers of central sensitization. Prospective data of 84 patients showed that tenderness of trigeminal sensory innervated muscles increased the migraine attack rate ($P = 0.035$).

Conclusion: The study suggests a possible peripheral influence on migraine pain in patients with neck pain associated with migraine attacks. The distinction of migraine patients based on the occurrence of neck pain associated with migraine attacks could be a useful biomarker in future migraine studies.

Disclosure of Interests: The authors have no conflict of interest to declare.

Other Primary Headache Disorders

IHC-LB-044

PCH-CU: Description of primary cough headache in a cough unit. A prospective study

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Objective: Description of characteristics, prevalence and comorbidities associated with cough headache in a Cough Unit.

Methods: From July 2018 to date, consecutive patients who attend the Cough Clinic were asked about the presence of headache with and without cough. The eligibility of the participants was determined via telephone interview. Neurological/ neuro-otological examination; and a modified Valsalva test were completed, MRI with cranio-cervical views. Results were tabulated and statistical analysis included χ^2 and Pearson correlation coefficient.

Results: At interim analysis, 245 patients completed the screening. Of these, 167 (68%) suffered from headache, of which 78 (47%) reported headache with cough. Fifty patients have completed the telephone interview (61% women, mean age of 45 ± 4 years) and 35 (70%) met the diagnostic criteria of cough headache according to the International Classification of Headache Disorders (ICHD-3). The remaining patients met the criteria for migraine. Among patients with cough headache, 90% had a previous history of migraine. Median time since headache onset was 6 years (range 3–11 years). The average attack duration was 1 hour, the most frequent location was occipital and cough was the only trigger in 65%. Associated symptoms included either vertigo, described as “spinning, whirling or being on a boat” (20%) or “dizziness”, described as “lightheadedness, giddiness or floating” (32%) for seconds in 52% of patients. The modified Valsalva test was positive in 37% but did not distinguish between primary and secondary headaches. The respiratory diagnosis: cough hypersensitivity syndrome was significantly related to the diagnosis of cough headache ($\chi^2 = 5.2$ $p = 0.02$). Four secondary headaches (8%) were identified: Chiari malformation, tuberculosis, fungal sinus infection and headache attributed to low CSF pressure.

Conclusion: In the presence of chronic cough, primary cough headache is more frequent in women with a history of migraine and could be related to cough hypersensitivity

syndrome. Secondary cough headache was not as prevalent as in previous series. The modified Valsalva test was not capable of distinguishing primary from secondary headaches.

Disclosure of Interests: Stephanie Becker reports no conflicts of interest.

David Moreno-Ajona reports no conflicts of interest.

Jan Hoffmann has received honoraria for consulting and/or serving on advisory boards for Allergan, Autonomic Technologies Inc. (ATI), Atheneum Partners, Chordate Medical AB, Eli Lilly, Hormosan Pharma, Novartis and Teva. He has received honoraria for speaking from Allergan, Autonomic Technologies Inc. (ATI), Chordate Medical AB, Novartis and Teva. JH also received financial compensation for serving as an Associate Editor, reviewing and/or writing manuscripts from Cephalalgia (Sage Publishing), Journal of Oral & Facial Pain and Headache (Quintessence Publishing) and Oxford University Press.

Surinder Birring reports no conflicts of interest.

Peter J Goadsby reports, over the last 36 months, grants and personal fees from Amgen and Eli-Lilly and Company, and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Biohaven Pharmaceuticals Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Impel Neuropharma, MundiPharma, Novartis, Teva Pharmaceuticals, Trigemina Inc., WL Gore, and personal fees from MedicoLegal work, Massachusetts Medical Society, Up-to-Date, Oxford University Press, and Wolters Kluwer; and a patent magnetic stimulation for headache assigned to eNeura without fee.

IHC-LB-090

Comparison of clinical profile of patients having chronic migraine with patients having new daily persistent headache of chronic migraine subtype

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Objective: To compare the clinical profile of patients having chronic migraine (CM) with patients having new daily persistent headache of chronic migraine type (NDPH CM)

Methods: An audit was conducted of the clinical letters of patients presenting with a phenotype of new daily persistent headache of chronic migraine type (NDPH-CM) and chronic migraine (CM) from a tertiary referral centre from 2014 to 2019.

Results: Patients with NDPH CM ($n=76$) and CM ($n=257$) were identified.

The age at first headache was lower in the CM group with respect to the NDPH-CM group (median and IQR: 14, 10–20 vs 19, 14–34; $p < 0.001$)

A total of 71% and 83% of the NDPH-CM and CM cohorts, respectively, were female ($p = 0.022$)

The total number of associated symptoms was greater in the CM group with respect to the NDPH-CM group (median and IQR: 6, 5–8 vs 5, 4–7; $p < 0.001$)

The total number of postdromal symptoms (median and IQR: 2, 1–3 vs 1, 0–2; $p = 0.008$) was greater in the CM group compared to the NDPH-CM group.

The total number of premonitory symptoms (median and IQR: 3, 2–5 vs 3, 2–4; $p = 0.182$) and cranial autonomic symptoms (median and IQR: 2, 1–4 vs 2, 0–4; $p = 0.798$) were not different in the 2 groups.

The total number of preventives used was also greater in the NDPH CM group compared to the CM group (median and IQR: 7.5–10 vs 6, 4–9; $p = 0.01$). Medication overuse was present in 33% of NDPH CM group and 51% of the CM subtype ($p = 0.006$)

Family history of headache was greater in the CM group compared to the NDPH-CM group (82% vs 53%) ($p < 0.001$).

Conclusion: There are significant differences between CM and NDPH-CM with regards to: age of headache onset, gender distribution, family history of headache, total number of associated symptoms, total number of postdromal symptoms and concomitant medication overuse.

Disclosure of Interests: The authors do not have any conflicts of interest for the above study.

IHC-LB-091

Clinical audit of patients with new daily persistent headache (NDPH)

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Objective: To analyse the clinical symptomatology, therapeutic profile and outcome of a cohort of patients with a new daily persistent headache (NDPH) phenotype.

Methods: An audit of patients who presented with a phenotype of new daily persistent headache (NDPH) from a tertiary referral centre between 2014 and 2019 was conducted using clinic documentation.

Results: Of patients identified ($n=133$), the chronic migraine (CM) subtype was identified in 87% ($n=115$) and the featureless subtype in 2% ($n=2$). Of the remaining patients, eight (6%) were under investigation for hemispheric continua, five (4%) were suspected to have low CSF pressure, one (0.7%) was found to have chronic paroxysmal hemispheric migraine and one (0.7%) had idiopathic intracranial hypertension.

The median age of onset of NDPH was 24 years with an interquartile range (IQR) of 14–38. The median time to diagnosis was 3 (IQR: 1–5) years. A past history of migraine was present in 45% of the cohort. A preceding event just before NDPH onset was found in 49% of patients. Within the CM subtype, 27% of patients had aura. The median number of cranial autonomic symptoms (CAS) was 1 (IQR: 0–3). The median number of premonitory symptoms among patients with the CM subtype was 2 (IQR: 1–4). The median number of postdromal symptoms within the CM subtype was 1 (IQR: 0–2).

Medication overuse was present in 33% of the cohort. The median number of preventives used were 5 (IQR: 3–8). At follow-up, four (3%) had gone into remission.

Conclusion: While the NDPH phenotype can be variable, the majority of patients have a CM subtype. They commonly present associated migrainous, cranial autonomic, premonitory and postdromal symptoms. A significant percentage of NDPH patients are refractory to treatment, requiring multiple preventive medications.

Disclosure of Interests: The authors do not have any conflicts of interest for the above study.

IHC-LB-045

Headache secondary to corticosteroid withdrawal: a case report

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Objective: Headache attributed to increased cerebrospinal fluid pressure (ICP) is a syndrome characterized by an elevation of intracranial pressure without hydrocephalus, with normal cerebrospinal fluid (CSF) composition and no alterations in the brain parenchyma.

Most of these cases are considered idiopathic, several possible etiologies have arisen. ICP secondary to corticosteroid withdrawal is poorly understood and rarely reported in the literature while observed primarily on pediatric population.

Methods: The following case presents an adult presentation of this unusual trigger of ICP.

Results: A 28-year-old male patient with a history of Crohn's disease treated with stable doses of azathioprine, mesalazine and meprednisone (60 mg/daily) for over 6 months. No personal history of headache. In October 2018, corticosteroid withdrawal was started. At week four (10 mg/daily), patient referred right pulsatile hemicranial headaches, intensity 9/10, associated to photophobia and phonophobia, increasing with Valsalva maneuvers, did not worsen with dorsal decubitus nor awaken the patient at night. Initially improved with acetaminophen; but after corticoid suspension, became persistent and increased intensity. Brain and orbital magnetic resonance imaging (MRI): no parenchymal alterations, intrasellar arachnoidocele and increased right optic nerve sheath liquid and tortuosity. Intracranial MRI angiography: slight tortuosity on the transverse sinuses. Ophthalmologic evaluation: mild right hyperemic papilledema, confirmed by optical coherence tomography. Lumbar puncture (LP): opening pressure 260 mm, CSF analysis and cultures normal.

After 1 week of corticosteroid therapy reintroduction (20 mg/daily), with a more gradual tapering, headache was completely resolved and remained asymptomatic 6 months after complete withdrawal. The patient was interpreted as a 7.1.2 headache attributed to intracranial hypertension secondary to toxic cause, according to the IHC-3.

Conclusion: Our case shows an unusual presentation of ICP syndrome with unilateral symptoms associated with withdrawal of corticosteroids. Performance of an LP and funduscopy should be considered on patients presenting a headache of recent onset while descending corticosteroid treatment.

Disclosure of Interest: None Declared.

Other Secondary Headache Disorders

IHC-LB-092

Systematic review and meta-analysis of efficacy, performance time, and accidental vascular puncture with ultrasound-guided versus fluoroscopy and CT-guided cervical medial branch blocks

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Abstract number: IHC-LB-092

Table 1. Trials Pertaining to Ultrasound-Guided Cervical Facet/Medial Branch Blocks and Radiofrequency Ablation

Authors (Yr)	Study Type	Jadad Score	Blinded Assessment/ Sample Size Justification	Description	Number of Patients/Groups	Primary Outcome	Main Findings
Eichenberger et al. (2006)	RCT	5	Y/N	Volunteers underwent an USG TONB with LA on one side and saline in the other using an OOP approach.	11/ crossover trial	Presence of cutaneous hypoesthesia in the distribution of the TON, needle position relative to fluoroscopic target point	Needle was correctly placed over the C2/C3 joint in all but one case, similarly cutaneous hypoesthesia was seen in all but one of the LA blocks.
Siegenthaler et al. 2011	CH	NA	N/Y	Examined the effect of a shortened fluoroscopic radiofrequency neurotomy procedure (fewer lesions),	15/1	Reduction in pre-procedural pain intensity.	A pain reduction of at least 80% was observed in 14 of the subjects at 15 days. Median duration of

(continued)

Abstract number: IHC-LB-092

Table 1. Continued.

Authors (Yr)	Study Type	Jadad Score	Blinded Assessment/ Sample Size Justification	Description	Number of Patients/Groups	Primary Outcome	Main Findings
Siegenthaler et al. 2012	CH	NA	Y/Y	using of ultrasound assistance to guide cannula placement Volunteers underwent USG needle placements with contrast injection simulating CMBB and TONB using an OOP approach.	60/1	Needle tip position and contrast distribution relative to conventional fluoroscopic target points	50% pain relief was 44 weeks. Overall accuracy was 77% for needle placement and 84% for contrast distribution. Results varied by level and was lowest at C7.
Finlayson et al. 2012	CH	NA	Y/N	Two phase study examining the accuracy of USG TONB and CMBB (C3-C6) using an IP approach in patients with neck pain.	53/ 1	Needle tip position and contrast distribution as assessed by post-procedural X-rays.	Phase 1:80.9% of needles placed correctly; phase 2: contrast covered appropriate area in 94.5% of injections.
Finlayson et al. 2013	RCT	3	N/Y	Patients with suspected cervicogenic headaches underwent a TONB using either fluoroscopy or an IP USG technique	40/ 2	Performance time was the primary outcome and secondary outcomes included success rates as well as sensory distribution of the blocks.	Ultrasound guidance was associated with a significantly shorter performance time (212.8 vs 396.5 seconds; P = 0.000) and fewer needle passes (2 vs 6; P = 0.000). Both imaging modalities resulted in similar success rates (95% vs 100%).
Obernauer et al. 2013	RCT	3	N/N	Patients undergoing cervical intraarticular facet blocks were assigned to CT guidance or USG using an IP approach	40/2	Primary outcomes were performance time and accuracy (as assessed by CT control). Secondary outcomes include pain reduction at 30 min and 1 month.	USG was associated with 100% accuracy and significant reduction in performance times (04:46 versus 11:12 min p < 0.05), as well as radiation dose. Pain relief was similar in both groups.
Finlayson et al. 2014	CH	NA	N/N	Patients with cervical pain underwent an USG CMBB at the C5 and C6 levels using a bi-planar (IP) technique.	40/1	Contrast distribution, as assessed by a blinded observer on anteroposterior and lateral x-ray views.	Appropriate contrast distribution was seen in 100% and 97.5% of C5 and C6 levels respectively
Finlayson et al. 2015	RCT	3	N/Y	Patients undergoing a C7 CMBB were randomized to either ultrasound or fluoroscopic guidance.	50/2	Performance time was the primary outcome and secondary outcomes included success rates, number of needle passes, as well as pain relief	US guidance was associated with a shorter performance time (233.6 vs 390.6 seconds; P < 0.001) and fewer needle passes. Both pain relief and success rates (92% > 96%) were

(continued)

Abstract number: IHC-LB-092**Table 1.** Continued.

Authors (Yr)	Study Type	Jadad Score	Blinded Assessment/ Sample Size Justification	Description	Number of Patients/Groups	Primary Outcome	Main Findings
Park et al. 2017	CH	NA	N/N	Retrospective chart review of patients with neck pain who had undergone CMBB with either fluoroscopic or USG (IP).	68 (USG) 58 (Fluoro)	Neck Disability Index and pain scores at 1,3 and 6 months after injection. Secondary measures included performance time, needle passes and complication.	similar between groups. USG was associated with a shorter performance time and fewer needle passes. Pain relief and functional improvement were similar for both groups. No major complications were noted.

Randomized control trial (RCT); cohort study (CH); third occipital nerve block (TONB); cervical medial branch block (CMBB); ultrasound-guided (USG); in-plane (IP); out-of-plane (OOP);

Objective: Cervical medial branch blocks (CMBB) are useful in differentiating of facetogenic pain from other sources of cervicogenic headaches. The purpose of this systematic review and meta-analysis is to compare the efficacy, performance time and pain reduction with ultrasound-guided (US-guided) CMBB vs. other used methods such as fluoroscopy and CT guidance. Additionally, the study assesses some complications such as vascular puncture, intraarticular spread, intra-foraminal and other aberrant spreads of the local anesthetic.

Methods: The protocol of this systematic review and meta-analysis was performed following the PRISMA recommendation data.

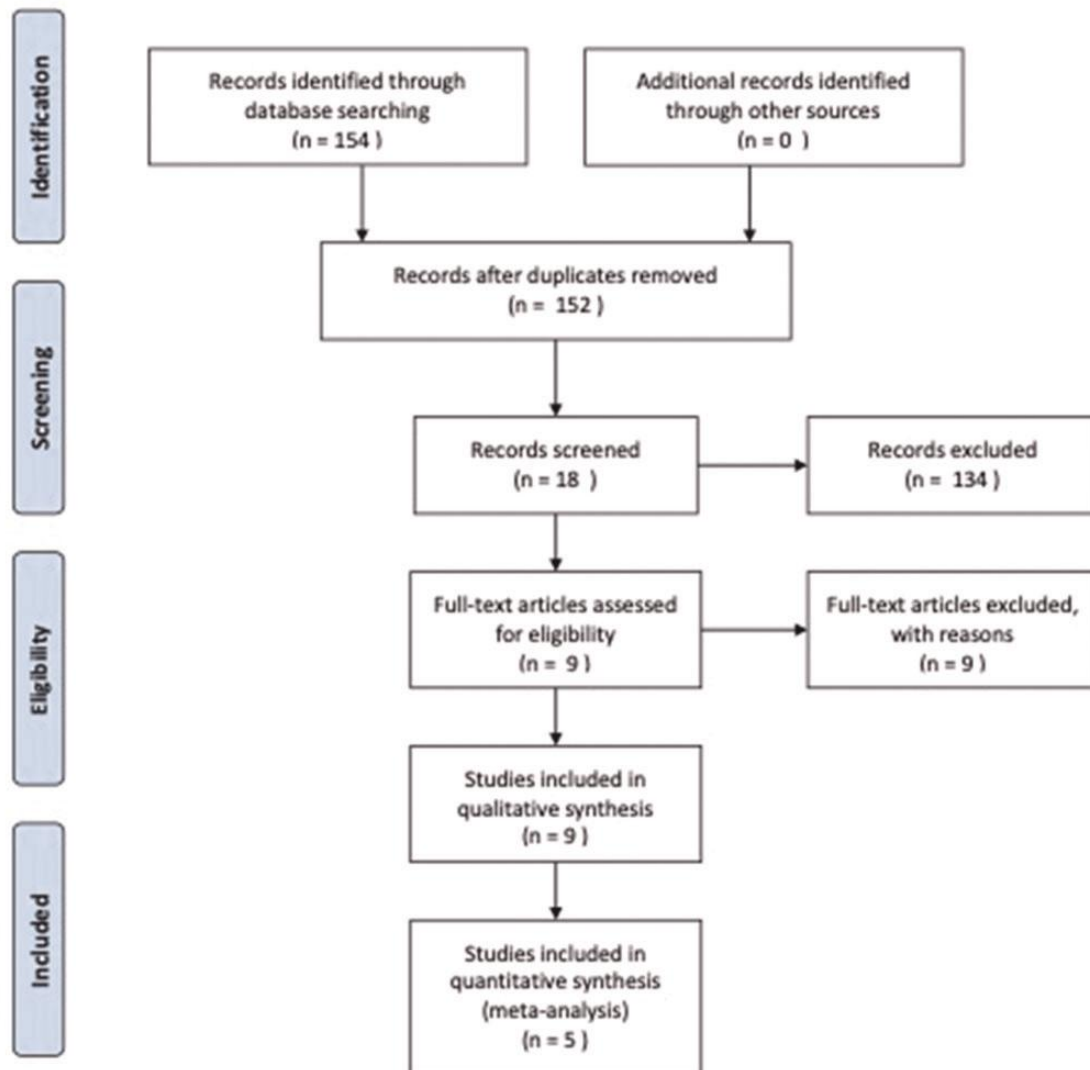
The following will be discussed in the presentation: protocol and registration, inclusion criteria, exclusion criteria, information sources and searches, study selection, data collection process, risk of bias in individual studies.

Statistical analysis was done using Comprehensive Meta Analysis© (CMA©) version 2.2.046 (Biostat© Englewood, NJ). Comparison of binary outcomes was done by estimation of the odds ratios (OR) with their 95% CI. Continuous outcomes were compared by calculation of the standardized mean differences (SMD) and their 95% CI. Estimates from included studies were pooled using the DerSimonian and Laird Random-Effects Method (REM) or the Mantel-Haenszel Fixed-Effects Method (FEM) depending on the presence or absence of significant heterogeneity, respectively.

Results: The results demonstrate that US-guided CMBB is a reliable alternative to the fluoroscopy and CT – guided CMBB, with demonstrated advantages in the efficacy, early identification, and prevention of adverse effects. The meta-analysis and discussion will be unfolded in the presentation.

Conclusion: This study demonstrated benefits of US-guided CMBB compared to fluoroscopy and CT Scan.

Disclosure of Interests: None. The study results were not available until 25/05/2019.



Abstract number: IHC-LB-092

Post-Traumatic Headache

IHC-LB-046

Non-Steroidal Anti-Inflammatory Drug Use and Post Traumatic Headache in Adults following a Concussion

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Objective: Posttraumatic headache (PTH) is common after concussion and non-steroidal anti-inflammatory drugs (NSAIDs) are routinely used for symptom relief. This study investigates the frequency and severity of PTH in concussed adults treated with NSAIDs during recovery and those who were not.

Methods: Concussed adults (n = 70) aged 19 to 78 with no history of treatment for PTH were evaluated within 30 days of injury at clinics in the North Texas Concussion Registry. Demographics, headache symptom severity (0-6), and NSAID use were recorded at initial evaluation and three-month follow-up. Chi square analysis and 2 (time) by 2 (NSAID use) repeated measures ANOVA with sex as a covariate were conducted to determine frequency and severity of headaches between PTH groups

treated with NSAIDs and those that were not treated with medications at initial evaluation and follow-up.

Results: There was no difference in headache frequency at initial evaluation and three-month follow-up between subjects who used NSAIDs ($n=42$) and those who did not ($n=30$), ($\chi=0.26$, $p=0.61$) regardless of sex. Subjects who used NSAIDs reported higher levels of headache symptoms initially than those who did not use NSAIDs, $F(1, 67)=5.29$, $p=0.03$. There was no interaction between time and NSAID use regarding headache severity, $F(1, 67)=1.83$, $p=0.18$. There was also no interaction between time and gender regarding headache severity, $F(1, 67)=3.64$, $p=0.06$. There was a main effect over time in reduction of headache severity, $F(1, 67)=54.51$, $p<0.001$. Differences in headache severity between the sexes was non-significant, $F(1, 67)=3.46$, $p=0.07$.

Conclusion: Regardless of sex, in this population of acutely concussed adults headache frequency was unchanged three months post-injury for who used NSAIDs compared to those who did not use any medication. Headache severity was initially higher for those who used NSAIDs, but not significantly so three months post-injury. Routine use of NSAIDs following a concussion may act to reduce symptoms but not frequency of headache during recovery in adults.

Disclosure of Interests: None.

Psychological and Behavioural Factors and Management

IHC-LB-047

Visual feedback to modulate pain perception in chronic migraine patients: a pilot study

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Objective: To investigate whether the exposure to different visual stimulating conditions may modulate pain perception assessed by the visual analogue scale (VAS) in chronic migraine patients.

Methods: To this aim we enrolled 10 female chronic migraine patients (mean age: 44.7 ± 12.4) recruited at

the IRCCS C. Mondino Foundation in the study. Using a visual feedback system, subjects were randomly exposed to 4 different types of facial expression: positive (happy/relaxed facial expression), neutral (neutral facial expression), negative (sad/distorted face) and control (white screen). At baseline, patients were evaluated on personal, clinical, psychological (Positive and Negative Affect Schedule, Hospital Anxiety and Depression Scale) variables, level of pain (VAS) and body image perception (Body Image Questionnaire). Subsequently, they were exposed to a 1x4 within-subject study design where they had to observe the different visual stimuli presented 3 times in a randomized order (each condition lasted 40 seconds). After the observation of each visual condition, the level of pain was assessed using the VAS.

Results: A repeated measure analyse (mixed effects model test) and the following multiple comparisons by using the Scheffe test showed a significant difference in pain ratings between the positive (20.5 ± 25.0) and the negative (36.2 ± 24.9) facial expressions ($z=-4.04$, $p=0.001$), and the positive facial expression (20.5 ± 25.0) and the white screen (35.3 ± 28.9) control condition ($z=3.82$, $p=0.002$).

Conclusion: Our results show that a positive visual feedback is a stimulus strong enough to modulate pain perception via the mediation of empathy mechanisms for positive emotions. Further, our study paves the way to the integration of conventional behavioral therapy with new cognitive behavioral training based on the adoption of visual feedback to further control pain perception in chronic migraine patients.

Disclosure of Interests: no conflict of interests.

IHC-LB-093

Systematic review of patient education and cognitively behavioral treatment for adults with migraine

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Objective: To evaluate the content and effectiveness of patient education and cognitive behavioural therapy for adults with migraine.

Methods: Predefined search using key terms of information sources including MEDLINE, EMBASE, PsycINFO and CINAHL databases. RCTs of the last 10 years (to April

2019) were included. Two reviewers independently searched and evaluated publications. The methodological quality of studies was assessed using the Cochrane Rob 2 tool.

Results: Across $n = 11$ studies, 1397 participants were recruited (84.2% females). Characteristics of education comprise explanations about links between thoughts and feelings, behaviour and relaxation techniques or aiming at improvements in life-style and stress coping, advice regarding diet, physical activity, or dealing with the pathophysiology of migraine, effective acute or prophylactic drug use. Professionals performing education were psychologists. The duration and frequency of education varied (three times for 1 h up to eight times for 2 h plus a retreat day). Different educational formats were used (workbooks, questionnaires, audiotapes, face-to-face sessions, online Behavioural Therapy, clinical visits, telephone contacts). Education was often enclosed in adjunct treatments (multi-modal therapy, prophylactic medical therapy, endurance training, relaxation techniques). Outcome measures related to pain (headache frequency, attack frequency, medication use (diary), function and disability (MIDAS; HIT-6), and psychosocial issues (e.g. HADS-anxiety, PHQ-9, Perceived stress scale-10). Due to strong heterogeneity the data could not be pooled for a meta-analysis.

Conclusion: Most of the studies with a good quality support a positive effect concerning the reduction of migraine frequency and improved quality of life. Behavioural approaches should be implemented in every treatment guideline. Besides psychologists also physical therapists specialized in the treatment of chronic pain should conduct the education. More randomized controlled trials are needed to evaluate the content and extend of education.

Disclosure of Interests: The authors declare no conflicts of interest.

IHC-LB-094

Could the migraine phase be predicted from the use of mobile phones? Social sensing in migraine

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Objective: The use of smart phones is closely related to human interaction. Thus, individual mobile activity could be used to predict migraine attacks and to study some cognitive and social changes. These changes may help us to define the different migraine phases.

To study if there is a correlation between migraine attacks and the social and cognitive activity and use of a smartphone.

Methods: A prospective observational study. We included patients with episodic (EM) and chronic migraine (CM) during 3 months. A mobile app monitored the daily use of the smartphone and migraine attacks. Moreover, we collected both sociodemographic and clinical data. We performed a comparative analysis between the migraine days (M) and 24 hours before the attack (24B), 24 and 48 hours after (24A and 48A) and headache-free days (F).

Results: 32 patients were recruited: 68.8% had EM and 31.2% had CM. The patients registered 764 entries: 50.5% headache-free and 25.0% with headache, 8.7% 24B, 9.2% 24A and 6.4% 48A. CM patients use more time the mobile phone and the social apps than EM ($p = 0.05$). The time of the attacks is significantly different between diagnostics (CM: 23.5% in the early morning, EM: 38.1% in the morning, $p = 0.01$) and CM have a longer attack duration ($p = 0.038$). A reduction of the use of the mobile phone has been reported during migraine days ($p = 0.01$) with respect to other days (F, 24B, 24A and 48A), but the use of social apps was significantly increased in 24 hours before the attack ($p = 0.05$).

Conclusion: The use of the smartphone depends on the migraine phase and the diagnostic: lower use in migraine days and EM and increase of use of social media before the attack. New technologies allow us to predict migraine attacks from changes in the social behavior and cognitive activity because these changes according to the migraine phase. This could be correlated with changes in brain activity.

Disclosure of Interests: PP-R has received honoraria as a consultant and speaker for: Allergan, Almirall, Chiesi, Eli Lilly, Novartis and Teva. AA has received honoraria as a speaker for Allergan. The authors declare no conflicts of interest to this work.

Tension-type Headache

IHC-LB-048

Excessive daytime sleepiness in tension-type headache: a population study

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Objective: Excessive daytime sleepiness (EDS) is a common sleep-related complaint in the general population and has been reported to be associated with headache. Tension-type headache (TTH) is the most commonly encountered headache and accounts for a significant amount of disease burden. A previous study reported a high prevalence of EDS in migraineurs and an association between EDS and migraine exacerbation. However, the association between EDS and TTH remains to be determined. In this study, we evaluated the prevalence of EDS in TTH individuals and examined the impact of EDS on the clinical presentation of TTH.

Methods: We used data from the Korean Headache-Sleep Study, a national survey that sought to identify headache and sleep characteristics in Korean adults. Participants with an Epworth sleepiness scale score greater or equal to 11 were considered as having EDS.

Results: Of the 2695 participants enrolled, 570 (21.2%) and 313 (11.6%) had TTH and EDS, respectively. EDS was highly prevalent in individuals with chronic tension-type headache (CTTH) than in those with non-headache

(35.7% vs. 9.4%, $p < 0.001$). The prevalence of EDS in episodic tension-type headache (ETTH) individuals with a headache frequency < 1 per month (8.3%, $p = 0.511$) and ETTH individuals with a headache frequency of 1–14 per month (13.5%, $p = 0.054$) was not significantly different from that in non-headache individuals (9.4%). TTH participants with EDS had a higher headache frequency (4.3 ± 8.1 vs. 1.7 ± 4.2 , $p = 0.013$), more severe headache intensity (Visual Analogue Scale, 5.0 [3.0–6.0] vs. 4.0 [3.0–6.0], $p = 0.008$), a higher impact of headache (Headache Impact Test-6 score, 47.1 ± 7.3 vs. 43.5 ± 7.6 , $p < 0.001$), and a higher prevalence of depression (12.7% vs. 3.2%, $p < 0.001$) compared to TTH participants without EDS.

Conclusion: Consequently, CTTH is associated with higher EDS prevalence compared to ETTH and non-headache. Moreover, TTH with EDS had more severe TTH symptoms compared to TTH without EDS.

Disclosure of Interests: The authors declare that they have no conflicting interests.

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