Abstracts

17th Biennial Migraine Trust International Symposium

Abstract Book


www.mtis2018.org
Searching this Abstract Book

How to search this Abstract Book

Click the search button below:

Enter your term in the search box. You can enter full or partial text for a speaker’s name, abstract number, category or topic. Clicking the search button will then list all successful matches for the search term, and clicking on any of the results in the list will take you immediately to the appropriate page.

The search window can be shown at any time by selecting “Edit > Search” or “Edit > Advanced Search” (depending on your software version) from the top file menu, or using the following shortcut keys:

“Shift - Control - F”
on a Windows operating system

“Shift - Command - F”
on an Apple operating system
Contents

How to search this Abstract Book ............................................................................................................................... 2
List of reviewers ............................................................................................................................................................ 4

Abstracts ......................................................................................................................................................................... 5

Epidemiology, comorbidity, outcomes and classification including big data ......................................................... 6
Experimental research ............................................................................................................................................... 36
General aspects of headache care .......................................................................................................................... 45
Genetics and biomarkers of headache disorders .................................................................................................... 66
Headache pathophysiology: basic science ................................................................................................................ 75
Headache pathophysiology: clinical .......................................................................................................................... 87
Migraine – acute therapy ......................................................................................................................................... 103
Migraine – preventive therapy .................................................................................................................................. 121
Other primary headaches ........................................................................................................................................ 221
Paediatric headache .................................................................................................................................................. 227
Psychological and behaviour factors ........................................................................................................................ 230
Secondary headaches ............................................................................................................................................... 237
TACs ................................................................................................................................................................................. 251

Author index ............................................................................................................................................................... 257
List of Reviewers

The Organising Committee of MTIS 2018 wish to thank the following people for reviewing the abstracts:

<table>
<thead>
<tr>
<th>Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afridi, S</td>
</tr>
<tr>
<td>Ahmed, F</td>
</tr>
<tr>
<td>Ashina, M</td>
</tr>
<tr>
<td>Charles, A</td>
</tr>
<tr>
<td>Dodick, D</td>
</tr>
<tr>
<td>Edvinsson, L</td>
</tr>
<tr>
<td>Goadsby, P</td>
</tr>
<tr>
<td>Holland, P</td>
</tr>
<tr>
<td>Kernick, D</td>
</tr>
<tr>
<td>Lipton, R</td>
</tr>
<tr>
<td>May, A</td>
</tr>
<tr>
<td>Paemeleire, K</td>
</tr>
<tr>
<td>Purdy, A</td>
</tr>
<tr>
<td>Silberstein, S</td>
</tr>
<tr>
<td>Tassorelli, C</td>
</tr>
<tr>
<td>Weatherall, M</td>
</tr>
</tbody>
</table>
Abstracts
**Abstracts**

**Epidemiology, comorbidity, outcomes and classification including big data**

**MTIS2018-001**

**PRAGMATIC CLINICAL TRIALS IN HEADACHE AND MIGRAINE RESEARCH: A SCOPING REVIEW**

S. Tanveer*
Johns Hopkins School of Public Health, Baltimore, United States

**Introduction:** This scoping review will evaluate the role of pragmatic clinical trials in headache and migraine treatment.

**Objectives:** The objective of this study was to conduct a scoping review\(^1\) on published research articles that utilized pragmatic clinical trial\(^2\) designs in order to identify gaps in the current headache and migraine clinical trial methodology.

**Methods:** A review of all published literature between the date ranges of 1 January 1990 to 30 March 2018 was conducted according to pre-determined inclusion and exclusion criteria. The following databases were included in the search strategy: PubMed, Web of Science, and SCOPUS. The author also hand-searched for relevant articles. We did not include articles that did not have a methods section (i.e., letters, editorials, opinion piece, and protocols). We also excluded retracted articles, full text articles in languages other than English, and animal studies.

**Results:** The review search strategy returned 33 results. Upon abstract and full text review, only five\(^3-7\) articles were determined to be relevant to the scope of this review. Articles that utilized a pragmatic clinical trial design ranged from manual therapy for headache, pharmacological treatment for acute migraine, care strategies for migraine, and chiropractic care for headaches.

**Conclusion:** Scoping reviews are a useful knowledge synthesis tool that can addresses exploratory questions and gaps in the literature. This review suggests the need for more pragmatic and patient-centered clinical trials in the field of headache and migraine. Moreover, further work is needed to elucidate the number of randomized control trials that are true pragmatic trials but are not labeled as such in the literature.

**References:**
Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-002

PREVALENCE OF PERIODONTITIS IN PATIENTS WITH MIGRAINE: RESULTS FROM A CROSS-SECTIONAL SURVEY IN SPAIN.


1Periodontology, Periodontology Unit, UCL Eastman Dental Institute and Hospital, University College London and Medical-Surgical Dentistry Research Group, Health Research Institute of Santiago de Compostela, London and Santiago de Compostela, 2Neurology, Headache Unit, Neurology Department, Vall d’Hebron University Hospital and 4Headache Research Group, Vall d’Hebron Institute of Research (VHIR), Universitat Autònoma de Barcelona, Barcelona, Spain, 3Periodontology, Periodontology Unit, UCL Eastman Dental Institute and Hospital, University College London, London, United Kingdom, 4Neurology, Hospital Clínico Universitario, Universidad Católica de Valencia, Valencia, 5Neurology, Hospital Universitario Basurto, Universidad del País Vasco/Euskal Herriko Unibertsitatea EHU/UPV, Bilbao, 6Neurology, Hospital Universitario Miguel Servet, Zaragoza, 7Neurology, Hospital Clínico Universitario de Valladolid, Valladolid, 8Neurology, Hospital de la Santa Creu i Sant Pau, Barcelona, 9Neurology, Hospital Universitario Virgen del Rocío, Sevilla, 10Neurology, Hospital Universitario La Princesa, 11Neurology, Hospital Universitario de Fuenlabrada, Madrid, 12Neurology, Hospital Clínico Universitario Lozano Blesa, Zaragoza, 13Neurology, Headache Unit, Hospital Clínico San Carlos, San Carlos Institute for Health Research (IdISSC), Complutense University of Madrid, Madrid, 14Periodontology, Periodontology Unit, Faculty of Odontology, University of Santiago de Compostela, Medical-Surgical Dentistry Research Group, Health Research Institute of Santiago de Compostela, 15Neurology, Headache Unit, Hospital Clínico Universitario, University of Santiago de Compostela, Clinical Neurosciences Research Laboratory, Health Research Institute of Santiago de Compostela, Santiago de Compostela, Spain

Introduction: Migraine and periodontitis (PD) are common disorders worldwide. Nevertheless, scarce information exists on the prevalence of PD in a large sample of migraineurs and if there is or not any difference between the two subtypes of migraine: episodic migraine (EM) and chronic migraine (CM).

Objectives: To investigate the prevalence of PD in patients diagnosed with migraine.

Methods: A cross-sectional survey was conducted including consecutive migraineurs attending Headache Units from 12 Spanish hospitals. PD diagnosis was determined administering a validated self-reported questionnaire. Socio-demographic and medical information was collected.

Results: 651 migraineurs were included. Overall, 327 migraineurs presented self-reported PD (50.2%). Migraineurs with PD were significantly older and presented a previous history of fibromyalgia, stress, anxiety, depression, and allodynia (all P<0.001). In addition, these patients took more topiramate as a preventive treatment (P=0.008) and simple analgesics as an acute treatment (P<0.001) than migraineurs without PD as well as performed less physical activity and had a lower educational level (both P<0.001). Self-reported PD was significantly more prevalent in CM patients than in EM subjects (53.9% vs. 44.6%, P=0.019).

Conclusion: PD prevalence was higher in migraineurs than the general population in Spain. Furthermore, PD was more conspicuous in CM.

This study was partially supported by grants from the Spanish Ministry of Economy and Competitiveness – Institute of Health Carlos III (PI15/01578).
LEPTIN AS A POTENTIAL BIOMARKER IN THE RELATIONSHIP BETWEEN PERIODONTITIS AND CHRONIC MIGRAINE.

Y. Leira 1*, P. Ameijeira 2, C. Domínguez 3, F. D’Aiuto 4, J. Blanco 5, R. Leira 6

1Periodontology, Periodontology Unit, UCL Eastman Dental Institute and Hospital, University College London and Medical-Surgical Dentistry Research Group, Health Research Institute of Santiago de Compostela, London and Santiago de Compostela, 2Periodontology, Periodontology Unit, Faculty of Medicine and Odontology, University of Santiago de Compostela, 3Neurology, Headache Unit, Hospital Clínico Universitario, University of Santiago de Compostela, Santiago de Compostela, Spain, 4Periodontology, Periodontology Unit, UCL Eastman Dental Institute and Hospital, University College London, London, United Kingdom, 5Periodontology, Periodontology Unit, Faculty of Odontology, University of Santiago de Compostela, Medical-Surgical Dentistry Research Group, Health Research Institute of Santiago de Compostela, 6Neurology, Headache Unit, Hospital Clínico Universitario, University of Santiago de Compostela, Clinical Neurosciences Research Laboratory, Health Research Institute of Santiago de Compostela, Santiago de Compostela, Spain

Introduction: Recently, an association was found between periodontitis (PD) and chronic migraine (CM). However, the exact mechanisms underlying this relationship remain unclear. Leptin, an adipocyte-derived hormone/cytokine, which is expressed during inflammation and infection seems to be overexpressed in PD and involved in migraine chronification.

Objectives: To evaluate the contribution of PD to serum leptin levels in CM.

Methods: In this case-control study, we included 150 subjects divided into healthy controls (n=58) and CM patients (n=92). Demographic, neurological, clinical data as well as full-mouth periodontal records were obtained. Serum leptin levels were measured by ELISA technique.

Results: Mean serum leptin levels were significantly higher in patients with CM in comparison to controls (57.6% vs. 36.2%, p=0.01 and 16.4 vs. 7.2 ng/mL, p<0.0001, respectively). Patients from the CM group who had PD showed significantly higher leptin concentrations than CM patients without PD (19.8 vs. 11.8 ng/mL, p<0.0001). Multivariable linear regression analysis showed that PD was an independent contributor to elevated leptin levels in CM patients (R²=0.270, p=0.013).

Conclusion: PD when present it contributes to elevated serum leptin levels, independently of other confounding factors. Therefore, it seems that CP via leptin could be involved in the process of migraine chronification. This study was partially supported by grants from the Spanish Ministry of Economy and Competitiveness – Institute of Health Carlos III (PI15/01578).
**Epidemiology, comorbidity, outcomes and classification including big data**

**MTIS2018-004**

**CHRONIC HEADACHE AMONG ADULT POPULATION OF MONGOLIA**

S. Enkhtuya 1,*, O. Luvsannorov 1, B. Tsenddorj 2, T. J. Steiner 3, 4

1Neurology, Mongolian National University of Medical Sciences, 2Neurology, Mungunguur hospital, Ulaanbaatar, Mongolia, 3Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway, 4Brain Sciences, Imperial College London, London, United Kingdom

**Introduction:** The headache is the third cause of years lost due to disability. Chronic headache defines the incidence of headache for >15 days per month on average for >3 months and fulfills the rest of the International Headache Society criteria. Medication-overuse headache is one of the most common chronic headache disorders and a public health problem. It is a condition characterized by chronic headache and overuse of different headache medications, and withdrawal of the overused medication is recognized as the treatment of choice.

**Objectives:** The aim of this study was to determine the 1-year prevalence and some risk factors of chronic headache in adult Mongolian population.

**Methods:** A cross-sectional, population-based survey consisting of semi-structured questionnaires was administered to randomly selected population aged 18–65 years, living in five geographically different regions of Mongolia using stratified multistage cluster sampling during the period from June to November 2017. The prevalence of chronic headache was calculated in the sample representing 2 million Mongolian adults.

**Results:** The surveyed totally 2043 participants; the one-year prevalence of all types of headache was 66.1%. The one-year prevalence of chronic headache was 11.2% (n=229), and 20.5% (n=47) of chronic headache declared having headache 30 days per month. About 70% (n=152) those with chronic headache also had medication overuse. Chronic tension-type headache and chronic migraine had one-year prevalence 1.3% (n=26) and 2.2% (n=45), respectively. The risk of chronic headache increased more than one fold and half when the participants were elderly participants, females, personal situation, low income and in those with low education. The most commonly overused medication was multi-therapy (acetylsalicylic acid, acetaminophen and caffeine) among the population.

**Conclusion:** We concluded that the prevalence of chronic headache in Mongolia is high compare to other countries worldwide. These patients require special attention and should be offered multidisciplinary medical support.

**References:**


THE ACTIVITY IMPAIRMENT IN MIGRAINE – DIARY (AIM-D): A NOVEL MIGRAINE-SPECIFIC PATIENT-REPORTED OUTCOME MEASURE TO ASSESS FUNCTIONING BASED ON ACTIVITY IMPAIRMENT IN EPISODIC AND CHRONIC MIGRAINE PATIENTS


1Endpoint Outcomes, Boston, 2Albert Einstein College of Medicine, Bronx, 3Neurology, Mayo Clinic, Arizona, Scottsdale, 4Independent Consultant, Orange County, 5Allergan plc, Irvine, United States

Introduction: Migraine is a chronic disease with debilitating symptoms that impact affected individuals through limitations in daily activities and social and leisure functioning. The impact of migraine on activity impairment has been highlighted in the literature and by clinical experts as an important and relevant aspect of the patient’s experience with the disease. To measure preventive treatment effects, including proximal effects on the performance of daily activities and physical impairment, it is essential that a content valid instrument be identified and/or developed.

Objectives: To develop a patient-reported outcome (PRO) measure to assess relevant impacts of migraine in episodic migraine (EM) and chronic migraine (CM) patients for use in clinical trials of migraine preventive treatments.

Methods: The AIM-D was developed using an iterative instrument development process involving (1) a review of the literature and relevant PRO measures; (2) interviews with clinicians; (3) mixed concept elicitation (CE) and cognitive interviews (CIs) in 20 EM and 20 CM patients; (4) concept confirmation and item generation based on qualitative analysis and input from clinical experts and PRO measurement experts; (5) three rounds of CIs (18 EM and 20 CM patients) of the draft AIM-D; and (6) finalization based on patient input from CIs. Qualitative analysis was conducted using ATLAS.ti.

Results: Qualitative analysis of the mixed CE/CIs, which confirmed conceptual saturation, helped to identify impacts that were relevant to migraine patients and to develop the draft AIM-D. The AIM-D includes items that assess usual household chores, errands, leisure activities at home, leisure or social activities outside the home, strenuous physical activities, walking, body movement, bending forward, and head movement. Response options for each item range from “not difficult at all” to “I could not do it at all” on a 6-point rating scale. The novel PRO measure was developed as an electronic handheld daily diary with headache and non-headache administration options to better elicit responses from migraine patients using a 24-hour recall period. Four additional items that assess difficulty in concentrating, difficulty in thinking clearly, activity level, and activity limitation were also developed and debriefed for future evaluation of the AIM-D. Changes were made after each of the first two rounds of CIs based on patient input and informed by the experts and research team. No changes were needed after the final round. Input from CIs confirmed that instructions, recall period, items, and response options were well understood by patients.

Conclusion: The AIM-D followed a comprehensive instrument development process in keeping with the US FDA 2009 guidance for PROs and measures functioning based on the performance of daily activities and physical impairment related to migraine. The results of this study provide evidence of the content validity of the AIM-D for use in EM and CM patients.

Disclosure of Interest: M. L. Cala Conflict with: Employee of Endpoint Outcomes, who was paid as a consultant by Allergan plc, C. Graham Conflict with: Employee of Endpoint Outcomes, who was paid as a consultant by Allergan plc, R. Lipton Conflict with: He receives research support from the NIH: 2P01 AG003949 (Program Director), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), 1RF1 AG057531 (Site PI), RF1 AG054548 (Investigator), 1RO1 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., N. Lyn Conflict with: Employee of Endpoint Outcomes, who was paid as a consultant by Allergan plc, D. Dodick Conflict with: Received compensation from serving on advisory boards and/or consulting within the past 5 years for: Allergan, Amgen, Novartis, Alder, Arteaus, Pfizer, Colucid, Merck, NuPath, Eli Lilly and Company, Autonomic Technologies, Ethicon J&J, Zogenix, Supernus, Labrys, Boston Scientific, Medtronic, St Jude, Bristol-Myers Squibb, Lundbeck, Impax, MAP, Electrocore, Tonix, Novartis, Teva, Alcobra, Zosano, ZP Opco, Insys, Ipsen, Acorda, eNeura, Charleston Laboratories, Gore, Biohaven, Biocentric, Magellan, Theranica, Xenon, Dr Reddy’s/Promius Pharma, Vedanta, Electrocore, CC Ford West Group, Foresight. Dr Dodick owns equity in Epien, GBS/Nocira, Second Opinion, Healint, and Theranica. Dr Dodick has received funding for travel, speaking, editorial activities, or royalty payments from IntraMed, SAGE Publishing, Sun Pharma, Allergan, Oxford University Press, American Academy of Neurology, American Headache Society, West Virginia University Foundation, Canadian Headache Society, Healthlogix, Universal Meeting Management, WebMD, UptoDate, Medscape/WebMD, Oregon Health Science Center, Albert Einstein University, University of Toronto, Starr Clinical, Decision Resources, Synergy, MedNet LLC, Peer View Institute for Medical Education, Medicom, Medlogix, Wolters Kluwer Health, Chameleon Communications, Academy for Continued Healthcare Learning, Haymarket Medical Education, Global Scientific Communications, Miller Medical Communications, MeetingLogiX, Wiley Blackwell. Dr Dodick, through his employer, has consulting use agreements with NeuroAssessment Systems and Myndshft. He holds board of director positions with King-Devick Technologies, and Epien Inc. He holds the following Patent 17189376.1-1466:vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis (no compensation), C. Burk Conflict with: Consultant for Allergan plc, J. Yu Conflict with: Employee of Allergan plc and receives stock or stock options, C. Evans Conflict with: Employee of Endpoint Outcomes, who was paid as a consultant by Allergan plc, H. Viswanathan Conflict with: Employed by Allergan plc, with ownership interest, including stock, stock options, patent or other intellectual property. Former employee of Amgen Inc. (until January 31, 2016), with ownership interest, including stock, stock options, patent or other intellectual property
**Epidemiology, comorbidity, outcomes and classification including big data**

**MTIS2018-006**

**EVALUATION OF THE 6-ITEM IDENTIFY CHRONIC MIGRAINE (ID-CM) SCREENER IN A LARGE MEDICAL GROUP**


1Neurology, Montefiore Medical Center, Bronx, 2Allergan plc, Irvine, 3Jefferson Headache Center, Philadelphia, 4Vedanta Research, Chapel Hill, 5DaVita Medical Group, El Segundo, 6Stanford University School of Medicine, Stanford, 7Independent Consultant, La Jolla, 8Albert Einstein College of Medicine, Bronx, United States

**Introduction:** Chronic migraine (CM) is associated with substantial economic burden and productivity loss, and is often underdiagnosed and undertreated. Survey-based studies have found that approximately 75-80% of persons meeting criteria for CM do not report having received an accurate diagnosis.

**Objectives:** The objective of this analysis was to assess the sensitivity and specificity of the 6-item Identify Chronic Migraine (ID-CM) screener.

**Methods:** Patients included in this analysis were enrolled in a large medical group and had at least 1 medical claim with an ICD-9/10 code for migraine in the 12-month pre-screening period. The 12-item ID-CM screener was then administered by e-mail, in person, or over the telephone to all patients enrolled into the study. The 12-item ID-CM screener is based primarily on 30-day patient recall and consists of questions that assess 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 is based on a subset of the 12-item version and consists only of the 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 physician trained to reliably administer the tool. The SSDI assesses HA symptoms, frequency, disability, and medication use based on 30-day and 90-day patient recall and served as the study gold standard for determining CM status. Migraine patients that were not administered the SSDI were excluded from this analysis. Additionally, migraine patients that had a medical claim with an ICD-9/10 code for CM in the 12-month pre-screening period or a migraine-related onabotulinumtoxinA claim in the 12-month pre-enrollment period were excluded.

**Results:** The analysis of the 6-item ID-CM screener included 109 patients with a migraine diagnosis who completed the ID-CM screener and the SSDI. The average (standard deviation) age of the patient sample was 48.7 (14.5) years and 91.7% of them 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 an accurate diagnosis of the disease. 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. The results support the real-world validity of the 6-item ID-CM screener and its use as a simple yet accurate tool to identify CM patients.

**Disclosure of Interest:** J. Pavlovic Conflict with: Received honoraria from Allergan and the American Headache Society, J. Yu Conflict with: Employee of Allergan plc and receives stock or stock options, S. Silberstein Conflict with: Consultant and/or advisory panel member, Dr. Stephen Silberstein receives honoraria from Alder Biopharmaceuticals; Allergan, Inc.; Amgen; Avanir Pharmaceuticals, Inc.; eNeura; ElectroCore Medical, LLC; Labrys Biologics; Medscape, LLC; Medtronic, Inc.; Neuralieve; NINDS; Pfizer, Inc.; and Teva Pharmaceuticals. His employer receives research support from Allergan, Inc.; Amgen; Cumberland Pharmaceuticals, Inc.; ElectroCore Medical, Inc.; Labrys Biologics; Eli Lilly and Company; Merz Pharmaceuticals; and Troy Healthcare, M. Reed Conflict with: Vedanta has received research funding from Allergan, Amgen, CoLucid, Dr. Reddy’s Laboratories, Endo Pharmaceuticals, GlaxoSmithKline, Merck & Co., Inc., NuPath, Novartis, and Ortho-McNeil, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study, S. Kawahara Conflict with: Served as a consultant and received consulting fees from DaVita medical Group, R. Cowan: None Declared, F. Dabbous: None Declared, K. Campbell Conflict with: Full-time employee of
17th Biennial Migraine Trust International Symposium
#MTIS2018

Abstracts

Allergan plc and owns stock in the company, R. Pulicharam Conflict with: Served as a consultant and received consulting fees from DaVita medical Group, H. Viswanathan Conflict with: Employed by Allergan plc, with ownership interest, including stock, stock options, patent or other intellectual property. Former employee of Amgen Inc. (until January 31, 2016), with ownership interest, including stock, stock options, patent or other intellectual property, R. Lipton Conflict with: He receives research support from the NIH: 2PO1 AG003949 (Program Director), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), 1RF1 AG057531 (Site PI), RF1 AG054548 (Investigator), 1RO1 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.
Abstracts

Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-007

A MULTICENTER, PROSPECTIVE, RANDOMIZED, OPEN-LABEL STUDY TO COMPARE ONABOTULINUMTOXINA AND TOPIRAMATE FOR HEADACHE PREVENTION IN ADULTS WITH CHRONIC MIGRAINE: PATIENT REPORTED FUNCTIONAL OUTCOMES FROM THE FORWARD STUDY

A. M. Blumenfeld 1,*, A. T. Patel 2, A. Manack Adams 3, J. F. Rothrock 4

1The Neurology Center, Headache Center of Southern California, Carlsbad, CA, 2Department of Rehabilitation Medicine, Kansas City Bone and Joint Clinic, Overland Park, KS, 3Global Medical Affairs, Allergan plc, Irvine, CA, 4Neurology, George Washington School of Medicine, Washington, DC, United States

Introduction: Patient-reported outcomes (PROs) can be important indicators of a migraine therapy’s real world effectiveness.

Objectives: To evaluate safety, tolerability, and PROs of onabotulinumtoxinA (onabotA) vs topiramate-immediate release (TPM) for chronic migraine (CM)

Methods: FORWARD, a multicenter, randomized study, compared onabotA 155U every 12 wks for 3 cycles with TPM 50-100 mg/day for up to 36 wks. The primary efficacy measure was proportion of patients with ≥50% reduction in headache (HA) days/mo vs baseline at wk 32. Adverse events (AEs) were recorded. PRO measures included: Controlled Oral Word Association Test (COWAT); 9-Item Patient Health questionnaire (PHQ-9); and the Work Productivity and Activity Impairment: Specific Health Problem (WPAI-SHP) questionnaire.

Results: 282 patients enrolled (onabotA, n=140; TPM, n=142); 148 completed treatment (onabotA, 85.7%; TPM, 19.7%). Primary reasons for withdrawal were lack of efficacy (onabotA, 5.0%; TPM, 19.0%) and AEs (onabotA, 3.6%; TPM, 50.7%). Using baseline observation carried forward (BLOCF) imputation, more patients on onabotA had ≥50% reduction in HA frequency vs TPM (40.0% vs 12.0%; P<0.001). Treatment-related AEs (TRAEs) were reported by 17.3% of onabotA and 69.0% of TPM patients. TPM was associated with a reduction in mean [SD] COWAT scores at wk 12 (−2.8 [5.7]), suggesting early cognitive changes in TPM recipients. The effect of TPM was potentially obscured by BLOCF methodology due to the large proportion of TPM withdrawals. OnabotA resulted in a small increase in mean [SD] COWAT scores at wks 12 (1.2 [8.1]) and 36 (2.8 [8.1]). At wk 36, onabotA had a significantly greater effect on mean [SD] PHQ-9 scores vs TPM (4.4 [4.2] vs 7.1 [5.8]; estimated mean difference: –1.86 [P<0.001]). Both treatments were associated with a slight reduction in WPAI-SHP Absenteeism and Presenteeism scores at week 36; onabotA significantly reduced mean Work Productivity Loss scores vs TPM.

Conclusion: Based on TRAEs and discontinuation rates, onabotA was associated with significantly better tolerability than TPM. PRO data suggest that changes in cognition may be seen as early as wk 12 in TPM recipients. OnabotA had a more favorable effect on depressive symptoms and improved work productivity loss and impairment in patients with CM vs TPM.

Disclosure of Interest: A. Blumenfeld Conflict with: Served on advisory boards and/or has consulted for Allergan, Amgen, Adler, Teva, Supernus, Promius, Eaglet, and Lilly; and has received funding for speaking from Allergan, Amgen, Pernix, Supernus, Depomed, Avanir, and Promius, A. Patel Conflict with: Allergan, Merz, and Ipsen , Conflict with: Speakers Bureau for Merz and Allergan, A. Manack Adams Conflict with: Full-time employee of Allergan plc and owns stock in the company, J. Rothrock Conflict with: 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. His parent institution has received funding from Allergan plc, Amgen and Dr. Reddy for clinical research he has conducted
Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-008

MIGRAINE PROGRESSION IN NATURAL SUBGROUPS OF MIGRAINE BASED ON COMORBIDITIES AND CONCOMITANT CONDITIONS: RESULTS OF THE CHRONIC MIGRAINE EPIDEMIOLOGY AND OUTCOMES (CAMEO) STUDY

R. B. Lipton 1*, V. T. Martin 2, M. L. Reed 3, K. M. Fanning 3, A. Manack Adams 4, D. C. Buse 5, P. J. Goadsby 6

1 Department of Neurology, Department of Epidemiology and Population Health, Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, 2 University of Cincinnati Headache and Facial Pain Center, University of Cincinnati College of Medicine, Cincinnati, OH, 3 Vedanta Research, Chapel Hill, NC, 4 Global Medical Affairs, Allergan plc, Irvine, CA, 5 Department of Neurology, Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, United States, 6 Institute of Psychiatry, Psychology & Neuroscience, Department of Basic and Clinical Neuroscience / Department of Neurology, NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College / University of California, San Francisco, London, United Kingdom

Introduction: Prior research has identified 8 natural subgroups of migraine based on profiles of comorbidities from the CaMEO Study.

Objectives: Test the hypothesis that these subgroups differ in prognosis as measured by progression to chronic migraine (CM).

Methods: Participants from the prospective, web-based baseline CaMEO Study were identified using quota sampling. Episodic migraine (EM) and CM were distinguished. Based on respondents’ self-report, 8 subgroups were identified using latent class analysis: Most Comorbidities, Respiratory/Psychiatric (Resp/Psych), Respiratory/Pain (Resp/Pain), Respiratory, Psychiatric, Cardiovascular, Pain, and Fewest Comorbidities. Modelling approaches included forward stepwise analysis of time to CM onset in individuals with EM at baseline across 7 comorbid classes, using Fewest Comorbidities as reference. Covariates including age, gender, income, body mass index, race, Migraine Disability Assessment (MIDAS), Migraine Symptom Severity Scale (MSSS), alldynia, and medication overuse at baseline were added to the model starting with the variable providing the most significant improvement in model fit, and continuing until no further improvement was observed.

Image:
Abstracts

**Results:** In the analysis population (n=8658), MIDAS was the first variable added to the forward stepwise model, as it provided the most statistically significant improvement in fit. Medication overuse was included as step 2, followed by comorbid class variable, allodynia, income, age, gender and MSSS (Table 1). BMI and race did not further improve fit and were not added. In the final model, Most Comorbidities had the highest risk of progression to CM, 3 times higher than Fewest Comorbidities (HR, 3.01 [95% CI: 2.17, 4.18]). Addition of age tended to increase the HR for all comorbid classes; Most Comorbidities increased from 2.49 (95% CI: 1.83, 3.39) before addition of age to 3.02 after (95% CI: 2.17, 4.20).

**Conclusion:** Identified comorbid classes of migraine are associated with risk of progression from EM to CM. Understanding the biological differences among these subgroups may help minimize migraine disease progression and optimize management.

**Disclosure of Interest:** R. Lipton Conflict with: Richard B. Lipton, MD has received grant support or honoraria from: Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, 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 University Press) and Informa. He holds stock options in eNeura Therapeutics and Biohaven. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS. Dr Lipton serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache., V. Martin Conflict with: In the past 12 months, Vincent T. Martin, MD has been a consultant for Amgen, Alder, Avanir, Promius, and Supernus and a speaker for

---

**Table 1. Forward Stepwise Model* for the Discrete Time Hazard to Chronic Migraine Onset in Comorbid Classes of Migraines in Individuals with Episodic Migraine at Baseline**

<table>
<thead>
<tr>
<th>LCA Class</th>
<th>Step 3 (Comorbid Class)</th>
<th>Step 4 (Allodynia)</th>
<th>Step 5 (Income ≥50k)</th>
<th>Step 6 (Age)</th>
<th>Step 7 (Gender)</th>
<th>Step 8 (MSSS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most Comorbidities</td>
<td>2.80 (2.06, 3.80)</td>
<td>2.59 (1.91, 3.53)</td>
<td>2.49 (1.83, 3.39)</td>
<td>3.02 (2.17, 4.20)</td>
<td>3.07 (2.21, 4.27)</td>
<td>3.02* (2.17, 4.18)</td>
</tr>
<tr>
<td>Resp/Psych</td>
<td>1.86 (1.39, 2.47)</td>
<td>1.75 (1.31, 2.33)</td>
<td>1.75 (1.32, 2.34)</td>
<td>1.87 (1.40, 2.49)</td>
<td>1.93 (1.44, 2.58)</td>
<td>1.87* (1.40, 2.50)</td>
</tr>
<tr>
<td>Resp/Pain</td>
<td>2.25 (1.68, 3.02)</td>
<td>2.13 (1.59, 2.66)</td>
<td>2.21 (1.64, 2.96)</td>
<td>2.61 (1.91, 3.57)</td>
<td>2.63 (1.92, 3.60)</td>
<td>2.57* (1.88, 3.51)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>1.40 (1.07, 1.82)</td>
<td>1.33 (1.01, 1.74)</td>
<td>1.35 (1.03, 1.76)</td>
<td>1.40 (1.07, 1.83)</td>
<td>1.42 (1.09, 1.87)</td>
<td>1.41* (1.07, 1.64)</td>
</tr>
<tr>
<td>Psych</td>
<td>2.22 (1.63, 3.03)</td>
<td>2.15 (1.58, 2.94)</td>
<td>2.10 (1.54, 2.87)</td>
<td>2.09 (1.53, 2.85)</td>
<td>2.12 (1.55, 2.89)</td>
<td>2.07* (1.52, 2.63)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>1.21 (0.84, 1.74)</td>
<td>1.21 (0.84, 1.74)</td>
<td>1.25 (0.87, 1.80)</td>
<td>1.46 (1.00, 2.13)</td>
<td>1.40 (0.96, 2.04)</td>
<td>1.41 (0.96, 2.05)</td>
</tr>
<tr>
<td>Pain</td>
<td>1.35 (0.93, 1.97)</td>
<td>1.30 (0.89, 1.90)</td>
<td>1.32 (0.91, 1.93)</td>
<td>1.48 (1.01, 2.17)</td>
<td>1.42 (0.96, 2.09)</td>
<td>1.41 (0.96, 2.07)</td>
</tr>
</tbody>
</table>

LCA=latent class analysis; MSSS=Migraine Symptom Severity Scale; Resp=respiratory; Psych=psychiatric.

* Step 1 added MIDAS and Step 2 added medication overuse and are not included in this table as the comorbid class only enters at Step 3.

*P<0.05, compared with the “Fewest Comorbidities” class.

*P<0.01, compared with the “Fewest Comorbidities” class.
Abstracts

Allergan, Avanir and Depomed. He has received research grant support from Allergan, Advanced Bionics, GlaxoSmithKline, Merck, Neuralieve, OrthoMcNeil, Pfizer, ProEthics, St. Jude's and is on the Advisory Board/Consulted for Allergan, OrthoMcNeil, Pfizer., M. Reed Conflict with: Michael L. Reed, PhD, is Managing Director of Vedanta Research, which has received research funding from Allergan, Amgen, Eli Lilly, GlaxoSmithKline, Merck & Co., and Promius, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study., K. Fanning Conflict with: Kristina Fanning, PhD, is an employee of Vedanta Research, which has received research funding from Allergan, Amgen, Eli Lilly, GlaxoSmithKline, Merck & Co., Novartis, and Promius, via grants to the National Headache Foundation. Vedanta has received funding directly from Allergan for work on the CaMEO Study., A. Manack Adams Conflict with: Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company., D. Buse Conflict with: In the past 12 months, Dawn C. Buse, PhD, has received grant support and honoraria from Allergan, Avanir, Amgen, Eli Lilly and Company, and Promius and for work on the editorial board of Current Pain and Headache Reports., P. Goadsby Conflict with: Peter J. Goadsby, MD, PhD has received personal fees from Akita Biomedical, Alder Biopharmaceuticals, grants and personal fees from Amgen, personal fees from Autonomic Technologies Inc., Cipla Ltd, Colucid Pharmaceuticals, Ltd, Dr Reddy's Laboratories, grants and personal fees from Eli-Lilly and Company, personal fees from Electrocore LLC, grants and personal fees from eNeura Inc, personal fees from Novartis, Pfizer Inc, Quest Diagnostics, Scion, Teva Pharmaceuticals, and Trigemina Inc., and personal fees from MedicoLegal work, Journal Watch, Up-to-Date, Oxford University Press outside the submitted work. In addition, Dr. Goadsby has a patent Magnetic stimulation for headache assigned to eNeura without fee.
LIFE WITH MIGRAINE, EFFECT ON RELATIONSHIPS, CAREER AND FINANCES, AND OVERALL HEALTH AND WELL-BEING RESULTS OF THE CHRONIC MIGRAINE EPIDEMIOLOGY AND OUTCOMES (CAMEO) STUDY

D. C. Buse 1, S. Murray 2, P. K. Dumas 3, A. Manack Adams 4, M. L. Reed 5, K. M. Fanning 5, R. B. Lipton 6

1Department of Neurology, Montefiore Headache Center; Albert Einstein College of Medicine, Bronx, NY,
2American Migraine Foundation Partner and Health and Wellness Author, Wenatchee, WA, 3Migraine Again LLC, Alpharetta, GA, 4Allergan plc, Irvine, CA, 5Vedanta Research, Chapel Hill, NC, 6Department of Neurology, Department of Epidemiology and Population Health, Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, United States

Introduction: Migraine can negatively affect many aspects of an individual’s life as well as the lives of those close to them.

Objectives: This analysis of CaMEO Study data evaluated and compared the effects of episodic (EM) and chronic migraine (CM) across a range of domains.

Methods: The CaMEO Study is a prospective, longitudinal, web-based survey study designed to characterize migraine impact, among other objectives, in a systematic US sample of people meeting modified ICHD-3 criteria: 19,891 respondents meeting said criteria were invited to complete the Family Burden Module. Answers by migraine respondents (probands) relating to the impact of migraine on family life, career and finances, and overall health—including how life would be without migraine—were recast as dichotomous variables for analysis. Descriptive analysis of items stratified by EM (<14 headache days/month) and CM (≥15 headache days/month) were reported. Comparative analyses utilized Chi-square and P values to indicate significant differences.

Results: 13,064 respondents (EM: 11,938 [91.4%]; CM: 1,126 [8.6%]) provided valid data. Approximately 20% of respondents not currently in a relationship (n=3,512) or in a relationship but not living together (n=1,393) indicated that headaches had contributed to relationship problems. Of those in a relationship and living together (n=8,154), 49.0% agreed somewhat/completely that they would be a better partner if they did not have headaches (EM: 46.2%; CM: 78.2%; P<0.001); 3.2% had delayed having children/had fewer children (EM: 2.6%; CM: 9.6%; P<0.001). Of 13,061 individuals responding to career items, 32.7% indicated that headaches had affected ≥1 item (EM: 30.0%; CM: 58.4%). Overall, 28.9% of respondents worried about covering household expenses (EM: 26.7%; CM: 52.9%), and 32.1% about long-term financial security (EM: 29.7%; CM: 57.4%). 16.4% reported poor or fair overall health (EM: 14.2%; CM: 40.5%). Across 9 “life-with-migraine” items, 69.6% of EM respondents (CM: 87.7%) reported ≥1 area that would be “better/a lot better” if they did not have headaches.

Conclusion: Migraine can negatively affect many aspects of life including relationships, career and financial outcomes, and overall health. People with migraine, particularly CM, feel that headaches affect many important areas of life and perceive that life would be better/a lot better without headache. Physicians managing migraine should consider the overall burden of disease.

Disclosure of Interest: D. Buse Conflict with: In the past 12 months, Dawn C. Buse, PhD, has received grant support and honoraria from Allergan, Avanir, Amgen, Eli Lilly and Company, and Promius and for work on the editorial board of Current Pain and Headache Reports., S. Murray: None Declared, P. Dumas Conflict with: Paula K. Dumas is the CEO and Managing Editor of Migraine Again LLC, and Partner in Migraine Health Ventures LLC, producer of the Migraine World Summit, and owns stock in each company. In the past 12 months, these companies have received advertising and research funding from Amgen, Novartis and Allergan plc., A. Manack Adams Conflict with: Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company., M. Reed Conflict with: Michael L. Reed, PhD, is Managing Director of Vedanta Research, which has received research funding from Allergan, Amgen, Eli Lilly, GlaxoSmithKline, Merck & Co., and Promius, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study., K. Fanning Conflict with: Kristina Fanning, PhD, is an employee of Vedanta Research, which has
received research funding from Allergan, Amgen, Eli Lilly, GlaxoSmithKline, Merck & Co., Promius, and Novartis, via grants to the National Headache Foundation. Vedanta has received funding directly from Allergan for work on the CaMEO Study. R. Lipton Conflict with: Richard B. Lipton, MD has received grant support or honoraria from: Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy’s Laboratories, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Pernix, Pfizer, Supernus, Teva, Trigemmia, 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. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS. Dr Lipton serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache.
Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-010

CHRONIC MIGRAINE PATIENTS DID NOT EXPERIENCE SIGNIFICANT IMPROVEMENT IN HEADACHE-RELATED DISABILITY AFTER UNDERGOING WEIGHT LOSS SURGERY

B. Torphy1,*, K. Ruffing2
1Headache, Diamond Headache Clinic, 2Psychology, Adler University, Chicago, United States

Introduction: Patients with chronic migraine (CM) are often encouraged to exercise to maintain a healthy weight, and if CM patients are overweight or obese they are frequently counseled to lose weight. Obesity is more common in CM than in episodic migraine (EM). The literature is rather scarce, however, regarding the impact of significant weight loss, such as that seen after bariatric surgery, on improvement in headache-related disability of CM patients.

Objectives: To determine if CM patients who underwent weight loss surgery experienced improvement in short-term and long-term headache-related disability after surgery.

Methods: Seven patients with CM who had previously undergone weight loss surgery, including gastric sleeve placement, gastric banding, and Roux-en-Y were identified at a tertiary headache center. The patients were administered the Migraine Disability Assessment Test (MIDAS) and asked to answer each of the five questions to reflect the following three time periods: 1. The three months preceding weight loss surgery 2. The three months following weight loss surgery and 3. The three months prior to the assessment date. The average time elapsed from surgery to the assessment date was six years (range 3 months to 14 years). MIDAS assessments were completed by five of the seven patients.

Results: There was no statistically significant difference in MIDAS scores before weight loss surgery, after weight loss surgery, and the three months prior to the assessments (p=0.55). Analysis of variance (ANOVA) was measured utilizing Statistical Package for the Social Sciences software.

Conclusion: Headache-related disability, as reflected in MIDAS scores, did not improve significantly in either the short-term (first three months) following weight loss surgery or the long-term (on average six years). Limiting factors in this study include the small sample size and the potential for recall bias given the time frame since surgery. Future research that includes a larger number of patients and is prospective is needed to draw more significant conclusions.

**THE MIGREX STUDY: IMPACT OF MIGRAINE IN SEXUAL FUNCTION**

MTIS2018-011

M. Torres-Ferrus 1,*, A. C. Lopez Veloso 2, V. Gonzalez Quintanilla 3, N. Gonzalez Garcia 4, J. Díaz de Teran Velasco 5, A. Gago Veiga 6, J. Camiña Muñiz 7, M. Ruiz Piñero 8, N. Mas Sala 9, V. J. Gallardo Lopez 10, P. Pozo-Rosich 1 and Juniors Committee from the Spanish Headache Society (GECSEN)

1Neurology, Vall d’Hebron University Hospital, Barcelona, 2Neurology, Gran Canaria Dr. Negrín University Hospital, Las Palmas de Gran Canaria, 3Neurology, Maqués de Valdecilla University Hospital, Santander, 4Neurology, Clínico San Carlos Hospital, 5Neurology, La Paz University Hospital, 6Neurology, La Princesa University Hospital, Madrid, 7Neurology, Rotger Clinic, Palma de Mallorca, 8Neurology, San Juan Hospital, Alicante, 9Neurology, Sant Joan de Déu Hospital, Manresa, 10Headache Research Group, Vall d’Hebron Research Institute, Barcelona, Spain

**Introduction:** Sexual dysfunction is a common symptom for many chronic disorders as well as pain syndromes.

**Objectives:** To determine the prevalence of sexual dysfunction in patients with migraine and its relationship with migraine features, comorbidities and the sexual perception of impact.

**Methods:** A multicenter study done in specialized headache clinics in Spain. We included patients with migraine according ICHD-3. Patients fulfilled an anonymous survey with demographic information, personal history, comorbidities, Arizona Sexual Experiences Scale (ASEX), Hospital Anxiety and Depression Scale (HADS) and a questionnaire about subjective impact of migraine on sexual activity. A univariate and logistic regression analyses were performed.

**Results:** 306 patients were included: 85.6% women, mean age 42.3±11.1 years. 62.1% had <15 headache days/month frequency, 77.5% were on preventive treatment and 24.3% met criteria for analgesic overuse. Subjectively, 62.2% of patients thought that migraine interfered with their sexual function and 41.8% had sexual dysfunction according to ASEX scale, with poor consistency (kappa coefficient=0.17). The presence of sexual dysfunction was correlated with older age, female gender, higher headache frequency, use of preventive medication, analgesic overuse, the presence of anxiety, depression, fibromyalgia and a HADS abnormal score (p<0.05). Only age [OR:0.33(0.14-0.75) p=0.009], female gender [OR:1.06(1.03-1.09) p<0.001] and HADS abnormal depression score [OR:1.19(1.12-1.27) p<0.001] were correlated with sexual dysfunction in the multivariate analysis.

**Conclusion:** Sexual dysfunction is frequent in migraine patients visited in a headache clinic. Headache frequency or use of preventive medication are not independently associated with sexual dysfunction.
INDIVIDUAL RISK FACTOR VARIABILITY AND OVERLAP IN FACTORS ASSOCIATED WITH MIGRAINE OCCURRENCE VS SEVERITY

K. J. Shulman¹, P. Prieto¹, M. Vives-Mestres¹, E. de la Torre²*, R. B. Lipton³
¹Curelator, Inc., Cambridge, MA, United States, ²European Headache Alliance, Valencia, Spain, ³Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, United States

Introduction: Migraine is a heterogeneous disease with significant individual variation in headache frequency, severity and disability over time. Trigger factors are usually studied using self-reported recall-based measures and presented as group means reflecting population averages. Protective factors and factors that modify severity are rarely studied. Long term diary studies create the opportunity to study within-person association of factors that modify risk and severity of attacks.

Objectives: Present 3 case reports to demonstrate within-person variability of risk factors associated with migraine occurrence and severity using two different N=1 analyses.

Methods: Curelator Headache®, a smartphone and web-based digital platform, was used to capture daily patient data and analyze risk factors of migraine occurrence using Cox regression and factors that modify severity using mixed model trajectory analysis. Individuals with migraine used the app daily for at least 90 days to enter details about headaches and factors that may be associated with their migraines. Risk factor profiles were derived for 774 individuals with migraine and 3 cases selected based on their clinical background. All items listed in the Table were significantly associated with occurrence factors that increased (trigger) or decreased (protector) short-term risk of migraine attacks and/or severity factors which increased (amplifier) or decreased (attenuator) pain.

Table: The table shows risk factor profiles from 3 selected cases to illustrate individual variability.

<table>
<thead>
<tr>
<th>Pt #</th>
<th>Age</th>
<th>Sex</th>
<th>Headaches/90 Days</th>
<th>Increased migraine severity/risk of occurrence</th>
<th>Decreased migraine severity/risk of occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Amplifier</td>
<td>Both</td>
</tr>
<tr>
<td>#439</td>
<td>27</td>
<td>Male</td>
<td>30</td>
<td>Time outdoors</td>
<td>Dehydration</td>
</tr>
<tr>
<td>#3133</td>
<td>45</td>
<td>Female</td>
<td>40</td>
<td>Anxiety</td>
<td>Nitrates</td>
</tr>
<tr>
<td>#6933</td>
<td>49</td>
<td>Female</td>
<td>29</td>
<td>Type of day</td>
<td>Pressure range</td>
</tr>
</tbody>
</table>
Results: Of 774 individuals, 63% had unique trigger profiles, 65% had unique protector profiles, 94% had unique amplifier profiles and 98% had unique attenuator profiles.

Conclusion: Individual N=1 analyses demonstrated limited inter-patient overlap of occurrence factors and severity modifiers, suggesting that factors associated with migraine frequency and severity may act differently in the same patient. Since risk factor profiles vary greatly among patients, data from individual N=1 analysis may help with the development of individualized recommendations as an alternative to relying on aggregated data.

EMIG (I): THE IMPACT OF DIGITAL PLATFORMS FOCUSED ON MIGRAINE PATIENT-CENTERED OUTCOME RESEARCH

V. J. Gallardo 1,*, J. Trochet 2, M. Torres-Ferrús 1,3, M. Sánchez del Río 4, J. M. Lainez 5, R. Leira 6, P. Pozo-Rosich 1,3
1Headache Research Group, Vall d’Hebron Research Institute, 2midolordecabeza.org, 3Neurology, Vall d’Hebron University Hospital, Barcelona, 4Neurology, Clínica Universitaria de Navarra, Madrid, 5Neurology, Hospital Clínico, Valencia, 6Neurology, Hospital Universitario Santiago de Compostela, Santiago de Compostela, Spain

Introduction: Patients are key stakeholders in all aspects of medical decision-making, and there is a growing emphasis on patient empowerment. The digital initiative midolordecabeza.org promotes the participation of patients with migraine with the aim of organizing the information on headache, including the latest research, and make it accessible and useful for all stakeholders.

Objectives: To validate and analyse the social impact of the digital platform focused on migraine patients with the aim of improving their medical decision-making.

Methods: Observational study to review the use of midolordecabeza.org, a website in Spanish for people (patients, physycians) interested in headache. We analysed the impact of this digital platform considering the average annual increase of users, visits, sessions and the duration of each one. We also studied the geographical distribution of access, social behaviour, electronic devices performance and temporary references with greater web traffic. We conducted open surveys to identify the clinical population and analyse the impact of their migraines, how they face to their migraine attacks, the answers they expect and the solutions they find.

Results: From June 2014 until February 2018, the instrument registered 828,071 users, 1,307,602 sessions and 2,844,113 visits with an average time per session for nearly two minutes. This implies an average annual increase of 78.7% of users, 51.5% of sessions and 47.7% of visits. Higher data traffic has been registered in Spanish-speaking regions such as Spain (32.2% of the total sessions), Mexico (15.6%) and Argentina (12.3%). Nevertheless, the platform has been widely disseminated throughout the world. In regards to social behaviour, the 68.0% of access were performed via mobile phone. Significant usage is registered during Spring and in the evening (7-11 pm). Regarding users: 76.0% are women between 25 and 40 years old (56.8%), 65.0% describe their migraine as a disabling disease with the presence of anxiety and depression as comorbidities, 55.0% ignore their type of headache and 47.0% do not have any medical follow-up, 62.0% do not know how to anticipate to their migraine attacks and 59.0% feel stigmatized, and 70.0% of patients feel dissatisfied with current therapeutic methods.

Conclusion: Migraine promotes a good research environment for the development of digital platforms due to its high prevalence, high socioeconomic impact, and migraineurs concern about available solutions and connectivity to the Internet.
**Epidemiology, comorbidity, outcomes and classification including big data**

**EMIG (II): HOW ARE MIGRAINE PATIENTS WHO USUALLY USE DIGITAL PLATFORMS FOCUSED ON PATIENT-CENTERED OUTCOME RESEARCH?**

V. J. Gallardo 1,*, J. Trochet 2, M. Torres-Ferrús 1,3, M. Sánchez del Río 4, J. M. Lainez 5, R. Leira 6, P. Pozo-Rosich 1,3  
1Headache Research Group, Vall d’Hebron Research Institute, 2midolordecabeza.org, 3Neurology, Vall d’Hebron University Hospital, Barcelona, 4Neurology, Clinica Universitaria de Navarra, Madrid, 5Neurology, Hospital Clínico, Valencia, 6Neurology, Hospital Universitario Santiago de Compostela, Santiago de Compostela, Spain

**Introduction:** Patients are key stakeholders in all aspects of medical decision-making, and there is a growing emphasis on patient empowerment. The digital initiative midolordecabeza.org promotes the participation of patients with migraine with the aim of organize the information about headache, including the latest research advances, and make it accessible and useful for all stakeholders.

**Objectives:** To describe the clinical characteristics of migraine-suffering population registered in the current digital platform.

**Methods:** Observational study to review the patients registered on the midolordecabeza.org website. We analysed and evaluated demographic data and their compliance in the migraine attacks record task commitment.

**Results:** 5,667 users had been registered. 83.5% were women, mean age 47.5±26.3 years old and an average onset age of 20.1±10.8 years. 64.6% of users were residents in Spain and the most common diagnoses were: 23.5% chronic migraine (CM), 14.8% migraine with aura (AM) and 9.2% migraine without aura (OM). 35.9% ignored their diagnosis and this proportion increased significantly in Spain (56.1%). After 4 years, 40.0% of users had registered 12,367 migraine attacks: 39.8% with moderate pain and 35.6% with severe pain. There is a follow-up of 46 users with more than 50 migraine attacks collected in long-term (39.1%>CM, 10.9%>AM, 6.5%>OM). There were significant differences in the increase of new users during the month of September (13.0%) and in the registration of migraine attacks from September to November (38.2% of the total attacks). The triggers associated with these attacks were stress (16.2%) and menstruation (10.2%), and the common accompanying symptoms were photophobia (9.3%), oppressive pain (8.0%) and visual aura (8.0%).

**Conclusion:** A large clinical and geographically heterogeneous cohort of patients with migraine is collected. Long-term migraine-attacks record remains low, indicating that adherence long-term strategies have to be developed (to facilitate patient empowerment.)
Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-015

CORRELATION OF MIGRAINE ATTACKS WITH SELF-REPORTED ALLODYNA

K. J. Shulman 1, M. Vives-Mestres 1, R. B. Lipton 2, P. J. Goadsby 3,*

1 Curelator, Inc., Cambridge, MA, 2 Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, United States, 3 NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College, London, United Kingdom

Introduction: Cutaneous allodynia is a common feature of migraine, likely due to sensitization of neurons in relevant pain pathway. Allodynia is associated with inadequate response to acute migraine treatment (1) and a risk factor for migraine chronification (2).

Objectives: To describe the correlation between allodynia and migraine attacks within individuals using a digital platform applying validated N=1 statistical algorithms to identify an association between daily allodynia, risk of migraine attack and level of suspicion for allodynia as a migraine antecedent.

Methods: Individuals with migraine registered with Curelator Headache®, using the app daily for 90 days to enter details about headaches and factors that may be associated with occurrence of a migraine attack, rating the likelihood of association on a scale of 1-10. Allodynia was determined by a Yes/No response to the question ‘Was your (head/neck) skin more sensitive to light touch etc. (today)?’. To be eligible for analysis, data must include at least 5 migraine attacks and allodynia must be reported on at least 5 days, but not all days. After 90 days within-person hazard ratios for association between allodynia and risk of migraine attack was computed using univariate Cox proportional hazard models. Allodynia was said to be associated with a migraine attack if the within person at p ≤0.05 and considered to be a migraine trigger if HR>1 or a migraine protector if HR<1.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Allodynia established</th>
<th>Allodynia not established</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected -yes</td>
<td>27</td>
<td>79</td>
<td>106</td>
</tr>
<tr>
<td>Suspected-no</td>
<td>40</td>
<td>109</td>
<td>149</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>188</td>
<td>255</td>
</tr>
</tbody>
</table>

Results: In the entire sample of 774 participants, mean migraine attack frequency was greater in 508 (66%) individuals reporting allodynia at least once vs. 266 (34%) who never reported allodynia (14.0 vs. 12.4, p<0.001). The table below shows the relation of allodynia as a diary-based migraine antecedent and patient report of allodynia as a migraine antecedent in 255 individuals with sufficient data on headache and allodynia to analyze. From this table, allodynia is an established migraine antecedent in 67/255 (26%). Using this diary result as the gold standard and self-report of allodynia as a migraine antecedent as a screen, suspected allodynia has a sensitivity of 27/67 (40.3%) and a specificity of 109/188 (58%).

Conclusion: Using daily diaries, two thirds of people with migraine report cutaneous allodynia using a single item screen. Allodynia was associated with higher migraine frequency in the entire sample. In a subgroup with sufficient data, allodynia was a statistically significant migraine antecedent in 26% of participants, though is more likely to be a premonitory feature than a trigger. Self-reported allodynia as an antecedent does not effectively identify persons with allodynia as an antecedent based on diary data.

References: (1) Lipton RB et al., Headache 2017; 57: 1026-40
(2) Louter MA et al., Brain 2013; 136: 3489-96

Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-016

REAL WORLD LONGITUDINAL ANALYSIS OF RESPONSE WITH AN ELECTRONIC PLATFORM
P. Prieto 1, E. de la Torre 2*, K. J. Shulman 1, M. Vives-Mestres 1, R. B. Lipton 3
1Curelator, Inc., Cambridge, MA, United States, 2European Headache Alliance, Valencia, Spain, 3Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, United States

Introduction: The “Access to Care” surveys from the EHA noted the top causes of dissatisfaction with care as drug ineffectiveness, difficulty seeing a headache specialist and having too much time between follow-up appointments (1). Migraine is a heterogeneous disease with significant individual variation over time. Clinical trial results are often based on self-reported recall-based measures and presented as group means reflecting population averages. Such results are limited and may not reflect how an individual may respond to treatment. There is a need for clinical tools that use objective detailed observational data to quickly identify an individual’s response to treatment over time.

Objectives: To evaluate the feasibility of using a digital platform to capture high-resolution patient outcomes and monitor individual (N=1) response to treatment remotely.

Methods: Individuals with migraine registered with Curelator Headache® and used the app daily for at least 90 days to enter details about headaches and medications. The population included those who were administered Botox at least once and used the Curelator app for at least 90 days after Botox. Three were selected based on clinical background for analysis of tracked days, total headache days, migraine days and MIDAS scores.

Results: We report 3 cases of individuals diagnosed with migraine who received Botox while using Curelator.
A 43 year old female with a baseline of 18 headaches/month, severe disability and eletriptan overuse was administered Botox and taken off gabapentin. After 3 months of improvement, gabapentin was reintroduced followed by 3 months of progressive regression to baseline headache frequency with increased disability. Eletriptan was discontinued and headache frequency gradually improved to 8/month with moderate disability, eliminating the need for further Botox in the following year. A 61 year old female with episodic migraine and mild/moderate disability started on Botox after worsening to 17 headaches/month. Despite eletriptan overuse, rapid improvement was seen on the first month and sustained up to the second Botox course. Headache frequency doubled following a switch to naratriptan, requiring treatment with steroids and Botox.
A 63 year old female with chronic migraine and severe disability had an initial response from 16 headaches/month to 13 headaches/month after Botox administration. Three months after a second course of Botox, headache frequency improved significantly to 4/month, yet disability remained severe.

Conclusion: Using a digital platform and N=1 statistical algorithms is an effective way to monitor migraine outcomes remotely. This technology could be useful to support clinical decisions regarding the need for and response to acute and preventative medications. Tracking individual patient outcomes offers the potential for better patient care and reduced healthcare costs.


Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-146

CORRELATION OF MIGRAINE ATTACKS WITH EXCESSIVE YAWNING
E. A. MacGregor 1,*, S. Donoghue 2, M. Vives-Mestres 2
1Barts Health NHS Trust, London, United Kingdom, 2Curelator Inc, Cambridge, MA, United States

Introduction: Repetitive yawning is a common premonitory migraine symptom [1,2]. In contrast to other common premonitory symptoms such as neck pain and tiredness, repetitive yawning is more specific and has a high predictive value for a migraine attack [3].

Objectives: We used a digital platform (Curelator Headache® - now called N1-Headache®) to determine 1) how many individuals recorded excessive yawning and 2) for how many individuals an association between excessive yawning and migraine attacks can be identified statistically.

Methods: Individuals with migraine registered to use Curelator Headache®. They then used this daily, entering details of headaches and factors possibly associated with attack occurrence: presence of yawning was determined by a Yes/No response to the daily question ‘Did you notice excessive yawning (today)?’. To be eligible for analysis, data must include 90 tracked days or more, at least five migraine attacks, more than 50 answers to the yawning question, and excessive yawning must be reported on at least 5% of days, but not all days. After 90 days all factors were analysed and for each individual the association between excessive yawning and migraine occurrence was determined via a univariate Cox proportional hazard model [4].

Results: Of 852 individuals with migraine, 285 (33.5%) were eligible for analysis. Excessive yawning was associated with increased risk of migraine attack in 72 (25.3%), with decreased risk in 4 (1.4%) and no significant within-person association was identified in 189 (66.3%). Risk could not be assessed in 20 (7%) due to convergence problems in the Cox model. Of the 72 with increased risk the median hazard ratio was 3 (IQR=4-2.2) meaning that, for them, when yawning is present the occurrence of migraine is about three times the rate per unit time as when there is no yawning.

Conclusion: In some individuals excessive yawning is a discernible symptom that is a sensitive predictor of migraine. Early identification of migraine provides an opportunity for early intervention. Future studies can assess effective strategies during the premonitory stage to abort an attack.

References:

Disclosure of Interest: E. A. MacGregor Conflict with: Clinical Advisory Board Member, S. Donoghue Conflict with: Employee of Curelator Inc, M. Vives-Mestres Conflict with: Employee of Curelator Inc
EFFICACY OF THE THERAPEUTIC INTERVENTION IN HEADACHE UNITS IN PATIENTS WITH CHRONIC MIGRAINE. EFUNCE II STUDY


1Hospital Clínico Universitario. Valencia, Valencia, 2Hospital Clínico Universitario Lozano Blesa, Zaragoza, 3Hospital Universitari Vall d'Hebron, Barcelona, 4Hospital Clínico Universitario, Valladolid, 5Complejo Hospitalario Virgen de la Macarena, Sevilla, 6Hospital Clínico Universitario, Santiago de Compostela, 7Clínica Universitaria de Navarra, Pamplona, Spain

Introduction: There is very few data in the literature confirming that the therapeutic intervention in headache units is superior to the attention received by patients in other levels of the health system. It is highly relevant to have these data to demonstrate the important role of these units in treating headache patients to patients themselves, health authorities and insurances companies.

Objectives: Evaluate the efficacy of the therapeutic intervention in headache units in headache patients and compare this intervention with other care levels as well as validate a protocol that could be applicable in the evaluation of headache units.

Methods: Multicenter prospective study performed in 7 university headache units in different regions of Spain. Every center should include 20 consecutive patients with chronic migraine that were referred to the headache unit for the first time. We evaluated the clinical situation, treatment received, paraclinical studies performed, degree of patients’ satisfaction, labor performance and disability (MIDAS) and quality of life (MSQOL and SF-12) studies. All these parameters were registered during the first consultation, after six months and one year later

Results: A total of 120 patients were included. 86% were women. Mean age was 46,5±11.9 years. All of them fulfilled the criteria for chronic migraine (IHCD III- Beta version). The headaches had begun 19,1±9,8 years before. Mean number of headache days in the last 3 months. 62,8±21,2. Mean number of days using analgesics in the last 3 months. 51,9±26,9. Mean age of migraine start 19.1±9,8. 70% were referred by neurologist or other specialist. Patients were attended 3-4 times in the year of follow-up

A significant reduction of number of days with headache, number of days of acute medication use, mean intensity of headaches, absenteeism and presenteeism, and use of health resources were observed. These clinical results were very related with improvement of quality of life (MAQOL and SF-12) and disability scales (mean MIDAS from 60 to 20). Only 28% of patients were satisfied or very satisfied at their arrival in comparison with 72% after attending the headache unit

Conclusion: This study confirms that Headache Units are efficient in treatment of chronic migraine patients, being clearly superior to other assistance levels. They offer a high degree of clinical improvement, patient satisfaction and important benefits regarding labor performance, disability and quality of life.
**Epidemiology, comorbidity, outcomes and classification including big data**

**MTIS2018-148**

**FACIAL PRESENTATIONS IN PRIMARY HEADACHE SYNDROMES**

C. Ziegeler*, A. May

**Introduction:** Facial involvement of the first trigeminal branch (V1) is common in primary headache disorders; but the involvement of the second (V2) and third (V3) branches is relatively rare, and its prevalence in primary headache disorders is not well investigated.

**Objectives:** We aimed to assess the prevalence of facial presentations (the involvement of V2 and V3) amongst primary headache patients treated in a university tertiary care center.

**Methods:** For the time period of 2010-2018 medical records of patients of our university headache and facial pain out-patient clinic were retrospectively investigated for a facial involvement and divided into three subtypes depending on pain localization and history. Type I was defined as pain mainly experienced in V1 with an additional facial spread. Type II describes pain now perceived solely in V2 and/or V3 in patients with a history of headache in V1. Type III describes pain that is perceived in V2 and/or V3 without any prior history of headache.

**Results:** In our extended database we had n=2,912 completed patient data sets of which 281 reported facial pain either as an independent or additional symptom. Among all migraine patients, 2.2% (n=43 out of 1,935) reported a facial involvement, most commonly in V2. Of these 43 patients, 25 (58.1%) experienced pain in V1 radiating to V2 and/or V3 (Type I), whereas 18 patients (41.9%) experienced the pain exclusively or predominately in V2 and/or V3 (II, III). In cluster headache 14.8% (n=42 out of 238) of the patients reported a facial involvement, of which 42.9% perceived the pain either exclusively or predominantly in V2 and/or V3 (II, III). A facial involvement was seen in 45.0% of paroxysmal hemicrania patients (n=9 out of 20), 23.8% of hemicrania continua patients (n=10 out of 42), and 20.0% of SUNCT/SUNA patients (n=3 out of 15).

**Conclusion:** Facial presentations in primary headache syndromes are not uncommon. A better understanding of the underlying mechanisms could potentially lead to a better understanding of primary headache syndromes in general.

Further research is needed to determine whether facial presentations in primary headaches represent a continuum of the same syndrome or indeed separate disease entities. We suggest subdividing these patients into the three above mentioned subtypes (Type I, II, III) to allow for a more homogenous definition of each group.
Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-149

VESTIBULAR ASSOCIATES IS MORE COMMON IN MIGRENEURS WITHOUT FAMILY HISTORY OF MIGRAINE

M. BOZDAG 1, N. OKSUZ 1, D. DERICI YILDIRIM 2, B. TASDELEN 2, A. OZGE 3,*

1NEUROLOGY, MERSIN UNIVERSITY, MERSIN, 2BIOSTATISTICS, 3NEUROLOGY, MERSIN UNIVERSITY, MERSIN, Turkey

Introduction: Vestibular signs and symptoms are often accompanied by other subgroups of migraine as well as vestibular migraine.

Objectives: The objective of this study was to evaluate the effect of family history on vestibular symptoms

Methods: This study included patients with definitive migraine diagnosis who had complete knowledge of migraine and vestibular symptoms (vertigo, dizziness, motion sickness) through Mersin University School of Medicine, Neurology Department Headache database. Migraine was diagnosed by the same specialist according to ICDH-3 criteria. Those with similar headache complaints at the family were considered as family history positive. After audiologic and vestibulocochlear evaluations patients with other vestibular pathologies and patients diagnosed with other headache syndromes were excluded in this study. Symptoms such as dizziness, vertigo and motion sickness were questioned during headache and headache free periods. Headache frequency, duration and severity were assessed by monthly headache diary. The Shapiro-Wilk test was performed to test the suitability of the normal distribution of the numerical data. Descriptive analyses were presented using median or mean±SD based on distribution normally or not. Categorical variables were summarized as count(percentage). Unadjusted comparisons were made using Mann-Whitney U test for continuous endpoints and the Chi-Square test for categorical endpoints. A multiple logistic regression model was used to identify independent predictors of family history and migraine type. Odds ratios with their 95% confidence intervals were estimated. A p value of less than 0.05 was considered statistically significant.

Table:

<table>
<thead>
<tr>
<th>Family History</th>
<th>Vertigo</th>
<th>Dizziness</th>
<th>Motion sickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>67 (9,4)</td>
<td>113 (15,8)</td>
<td>134 (18,7)</td>
</tr>
<tr>
<td>No</td>
<td>649 (87,9)</td>
<td>603 (84,2)</td>
<td>581 (81,39)</td>
</tr>
</tbody>
</table>

| P              | 0,001  | <0,001   | <0,001         |

Results: 793 patients were included in the study and 685 (86.4%) were female. The mean age was 35.35 ± 12.73 years. The median of headache duration as 24.0 [5-48] hours; headache frequency as 6.0 [3-15] days/month and headache severity as 8.0 [7-10] points according to VAS (visual analog scale) were detected. Family history of migraine in 716 patients (90.3%), vertigo in 96 patients (12.1%), dizziness in 154 patients (19.4%) and motion sickness in 167 patients (21.1%) were determined. There was a statistically significant relationship between vestibular associates and family history. (vertigo p < 0.001, dizziness p<0.001, motion sickness p<0.001).

Vestibular associates were more common in migreneurs without family history of migraine.
In migraineurs without family history, dizziness rate was 3.175 times (OR=3.175, 95% CI 1.690-5.966, p<0.001) and vertigo rate was 2.45 times higher (OR=2.45, 95% CI 1.27-4.72, p<0.001).

**Conclusion:** In our study, it was determined that family history of migraine did not have a significant effect on frequency and severity of migraine-accompanying vestibular symptoms.
Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-150

IDIOPATHIC INTRACRANIAL HYPERTENSION AND RISK OF CARDIOVASCULAR DISEASES IN WOMEN: UK POPULATION BASED MATCHED COHORT STUDY

K. Nirantharakumar 1,2, A. Subramanian 1, N. J. Adderley 1, A. Yiangou 3,4,*, K. M. Gokhale 3, S. Mollan 3,5, A. J. Sinclair 3,4

1Institute of Applied Health Research, University of Birmingham, 2Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, 3Metabolic Neurology, Institute of Metabolism and Systems Research, University of Birmingham, 4Department of Neurology, University Hospitals Birmingham, 5Birmingham Neuro-Ophthalmology, Queen Elizabeth Hospital, Birmingham, United Kingdom

Introduction: Cardiovascular disease risk has not been previously evaluated in idiopathic intracranial hypertension (IIH).

Objectives: To estimate risk of composite cardiovascular events, heart failure, ischaemic heart disease, stroke/transient ischaemic attack, hypertension, and type 2 diabetes in women with idiopathic intracranial hypertension compared to general population controls matched on body mass index and age. To evaluate prevalence and incidence of the condition.

Methods: A population-based retrospective cohort study was performed through The Health Improvement Network (THIN), a nationally representative electronic primary care records database between 01/01/1990, and 01/05/2016. Women with idiopathic intracranial hypertension (n=2083) were compared to a control cohort (n=18,439) matched for age, gender and body mass index. Adjusted hazard ratios of cardiovascular outcomes calculated using Cox regression. Primary outcome was a composite of any cardiovascular disease. Secondary outcomes included each of the cardiovascular disease outcome separately and type 2 diabetes, hypertension, fragility fractures, and death.

Results: Higher absolute risks for all cardiovascular outcomes were observed in idiopathic intracranial hypertension compared to controls. Idiopathic intracranial hypertension was positively associated with composite cardiovascular events (adjusted hazard ratio 2.19, 95% confidence interval 1.63 to 2.93, p<0.001), heart failure (2.79, 1.51 to 5.15, p=0.001), IHD (1.84, 1.16 to 2.91, p=0.009), stroke or transient ischaemic attack (1.97, 1.33 to 2.92, p=0.001), and hypertension (1.43, 1.18 to 1.75, p<0.001). There were no statistically significant differences in type 2 diabetes, fracture and mortality rates. Both incidence and prevalence of IIH increased from 2005 to 2015: incidence from 2.5 to 6.7 per 100,000 person years and prevalence from 31 to 68 per 100,000 females. Incidence increased markedly in those with BMI >30Kg/m2 and was highest in the most deprived Townsend quintile.

Conclusion: Idiopathic intracranial hypertension in women is associated with increased cardiovascular risk compared to a cohort matched for age, gender and body mass index. The absolute risk for this young population was low, but noteworthy considering the young age and relatively short study period. There is a growing burden of the disease, most marked in those with obesity. This data suggests that management of risk factors for cardiovascular disease may reduce long-term morbidity.

Epidemiology, comorbidity, outcomes and classification including big data

MTIS2018-151

TENSION-TYPE HEADACHE IN A MEXICAN POPULATION. RESULTS FROM PREMECEF
A. Marfil*, S. Barrera-Barrera 1
1CLINICA DE CEFALIAS, HOSPITAL UNIVERSITARIO, UANL, Clinica De Cefaleas, UANL, Monterrey, Mexico

Introduction: Clinical presentation of most headaches is not well known in Mexican population.
Objectives: To communicate results from PREMECEF (Primer Registro Mexicano de Cefaleas, First Mexican Registry on Headaches) regarding tension-type headache (TTH).
Methods: PREMECEF is a database that works as an electronic medical record oriented to headaches. It is filled by physicians. It was launched in July, 2017 and currently has three regional hospitals participating, one private. Data collected to June 30, 2108 are presented.

Results: Of 485 records, 136 (28%) were TTH, with 104 (76.5%) female, median age 41.5 (SD 18.3) y/o; TTH subtypes, 93 (68.4%) were chronic, with initial frequency of 1 episode/d in 25 (18.4%), and the same current frequency in 26 (19.1%). Oppressive quality 83 (61%), duration 6 - 12 hours in 14 (10.3%), holocranial in 20 (14.7%), occipital irradiation in 11 (8.1%), mainly afternoon in 10 (7.4%), prodrome in 12 (9.6%), accompanying symptoms in 80 (58.8%) with nausea: 31 (22.8%), vomiting, 18 (13.2%), phonophobia and photophobia in 17 (12.5%), kinesophobias in 11 (8.1%), alldynia in 5 (3.7%), dysautonomia in 11 (8.1%), triggers in 31 (22.8%). Sleep quality: sleep time 6 - 8 hours, 56 (41.2%), in 15 (11%) the sleep has good quality; 6 (4.4%) had bruxism.

Conclusion: TTH is the most frequent headache. Our figures show a higher than expected presence of accompanying and prodromal symptoms. Kinesophobia, alldynia and dysautonomias could be due to other, non-recognized, headaches. Poor sleep quality is highly prevalent. TTH clinical profile in our simple has some characteristics that deserve further study. This is the first of its kind study in our country.
**Experimental research**  
**MTIS2018-017**  
**ROLE OF TRPA1 CHANNEL AND CGRP DURING CORTICAL SPREADING DEPRESSION**  
M. Wang*, L. Jiang

**Introduction:** Calcitonin-gene-related peptide (CGRP) is a target for migraine therapy; CGRP release is known to be associated with the activation of the transient receptor potential ankyrin type-1 (TRPA1) channels. However, the role of CGRP and TRPA1 in migraine mechanism has not been fully understood.

**Objectives:** The aim of this study is to investigate whether deactivation of TRPA1 and blockade of CGRP could prevent the occurrence of cortical spreading depression (CSD) and if there is a functional link between TRPA1 and CGRP during CSD.

**Methods:** CSD was induced by KCl application in the mouse brain slice and recorded using intrinsic optical imaging.

**Results:** The results showed that deactivation of TRPA1 by a selective TRPA1 antagonist, A967079, markedly prolonged the CSD latency and reduced magnitude, indicating a reduced cortical susceptibility to CSD under TRPA1 deactivation. This inhibitory action of A967079 on CSD was reversed by application of exogenous CGRP. Consistent to TRPA1 deactivation, an anti-CGRP antibody also suppressed CSD in the mouse brain slice, which was prevented by a TRPA1 agonist, allyl-isothiocyanate (AITC).

**Conclusion:** This data suggest that there is a bidirectional positive interaction between TRPA1 activation and CGRP in modulating CSD, indicating both deactivation of TRPA1 channels and blockade of CGRP would have therapeutic benefits in preventing migraine with aura.

A PHASE II RANDOMISED CONTROL TRIAL ASSESSING THE SAFETY, TOLERABILITY AND EFFICACY OF AN 11β-HYDROXYSTEROID DEHYDROGENASE TYPE 1 INHIBITOR IN IDIOPATHIC INTRACRANIAL HYPERTENSION: IIH:DT.

K. Markey\(^1\)\(^2\)*, R. Ottridge\(^1\), J. Mitchell\(^2\)\(^3\), C. Rick\(^3\), R. Woolley\(^3\), N. Ives\(^3\), T. Matthews\(^2\), A. Krishnan\(^4\), P. Shah\(^5\), W. Scotton, S. Mollan\(^2\), A. Sinclair\(^1\)\(^2\)

\(^1\)University of Birmingham, \(^2\)University Hospital Birmingham, \(^3\)University of Birmingham, Birmingham, \(^4\)The Walton Centre Foundation Trust, Liverpool, \(^5\)NHS Greater Glasgow and Clyde, Glasgow, United Kingdom

**Introduction:** Pharmacological therapies in idiopathic intracranial hypertension (IIH) are limited and can be poorly tolerated. Novel treatments have not been assessed previously in early phase clinical trials.

**Objectives:** We investigated the safety, tolerability and efficacy of a novel drug, an 11β-hydroxysteroid dehydrogenase type-1 inhibitor (AZD4017), in a phase 2 multicentre randomised, double-blind, placebo-controlled trial.

**Methods:** Thirty females aged between 18-55 years with active IIH (lumbar puncture (LP) pressure >25 cmH2O and papilloedema) were to be randomised 1:1 to receive either 400mg twice daily oral AZD4017 or matching placebo for 12 weeks. The primary outcome was the difference in LP pressure at week 12. Secondary outcomes included: headache frequency, severity and analgesic use, HIT-6 scores, papilloedema grading, Logmar visual acuity and visual field mean deviation.

**Results:** LP pressure decreased from 33.7(6.3) to 29.7(5.2) cmH2O at 12 weeks for AZD4017 and from 32.7(4.8) to 31.3(6.7) cmH2O for placebo (mean difference: -2.8, 95%CI:-7.1 to 1.5; \(p=0.2\)). Visual field mean deviation (MD) (worst eye) changed from -6.1dB (5.4) to -3.4dB (3.2) at 12 weeks for AZD4017 and from -3.4dB (6.8) to -2.2dB (3.1) for placebo (mean difference: 0.3, 95%CI:-2.0 to 2.7, \(p=0.8\)). There was no difference in headache outcomes, HIT-6 scores, visual acuity and papilloedema between AZD4017 and placebo at week 12. Only 9 adverse events were deemed to be drug-related and no patients withdrew. One unrelated serious adverse event was recorded two days post-randomisation.

**Conclusion:** This is the first ever phase 2 trial in IIH to assess a novel agent, AZD4017. The treatment was safe and tolerable over the 12 week study period. We noted a trend for improvement which would be interesting to evaluate in a larger phase 2B or 3 randomised controlled trial.
**Experimental research**

**MTIS2018-019**

VAGUS NERVE STIMULATION MODULATES THE CRANIAL TRIGEMINAL-AUTONOMIC REFLEX – A COMPARISON TRIAL OF DIFFERENT SHAM-CONDITIONS.
C. F. Schroeder¹,*, M. Möller¹, A. May¹

¹Department of Systems Neuroscience, University Medical Center Eppendorf, Hamburg, Germany

**Introduction:** Non-invasive vagal nerve stimulation (nVNS) has been proposed as a novel treatment for migraine and cluster-headache patients (1-3). Cranial autonomic symptoms such as lacrimation and conjunctival injection are characteristic features in some primary headache disorders (4). Recently, we were able to show that nVNS modulates the trigeminal autonomic reflex in healthy participants. However, a study, using nVNS in order to treat cluster headache attacks, failed to find overall group effects between nVNS and sham treatment as responses to sham treatment were noticeably high (5).

**Objectives:** The purpose of this study was to compare the effects of nVNS (electroCore stimulation device) on the trigeminal-autonomic reflex with sham nVNS (as used in clinical studies), no stimulation and verum stimulation at the back of the neck.

**Methods:** 28 healthy participants (15 female, 13 male, mean ± SD age= 26.29 ± 4.57) were recruited and participated in a single-blind, within-subject design. The four different conditions (i) no stimulation, (ii) verum stimulation of the posterior neck, (iii) electroCore sham stimulation and (iv) regular nVNS were applied in a pseudorandomized order for 3 x 2 minutes. Lacrimation, as a quantifiable physiological autonomic output, was subsequently provoked using kinetic oscillation stimulation (KOS) (Chordate Medical AB, Stockholm, Sweden) of the nasal mucosa (6) and quantified using a Schirmer’s II test before the stimulation (baseline), as well as during the KOS procedure. As an indicator of autonomic activation, the mean difference between lacrimation at baseline and lacrimation after one minute of KOS was calculated.

**Results:** The regular nVNS treatment resulted in a significant reduction of ipsilateral KOS-induced lacrimation compared to no stimulation (p=0.003) and stimulation of the posterior neck (p=0.02). Surprisingly the same effect was observed after stimulation with the electroCore sham device (p=0.003; p=0.001). There was no significant difference between nVNS and stimulation with the electroCore sham device.

**Conclusion:** KOS-induced lacrimation was significantly reduced after regular nVNS stimulation compared to no stimulation and stimulation of the posterior neck. However, after stimulation with the electroCore sham device the lacrimation was also significantly reduced. These data suggest that regular nVNS and the sham device used in randomized trials activate the vagal system and only stimulation of the posterior neck may be considered a true sham for regular nVNS stimulation.
References:


Disclosure of Interest: C. Schroeder: None Declared, M. Möller: None Declared, A. May Conflict with: Unrestricted scientific grant from electroCore and Chordate Medical
Abstracts

Experimental research

MTIS2018-020

A NOVEL MICROELECTRONIC TECHNIQUE FOR TRIGGERING AND RECORDING OF CORTICAL SPREADING DEPRESSION.

G. Faas¹*, G. Kechechyan¹, C. Yeh¹, A. Charles¹
¹Neurology, UCLA, Los Angeles, CA, United States

Introduction: Cortical spreading depression (CSD) is believed to underlie the migraine aura, and has been used extensively as a translational model for migraine. CSD can be reliably induced in a controlled manner in a variety of experimental setting, making it an appealing model to study migraine mechanisms and their potential modulation by migraine therapies. Although CSD models have given us many important insights thus far, the results of CSD measurements may be confounded by the fact that the triggering and recording of CSD is invasive, requiring penetration of the skull and the brain tissue with electrodes or optical fibers. Furthermore, the majority of CSD measurements have been done in animals under anesthesia, and the small number of studies of involving awake animals have been limited because of the requirement for implantation of electrodes.

Objectives: Our objective was to expand and improve upon the current techniques with as ultimate goal to induce CSDs and continuously measure neurovascular activity in a minimally invasive way in awake and freely moving animals.

Methods: We have developed a technique in which we use skull-mounted microelectronics in optogenetic mouse models to trigger and record spontaneous and CSD-associated neurovascular activity without compromising the skull. Moreover, since these electronics are minimally invasive, neurovascular activity can be studied continuously over long periods of time, with high temporal resolution, in awake animals.

Results: Using this approach, we observe consistently quantifiable changes in neurovascular activity associated with CSD that are comparable to what are observed with video recording of CSD in invasive preparations. We can correlate CSD events with changes in behavior, and evaluate the effects of repetitive CSD events over extended time periods, as well as the modulation of these events by potential migraine therapies.

Conclusion: This new technique will significantly refine the use of CSD as a model for understanding migraine mechanisms and for the development of new treatments.
**Abstracts**

---

**Experimental research**

**MTIS2018-021**

**KYNURENINES: NEW TARGETS IN MIGRAINE: PRECLINICAL AND CLINICAL STUDIES**

V. Imre László

---

**Introduction:** Kynurenines: new targets in migraine

László Vécsei
Department of Neurology and MTA-SZTE Neuroscience Research Group, Albert Szent-Györgyi Clinical Center, University of Szeged, Semmelweis str. 6, 6725-Szeged, Hungary

In mammals, the vast majority of dietary tryptophan is metabolized via the kynurenine pathway. Interest in kynurenine has increased markedly since it became clear that two of its metabolic products quinolinic acid and kynurenic acid (KYNA), act as agonist and antagonist, respectively, at receptors for excitatory amino acids. KYNA was detected in the canine urine as early as 1853 (Liebig, 1853) and was long recognised as a side product of tryptophan metabolism.

**Objectives:** The role of the kynurenine system in migraine: preclinical and clinical studies

**Methods:** Trigeminal stimulation in rats, immunohistochemistry, analysis of kynurenine metabolites

**Results:** We found that in rats electrical stimulation of the trigeminal ganglion (which is a reasonably effective model for trigeminal activation in migraine) results in decreased kynurenine-amino-transferase immunoreactivity in dural macrophages, Schwann cells and mast cells, which is paralleled by an increase in the number of neuronal nitric-oxide immunoreactive nerve fibers in the dura mater. In chemically induced animal model of migraine, a derivative of KYNA was able to inhibit nitroglycerine-induced increase of c-fos and Calcitonin gene-related peptide (CGRP) expression in rat trigeminal nucleus caudalis (TNC). Recently we demonstrated that KYNA inhibits the electrical stimulation induced Pituitary Adenylate Cyclase-Activation Polypeptide (PACP) expression in TNC.

**Conclusion:** Our results provided the direct evidence that NMDAR inhibition can prevent the overexpression of PACAP in an experimental model of migraine and support the idea that therapies aimed at the modulation of glutamatergic transmission, including the use of KYNA derivatives may be therapeutic value in migraine. Furthermore, it was found altered kynurenine pathway metabolites in serum of chronic migraine patients. The large increase in the levels of anthranilic acid (ANA) encourages research aimed at establishing whether ANA has any role in the regulation of nociceptive transmission (Curto et al. 2015).


Supported by GINOP-2.3.2-15-2016 00034
Experimental research

MTIS2018-022

EFFECTS OF SUBTHRESHOLD SINGLE PULSE TRANSCRANIAL MAGNETIC STIMULATION (STMS) ON DOPAMINERGIC ACTIVITY OF HYPOTHALAMIC A11 NUCLEUS.

J. Lloyd 1,*, R. AbuukarAbdullahi 1, M. Jones 2, S. McMahon 3, A. Andreou 4,5

1Headache Research - Wolfson CARD, King’s College London, 2Zenith Neuroteck Ltd, 3Neurorestoration Department - Wolfson CARD, King’s College London, 4Headache Centre, Guy’s and St Thomas’s NHS Trust & Wolfson CARD, King’s Health Partners, 5Headache Research - Wolfson CARD, King’s College London, London, United Kingdom

Introduction: Single-pulse transcranial magnetic stimulation (sTMS) is a non-invasive neuromodulation technique shown to be a successful acute preventative treatment for migraine patients. sTMS uses a single magnetic pulse of 170 μs duration to induce weak cortical electrical currents via electromagnetic induction. Migraine pathophysiology has been shown to involve altered activity of hypothalamic region. The dopaminergic A11 nucleus appears to be of particular importance/interest.

Objectives: The aim of this experiment was to investigate if sTMS could affect the neuronal activity of dopaminergic cells in the A11 nucleus.

Methods: All procedures were performed under a UK Home Office Licence in accordance to the 1986 Animal (Scientific Procedures) Act in anaesthetised male adult Sprague-Dawley rats. Two 600 V (~1.1 T) pulses were fired from a custom made (11 mm diameter; rise time 170 us) sTMS coil. Tungsten microelectrodes were used for extracellular recordings from the A11 nucleus. Spontaneous recording of A11 region was recorded for 60 minutes after 2x 600 V sTMS pulses. Post-hoc spike analysis was used to isolate dopaminergic firing and data were compared to baseline.

Results: No significant difference was found in spontaneous dopaminergic firing of the A11 region following application of 2x 600 V sTMS (F14.59, 10.35 = 2.121, P = 0.91)

Conclusion: sTMS does not have any effect on the firing rate of the dopaminergic A11 nucleus, suggesting that other brain areas may be involved in the preventive mechanisms of A11


Disclosure of Interest: J. Lloyd: None Declared, R. AbuukarAbdullahi: None Declared, M. Jones Conflict with: CEO of Zenith Ltd, S. McMahon Conflict with: MRC Board Member, A. Andreou Conflict with: Grant from Migraine Trust
**Experimental research**

**MTIS2018-152**

**EMG-GUIDED BOTULINUM TOXIN A ALLEVIATES SEVERELY DISABLED HEADACHE PATIENTS WITH HYPERACTIVE MUSCLES. A DOUBLE-BLIND RANDOMIZED PLACEBO-CONTROLLED CROSS-OVER STUDY.**

D. S. Knudsen*, H. Kasch

**Introduction:** In chronic refractory headaches a mixture of migraine with or without aura (MwoA) and tension-type headache (TTH), may often co-exist. Likewise, post-traumatic and post-whiplash headache (whiplash associated disorder, WAD) may have features of both TTH and MwoA. If intense, persisting neck-tenderness/muscle stiffness and jaw-clenching/bruxism co-exist, these hyperactive muscles may be treated by botulinum toxin A (BTX-A).

**Objectives:** In chronic refractory headaches a mixture of migraine with or without aura (MwoA) and tension-type headache (TTH), may often co-exist. Likewise, post-traumatic and post-whiplash headache (whiplash associated disorder, WAD) may have features of both TTH and MwoA. If intense, persisting neck-tenderness/muscle stiffness and jaw-clenching/bruxism co-exist, these hyperactive muscles may be treated by botulinum toxin A (BTX-A).

**Methods:**

59 consecutive chronic headache patients naïve to BTX-A treatment (Male:13; Female:46, age: 39.5±11.2, mean VAS headache 6.9±1.6; median duration 71.5mths) with hyperactive muscles. The diagnoses were: MwoA=11; TTH=25; PTH=7; WAD=15; other=1.

Some of the patients with more than one diagnosis, were categorized by the main diagnosis.

EMG from the cervical, capital splenius and the semi spinal muscles was measured. If measures of turns/sec were above 250, patients otherwise fulfilling criteria for participation were randomized to either 75 units of Dysport (conc: 200u/ml) or a similar volume of isotonic saline in a double-blind cross-over study of 2×4 months periods. Half of the patients were randomized to treatment with saline first and Dysport second and the other half to treatment with Dysport first and saline second, using a computer program called minimize.

**Results:**

Treatment outcome was evaluated by the patient’s charts.

During active treatment 43% reported headache relief as compared to 21% during placebo (Kruskal-Wallis(K-W), p<0.009). During active treatment 19% had 2 months+ of 50% pain-relief. During active treatment significantly more complained about heaviness of the head, 48%, but no other Adverse events (AE’s) were more common during active treatment. (K-W, p<0.003). During placebo 4% reported heaviness of the head, 8% had flulike symptoms (7% in active treatment), 12% had muscle soreness (29% in active treatment) and 0% reported worsening of the headache (5% in active treatment).

**Conclusion:**

Severely affected headache patients with hyper active muscles, may respond to low dosages of EMG guided BTX-A injections in the neck muscles. However more studies are necessary, before recommendations for clinical use can be made.
**Abstracts**

**Experimental research**

**MTIS2018-153**

**ALTERATIONS IN REGIONAL CEREBRAL BLOOD (RCBF) IN VISUAL SNOW ASSESSED USING ARTERIAL SPIN-LABELLED (ASL) FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI)**

F. Puledda 1,*, F. Zelaya 2, C. Schankin 3, P. Goadsby 1

1Basic and Clinical Neuroscience, 2Centre for Neuroimaging Sciences, Institute of Psychiatry, Psychology and Neuroscience, King’s College London, London, United Kingdom, 3Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

**Introduction:** Patients with visual snow suffer a pan-field, dynamic visual disturbance described as continuous TV-static-like tiny flickering dots. The proposed 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 (1). The only previous neuroimaging study in patients with visual snow showed hypermetabolism in the area of the lingual gyrus using [18]F-FDG PET (2).

**Objectives:** In order to understand more about the pathophysiology of visual snow and to confirm previous neuroimaging results, we aimed to measure the changes in regional cerebral blood flow (rCBF) in patients with this condition. We used a 3D pseudo-continuous arterial spin labeling (3D-pCASL) fMRI sequence, which was performed on a 3T General Electric MR750 MRI scanner.

**Methods:** These are preliminary results of an ongoing study. Subjects (n=19) and age and gender matched healthy volunteers (n=19) were recruited following screening and informed consent. All subjects underwent a structural T1, T2 and FLAIR sequences followed by two six minute pCASL scans. During the pCASL scans, subjects were instructed to either look at a blank screen (baseline sequence) or at a simulation of visual snow (stimulation) on the same screen. Scanning was conducted over 70 minutes in a single session. Imaging was analysed using SPM 12 (www.fil.ion.ac.uk/SPM).

**Results:** A full factorial analysis was conducted to compare the rCBF of patients to healthy volunteers, both at baseline and during visual stimulation. Using a whole brain, voxel-wise analysis we found that, at baseline, patients with visual snow exhibit a significant increase in rCBF in large clusters that include the left cerebellum, bilateral cuneus and precuneus and parts of the occipital and parietal cortices (p<0.001). We also found that when subject to the visual snow stimulus, patients showed a significant increase in rCBF in the left cerebellum, left insula, left parietal and left occipital cortices (p<0.001). No significant reductions in rCBF were detected.

**Conclusion:** Patients with visual snow present significant increase in blood flow in various brain regions, namely the cerebellum, cuneus, precuneus, insula, occipital and parietal cortices, both at baseline and when subject to a visual stimulus simulating the snow itself.

This study suggests that measures of regional CBF using ASL may provide a sensitive surrogate marker of differences in resting state neuronal activity, in subjects who experience visual snow syndrome. These results are consistent with those reported in previous investigations using Positron Emission Tomography.

**References:**


General aspects of headache care
MTIS2018-023

CHOCOLATE AS A RISK FACTOR FOR MIGRAINE ATTACKS IN INDIVIDUALS

S. Donoghue*, M. Vives-Mestres¹, S. Silberstein²
¹Curelator Inc., Barcelona, Spain, ²Headache Center, Jefferson University, Philadelphia, United States

Introduction: There is widespread belief that chocolate can trigger migraine attacks, but little supportive evidence. A review by Lippi et al (1) concludes that the risk of migraine attacks after eating chocolate is lower than for other believed triggers (e.g. stress, lack of sleep, fasting) and in double-blind studies the risk is similar to placebo. To further explore this we used a digital platform (Curelator Headache®) which uses an App to record daily, self-reported intake of chocolate and N=1 analytics to correlate this with migraine attack risk.

Objectives: To determine in individuals with migraine 1) how many suspect chocolate as a trigger and 2) for how many can a statistical association between chocolate ingestion and time to migraine attack be identified.

Methods: Individuals with migraine registered to use Curelator Headache® and answered questions about their suspected triggers, including chocolate, and their importance (1=low; 10=maximal). They then used Curelator Headache daily for 90 days, entering details about headaches and tracking factors that may affect time to migraine attack occurrence. After 90 days all factors were analyzed and for each individual the association between daily self-reported chocolate ingestion (no/some/a lot) and time to migraine attack was determined via a univariate Cox proportional hazard model (2).

Table:

<table>
<thead>
<tr>
<th>Suspected?</th>
<th>Associated?</th>
<th>Not suspected</th>
<th>Low (1-3)</th>
<th>Medium (4-6)</th>
<th>High (7-10)</th>
<th>No answer</th>
<th>TOTAL n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated trigger</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>10 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Associated protector</td>
<td>4</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>16 (2.1)</td>
<td></td>
</tr>
<tr>
<td>No association</td>
<td>259</td>
<td>154</td>
<td>84</td>
<td>52</td>
<td>31</td>
<td>580 (74.9)</td>
<td></td>
</tr>
<tr>
<td>Not analyzed</td>
<td>70</td>
<td>35</td>
<td>20</td>
<td>32</td>
<td>11</td>
<td>168 (21.7)</td>
<td></td>
</tr>
<tr>
<td>TOTAL n (%)</td>
<td>339 (43.8)</td>
<td>198 (25.6)</td>
<td>107 (13.8)</td>
<td>88 (11.4)</td>
<td>42 (5.4)</td>
<td>774</td>
<td></td>
</tr>
</tbody>
</table>

Results: The table shows statistical associations between chocolate and attack risk according to the degree of suspicion of chocolate as a trigger, in 774 individuals with migraine. Very few associations were found. There was no clear association between degree of suspicion of chocolate and the proportions of individuals in whom an association was identified. Not analyzed individuals had insufficient data for analysis, due to either constant or low variability in chocolate intake (61: 36.3%) or low number of migraine attacks, or there were convergence problems in the Cox model.

Conclusion: Chocolate is widely suspected as a trigger but in very few individuals was an association with migraine attacks identified statistically, and then with either increased (potential trigger) or decreased risk (potential protector) in almost equal numbers. However intake of chocolate was insufficiently variable or there were too few migraine attacks to allow analysis in one-fifth of individuals, making analysis for them impossible. Eighteen individuals reported no chocolate intake, possibly indicating avoidance.
References:

Disclosure of Interest: S. Donoghue Conflict with: Curelator Inc. consultant, M. Vives-Mestres Conflict with: Curelator Inc. employee, S. Silberstein Conflict with: Consultant to Curelator Inc.
Abstracts

General aspects of headache care

MTIS2018-024

DIAGNOSTIC ERROR ERRORS RATES IN DIAGNOSING IDIOPATHIC INTRACRANIAL HYPERTENSION


Introduction: IIH is a syndrome characterised by raised intracranial pressure of unknown cause most commonly in obese woman. IIH causes significant morbidity including disabling headaches and permanent visual loss therefore identification of optic nerve swelling with normal imaging in a young woman with chronic headache is highly suggestive. However the high incidence of primary headache disorder among young woman and the increasing prevalence of obesity makes identification of patients who truly have IIH more challenging. With the growing awareness of IIH many overweight woman with isolated headaches are subjected to invasive tests and treatments before being referred to a specialist centre.

Objectives:
To quantify the rate of diagnostic error amongst patients with IIH. Additionally, to identify factors contributing to diagnostic error.

Methods:
Sequential patients referred with a diagnosis of IIH to the Birmingham tertiary neuro-ophthalmology IIH clinic were prospectively included (October 2013 - February 2017). A diagnostic error taxonomy tool was applied to cases referred as “definite” or “possible” IIH. Discrepancy between referred and final diagnosis were recorded.

Results: 210 patients were referred, (96.2% female), 138/212 (65%) with definite IIH and 74/212 (35%) with possible IIH. Of those diagnosed with definite IIH 25% were not IIH and out of those diagnosed with possible IIH 57% were not IIH. Reasons for diagnostic error included incorrectly identifying papilloedema where in fact pseudopapilloedema existed and diagnosing IIH following an isolated lumbar puncture (LP) pressure > 25cmCSF (but in the absence of the other diagnostic criteria for IIH). Mis-diagnosis lead to 43% receiving unnecessary acetazolamide (or other diuretics) and 14% having multiple LP’s.

Conclusion: We noted a high diagnostic error rate amongst IIH patients referred to a tertiary centre for ongoing management. Where there is doubt about the presence of true papilloedema early specialist review may reduce unnecessary treatment and LP’s.

2. Schif Et al Diagnosing Diagnosis Errors: Lessons from a Multi-institutional Collaborative Project
3. Markey KA et al Mollan SP et al
CORRELATION OF MIGRAINE ATTACKS WITH NECK PAIN AND TENSION.
S. Donoghue 1*, M. Vives-Mestres 2, A. MacGregor 3
1Curelator Inc., Skipton, United Kingdom, 2Curelator Inc., Barcelona, Spain, 3Barts Health NHS Trust, London, United Kingdom

Introduction: Neck pain associated with migraine attacks is common and usually first noticed close to time of headache onset (1,2). However because it can occur prior to headache, it can be perceived as a migraine trigger. We used a digital platform (Curelator Headache®) to record daily neck pain/tension and correlate this with risk of migraine attack, in individuals.

Objectives: To determine 1) how many people suspect neck pain/tension as a migraine trigger and 2) for how many an association between neck pain/tension and migraine attacks can be identified statistically.

Methods: Individuals with migraine registered to use Curelator Headache® and answered questions about factors they suspect contribute to attack occurrence, including neck pain/tension, and their importance (1=low; 10=maximal). They then used Curelator Headache® daily for 90 days, entering details of headaches and factors possibly associated with attack occurrence: presence of neck pain/tension was determined by a Yes/No response to the question ‘Did you notice neck pain or tension (today)?’. After 90 days all factors were analyzed and for each individual the association between neck pain/tension and migraine attacks was determined via a univariate Cox proportional hazard model (3) using a) all data and b) relating attack occurrence with previous day neck pain data (lagged analysis).

Table:

<table>
<thead>
<tr>
<th>Suspected?→ Association?↓</th>
<th>Not suspected</th>
<th>Low (levels 1-3)</th>
<th>Medium (levels 4-6)</th>
<th>High (levels 7-10)</th>
<th>No answer</th>
<th>TOTAL n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated ‘trigger’</td>
<td>19</td>
<td>13</td>
<td>31</td>
<td>92</td>
<td>6</td>
<td>161 (20.8)</td>
</tr>
<tr>
<td>Associated ‘protector’</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No association</td>
<td>56</td>
<td>40</td>
<td>81</td>
<td>147</td>
<td>16</td>
<td>340 (43.9)</td>
</tr>
<tr>
<td>Not analyzed</td>
<td>72</td>
<td>37</td>
<td>47</td>
<td>99</td>
<td>18</td>
<td>273 (35.3)</td>
</tr>
<tr>
<td>TOTAL n (%)</td>
<td>147 (19)</td>
<td>90 (11.6)</td>
<td>159 (20.5)</td>
<td>338 (43.7)</td>
<td>40 (5.2)</td>
<td>774</td>
</tr>
</tbody>
</table>

Results: The table shows statistical associations between neck pain/tension and attack risk according to the degree of suspicion as a trigger in 774 individuals (non-lagged analysis). Neck pain/tension was associated with increased risk of attacks (‘trigger’) in about one-fifth of individuals, but never found as a ‘protector’. There was an association between degree of neck pain/tension suspicion as a trigger and frequency of statistical confirmation of an association with attacks. Not analyzed individuals had insufficient data for analysis, due to constant or low variability in neck pain/tension (128: 46.9%), low number of attacks or convergence problems in the Cox model. In the lagged analysis, only 4.9% individuals had an association between attacks and preceding day neck pain/tension.

Conclusion: Neck pain/tension was widely suspected as a migraine trigger. In one-third of individuals with adequate data there was a statistical association between same day neck pain/tension and migraine headache. However neck pain/tension the day before headache started was much less commonly correlated with attacks: this supports the view that neck pain/tension is more likely a migraine symptom rather than a trigger.
References:
1. Calhoun AH et al 2010; Headache 50: 1273-77
2. Lampl C et al 2015; J Headache and Pain 16: 80-84

**General aspects of headache care**

**MTIS2018-026**

**HEADACHE GAUGE - A REAL-LIFE TOOL FOR HEADACHE IMPACT EVALUATION**

R. Gil-Gouveia¹ ²,*, I. B. Marques¹, S. Machado¹, E. Parreira¹, I. P. Martins³

¹Headache Center, Hospital da Luz, ²Headache Outpatient Clinic, ³Headache Outpatient Clinica, Centro Hospitalar Lisboa Norte, Lisboa, Portugal

**Introduction:** Primary headaches, in particular migraine, are frequent chronic and disabling disorders which have several therapeutic options. Monitoring treatment efficacy is complex as there is no consensual scale acknowledged to be the gold standard for measuring neither the impact of headache nor the treatment effect.

**Objectives:** To develop and validate a quantitative, fast and user-friendly tool the, “Headache Gauge (HG)” a composite score to monitor the impact of headache taking into account three dimensions of headache severity (frequency, duration and functionality), that can be applied in all cultural contexts and that is not time-locked to a specific time period.

**Methods:** Headache Gauge was calculated in two consecutive consultations in a sample of primary headache patients recruited in a headache clinic. Convergent validity was evaluated by its correlation with headache frequency, headache impact scales (MIDAS, HIT-6, HURT) and quality of life evaluation (SF12).

**Results:** Preliminary data of the first 100 patients included is presented, with 74% of patients having completed the study. Six were male, average age was 39.7 ± 9.6 years and average disease duration was 19.2 ± 11.5 years. Migraine was diagnosed in 90% of patients, 10% had tension-type headache. Revaluation occurred 94.9 ± 19.5 days (range 63 to 171 days) after inclusion. Average improvement of all scale scores was observed from the first to the second evaluation, although significant difference was found only in headache days, headache gauge, MIDAS and HIT-6. Headache Gauge scores correlated highly with headache frequency (Pearson 0.470, p< 0.0001) and HURT scale (Pearson 0.382, p= 0.001). When considering only the group of patients in whom both doctors and patients agreed on subjective outcome (N=48), only reduction in Headache Gauge and HURT scores distinguished both patient groups.

**Conclusion:** Headache Gauge is easy to apply, uses routine clinical data, and it seems more sensitive to headache change than the existing accepted impact scores for migraine; it has the potential to be relevant in real-life clinical monitoring. It can probably be useful in tension-type headache. More data is needed to confirm these findings.
**General aspects of headache care**

**MTIS2018-027**

**APPROPRIATENESS OF IMAGING REFERRALS FROM A TERTIARY HEADACHE CLINIC**

S. Dorsey, A. Zaidi*, A. Ijaz 1, A. Buture 1, F. Ahmed

1Neurosciences, Hull York Medical School, Hull, United Kingdom

**Introduction:** Headache remains a leading cause of morbidity affecting 50% of people worldwide. Vast majority of headaches are benign and neuroimaging is used to exclude secondary based on presence of red flags. However, too often the imaging is requested on non-medical grounds such as reassurance that raises financial and ethical issues. Indeed all too frequently scans detect incidental findings that not only increase patient anxiety but can lead to further investigations. It is often perceived that Neurologist or headache physicians scan many patients for reassurance that could be undertaken in primary care.

**Objectives:** We aimed to evaluate our practice on imaging referrals. The study was approved by the IRB authorities.

**Methods:** Data for all new patients attending the Hull headache clinic from October 2017 was collected that is ongoing. The data included patient age and sex, the grade of doctor performing the assessment, the clinical diagnosis, type of scan and the reason for neuroimaging if requested. Patients who had neuroimaging prior to the clinic appointment were excluded.

**Results:** Of the 173 patients seen, 55 (31.7%) had imaging prior to clinic attendance. Of the remaining (N=118) 30 (25.4%) were scanned of which 21 (17.7%) were scanned for medical reasons e.g., new daily persistent headache, first episode of cluster headache, change in characteristic of existing migraine or red flag features and only 9 were imaged for reassurance (N=6) or patients’ insistence (N=3).

**Conclusion:** Only 25% of patients referred to a tertiary headache clinic were referred for imaging of which only 7.6% were scanned for reassurance. This is against the general perception that a third of patient from headache clinics are imaged purely for reassurance. However, as the data collection was prospective, it may have impacted on imaging requests. We aim to look retrospectively on the practice prior to the study.

**Disclosure of Interest:** S. Dorsey: None Declared, A. Zaidi: None Declared, A. Ijaz: None Declared, A. Buture: None Declared, F. Ahmed Conflict with: Advisory Board for Novartis, Allergan, Electrocore, Eneura receive honorarium paid to Migraine Trust and British Association for the study of Headache
General aspects of headache care

MTIS2018-028

AUDITING SUDDEN ONSET HEADACHE IN THE ACUTE MEDICAL UNIT
F. McCann*, R. Forbes

Introduction: 54 year old lady admitted with 2 week history of a sudden onset headache. Previous SAH – aneurysm coiled. Neurology exam, CT brain, Ct venogram and Lumbar puncture (LP) were normal. Ongoing headache during admission. Discharged after it had resolved. Presented following day with GCS of 3 post sudden headache. CT brain revealed SAH. She passed away.

Southern Trust Guidelines. “if a CT brain and LP performed at an appropriate time are both negative you have excluded SAH”. Guidelines also say that “consider a Neurology Referral in instances where SAH is excluded but there is a persistent headache.”

Objectives: PHASE 1: aim was to recognise the standard of investigations of patients who present with sudden onset headaches to Acute Medical Unit (AMU)
* If Ct head and LP were normal did they get further imaging?
* How often was neurology advice sought?
* Did a background of previous SAH influence the decision to do further imaging/seek specialist advice?

PHASE 2: Aims:
(1) Ensure all patients admitted with sudden onset headache were reviewed by a neurologist
(2) Arrange follow up at clinic and record clinical features of headache + investigations performed
(3) Gather data about this cohort of patients
(4) Identify possible reasons for low LP rate

Methods: PHASE 1: cohort of 40 patients from the medical admission list who presented with a sudden onset headache, over a 2 year period. NIECR was used to gather details about their admission.

PHASE 2: all patients admitted with sudden onset headache were seen by the neurologist and offered 8 week out-patient follow up at a consultant-led Acute Headache Review Clinic (AHRC). In the AHRC we record features of the incident headache, clinical examination and investigations.

Results: PHASE 1: Out of total 40 patients admitted to the AMU:
- All had CT brain done within 24 hours
- LPs performed in 38%
- Further imaging requested in 25%
- 18% had neurology consultations

PHASE 2: to date we have offered 30 people review at AHRC. 3 people did not attend. All patients were assessed by a neurologist during admission, and had a CT Brain performed. LP was performed in 47% of cases. Aa minority had ‘true’ sudden severe headache with immediate maximal pain. 80% of patients had further imaging.

Conclusion: PHASE 1: The low rate of LP and neurology input were surprising as the unit has access to a neurology liaison service every week day.

PHASE 2: Less than 50% of cases were true "sudden onset headaches". History taking may help target investigations more appropriately. The initial low rate of LP may reflect this. Engagement of neurology staff in AMU increases the demand for specialised investigations when initial CT/CSF is non-diagnostic. Over 50% of patients had abnormal c-spine exam-a potentially modifiable risk factor for acute headache.


Southern Health and Social Care Trust Guidelines
**General aspects of headache care**  
MTIS2018-154

**ORGANIZATION, MANAGEMENT AND TREATMENT OF IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH) IN A TERTIARY HEADACHE CLINIC - HOW TO CHARACTERIZE AND IMPROVE PATIENT CARE.**

M. Eriksen*

Introduction:

Background:

Observations in the Pain- and Headache Clinic in Aarhus have led to questions about the patient care offered to patients diagnosed with IIH.

Objectives: Background:

Observations in the Pain- and Headache Clinic in Aarhus have led to questions about the patient care offered to patients diagnosed with IIH.

Methods:

Method:

Both quantitative and qualitative data were included in order to generate a broader insight and understanding into the answer in how to improve patient care to patients diagnosed with IIH. The medical records of 33 identified patients diagnosed with IIH and undergoing treatment at the Pain-and Headache Clinic during 2017 were investigated. Four persons were furthermore chosen systematically for a telephone interview. The investigation of the medical records was turned into statistical material and the telephone interview was coded and abstracted into categories and through a further abstraction into four key themes that seemed of importance to improvement of patient care to patients diagnosed with IIH.

Table:

Analysis:

By analysing the data, four key themes appeared. The four key themes were coordination, help to lose weight, better health care service and education/information.

Analysis:

By analysing the data, four key themes appeared. The four key themes were coordination, help to lose weight, better health care service and education/information.

Results:

Results:

The four themes; Coordination, Help to Lose Weight, better Health Care Service and Education/Information appeared to be of importance to the patients in characterizing and improving patient care to patients diagnosed with IIH. In order to improve the present patient care, new strategies and a multidisciplinary approach need to be devised on the basis of the four themes. As the incidence of IIH is expected to rise in the future due to the obesity epidemic there is a developing need of centres with expertise in IIH involving organization, management, and treatment of IIH and continued and ongoing curiosity of development in the management, organisation and treatment are of importance in offering the best quality of patient care.

Keywords:

Idiopathic intracranial hypertension; Pseudo tumour cerebri; Patient care; Treatment; Organisation; Compliance; Adherence; Management and IIH, qualitative analysis method.

Conclusion:

The four themes; Coordination, Help to Lose Weight, better Health Care Service and Education/Information appeared to be of importance to the patients in characterizing and improving patient care to patients diagnosed with IIH. In order to improve the present patient care, new strategies and a multidisciplinary approach need to be devised on the basis of the four themes. As the incidence of IIH is expected to rise in the future due to the obesity epidemic there is a developing need of centres with expertise in IIH involving organization, management, and treatment of IIH and continued and ongoing curiosity of development in the management, organisation and treatment are of importance in offering the best quality of patient care.
Abstracts

**Keywords:**
Idiopathic intracranial hypertension; Pseudo tumour cerebri; Patient care; Treatment; Organisation; Compliance; Adherence; Management and IIH, qualitative analysis method.
General aspects of headache care

GREATER OCCIPITAL NERVE BLOCKADE: AN EVALUATION OF 1577 INJECTIONS

M. Weatherall 1*, D. Vanniasegaram 2
1Department of Neurology, Buckinghamshire Healthcare Trust, Aylesbury, 2Imperial College School of Medicine, London, United Kingdom

Introduction: Greater occipital nerve blockade is widely used as a treatment for primary and secondary headache disorders. We performed a service evaluation of 1577 injections performed in 861 patients over a ten year period.

Objectives: The primary objective was to establish the safety and frequency of adverse events in a large cohort of patients, including a significant number who underwent repeated injections. Secondary objectives included recording patient-reported outcomes to provide real world data on the utility and consistency of the intervention.

Methods: A retrospective review of medical records was undertaken by the authors. Information was recorded on the age and sex of the patient, the main headache diagnosis, the location and quantity of materials injected, immediate complications, and if available, subsequent adverse events and patient-reported outcome (frequency and severity of headaches).

Results: Records of 1577 injections performed in 861 patients (662 F, 199 M) were identified. Immediate complications were recorded in 32 cases, most commonly syncope or near-syncope. 12 patients reported immediate symptoms in ipsilateral trigeminal territory, presumably mediated through activation of the trigeminocervical complex. Delayed effects were reported in 145 cases, mostly commonly persistent pain at the injection site. Serious side effects were rare: 4 cases of alopecia were recorded, one patient had a significant localised allergic reaction, and there was one case of central serous retinopathy closely temporally related to the injection. 20 injections were given to women whilst pregnant, and 30 whilst breast-feeding, with no significant adverse consequences. 21 patients had ≥7 injections; 2 of the cases of alopecia occurred in this group but there was otherwise no evidence of any cumulative risk of adverse events from repeated injections. Follow-up data was available for 733/861 first injections. 261 patients (36%) reported an excellent or good response, 184 (25%) a fair or minimal response, 256 (35%) no response, and 32 (4%) were worse. For those who responded, the median duration of effect was two months. 24/34 (71%) patients who did not respond to a first injection failed to respond to a second injection, or got worse. Conversely, 70/119 (59%) of those who reported a good response to the first injection, did as well or better with a second injection, although 32 of these patients (27%) did not respond second time around.

Conclusion: Greater occipital nerve blockade is a safe intervention for patients with primary and secondary headache disorders. Serious adverse events are very rare; with the possible exception of alopecia, repeated injections are not associated with higher risks of adverse effects. More than 50% of patients will derive some benefit from the intervention. Response to the first injection is a good guide to likely response to further injections.
NITRATES IN FOOD AS A RISK FACTOR FOR MIGRAINE ATTACKS
S. Donoghue 1*, M. Vives-Mestres 1, E. Virre 2
1Curelator Inc., Cambridge MA, 2Departments of Neurosciences, UCSD, La Jolla CA, United States

Introduction: Nitrates are used as preservatives in foods such as processed meats. High doses cause headaches and may trigger migraine attacks in susceptible individuals (1). However there is less evidence that nitrates consumed in food trigger migraine, but some indirect evidence (2). Nevertheless it is listed as a causative agent in ICHD-3beta. To explore whether daily variation in nitrate intake in food is associated with increased (or decreased) risk of having migraine attacks, we used a digital platform, Curelator Headache® (now called N1-Headache®) to statistically compare, in individuals, daily intake of nitrates and occurrence of attacks.

Objectives: To determine in individuals with migraine 1) how many suspect nitrates as a migraine trigger and 2) for how many an association between nitrate intake and occurrence of migraine attacks can be identified statistically.

Methods: Individuals with migraine registered to use Curelator Headache via website or the App Store and answered questions about personal suspected triggers, including nitrates, and their importance (1=low; 10=maximal). They then used Curelator Headache® daily for 90 days, entering details about headaches and tracking factors that may affect migraine attack occurrence. After 90 days all factors were analyzed and, for each individual, the association between self-reported daily nitrate intake (none, some, a lot) and time to migraine attack was determined via a univariate Cox proportional hazard model.

Results: Table 1 shows statistical associations between nitrates and attack risk according to the degree of suspicion as a trigger in 774 individuals.
Nitrates was suspected as a trigger at baseline by almost half of individuals, mostly at the ‘low’ or ‘mildly’ suspected levels. Only a low number of associations were found therefore it was not possible to test the relation between degree of suspicion and the proportions of individuals with associations. Not analyzed individuals had insufficient data for analysis, due to constant or low variability in nitrates intake (404, 52.2%), low number of attacks or convergence problems in the Cox model.
Conclusion: Although often suspected as a trigger, nitrates in food are not a common trigger. In those individuals who suspect, positive (possible trigger) and negative (possible protector) associations were found in an almost equal and very small number of individuals. In one third of individuals intake of nitrates was reported as constant or with low variability making analysis impossible. For 20% of individuals intake was consistently reported as ‘none’, possibly indicating avoidance of nitrate-containing foods.

References:  
Gonzalez A et al. mSystems 2016; 1(5): e00105-16

Disclosure of Interest: S. Donoghue Conflict with: Curelator Inc. Consultant, M. Vives-Mestres Conflict with: Curelator Inc. employee, E. Virre: None Declared
PATIENTS WHO USE THE EMERGENCY DEPARTMENT FOR MIGRAINE: A STUDY OF ATTENDANCE AND TREATMENT CHARACTERISTICS

A.-M. logan, I. reid, M. yogarajah, H. jarman, N. nirmalanathan
1St Georges University NHS Foundation Trust, 2St George's Medical School, St George's University of London, London, United Kingdom

Introduction: Primary headache is a common cause of Emergency Department (ED) attendance[1] and a challenge for clinicians who need to distinguish primary from secondary headaches in a safe and timely way.

Objectives: In this retrospective cross sectional study of electronic records in a UK major urban Emergency Department we identified Migraine/ Probable Migraine (PM) from other primary headaches in order to establish how patients with migraine present and are managed in the acute setting.

Methods: Data was collected for all patients with available electronic records, triaged as attending for headache, aged 16 years and over, from 1st December 2016 to 30th April 2017 as part of a service evaluation study. The International Classification of Headache Disorders (ICHD) 3rd edition[2] was used to classify headaches using C, D and E criteria of the classification for Migraine/PM. Non primary headaches were classified based on ED/specialty diagnosis and inability to fulfil the ICHD criteria. Attendances were recorded during the study period as the Index Event and two years prior to this. Further analysis of the Migraine/PM group only was carried out to show attendance and treatment characteristics.

Image:
Abstracts

Results: Data was collected for 802 consecutive patients. 356 (46.5%) attendances were for non-primary headache, 196 (25.6%) for Migraine/PM and 213 (27.8%) for undefined headache due to lack of recorded headache features. 62 (31.6%) of Migraine/PM attendances and 67 (31.5%) undefined headache attendances resulted in brain imaging. 62 (31.6%) of Migraine/PM attendances and 67 (31.5%) undefined headache attendances resulted in brain imaging. 37 (18.9%) in the Migraine/PM group were transported to ED by emergency vehicle. Timing analysis showed that 35% of attendances were acute, within 24 hours of the headache starting (Table 1). 59 (30.1%) of patients reported taking no treatment prior to ED attendance, 72 (36.7%) had used a low dose analgesic, 20 (10.2%) had used a triptan / analgesic combination and 20 (10.2%) an opiate preparation. In 49 (25%) of attendances treatment was not wanted / recorded, in 54 (27.6%) opiates were given. Triptans were used in 3 (1.5%) attendances.

Conclusion: This study shows how the ICHD classification[3] can be used to identify migraine in ED and highlights the frequent use of opiates[4] and scans[5] for migraine patients that has been seen acutely in other health systems. The proportion with undefined headache diagnoses adds weight to the calls for the use of a protocolised approach to headache management in ED [6, 7]. The use of emergency vehicles and the numbers of patients attending with non-acute symptoms may reflect the patient’s perception of the urgency of their need for headache care and warrants further investigation.

General aspects of headache care

MTIS2018-158

SELF-MANAGEMENT FOR PATIENTS WITH EPISODIC MIGRAINE: A PILOT OF COMMUNITY BASED GROUP EDUCATION SERVICE.

A.-M. logan¹,*, N. nirmalanathan¹
¹Headache Service, Neurology Department, St George’s University Hospitals NHS Foundation Trust, London, United Kingdom

Introduction: Self-management interventions have been shown to have a positive impact in patients with migraine[1]. Pressures on health services mean that new models of care are being sought, engaging patients in an active role in their migraine management.

Objectives: To assess the impact of a pilot community based group education service for patients with episodic migraine.

Methods: Episodic migraine patients were referred following a new hospital appointment to prevent further attendances or by their GP to prevent a hospital referral, to a 2 hour group session run by the Headache Practitioner. The session covered what migraine is, treatments, triggers, medication overuse, diaries, as well as living well with headache through advice on exercise, sleep and managing anxiety. Quantitative data of headache frequency, headache disability (HIT6)[2], diagnosis and referral was collected at the group with the HIT6 repeated at a subsequent telephone call. Qualitative data was recorded through a short questionnaire and comments recorded at the group and telephone call.

Image:

Table 1. HIT6 change pre/post education group

<table>
<thead>
<tr>
<th></th>
<th>Pre group HIT 6 (mean)</th>
<th>Post group HIT 6 (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP</td>
<td>66</td>
<td>58</td>
</tr>
<tr>
<td>Hospital</td>
<td>65</td>
<td>60</td>
</tr>
</tbody>
</table>
Results: 56 patients were referred, 82.1% were female, 17.9% male. 27 (48.2%) patients had high frequency migraine (HFEM) ≥8 migraine days per month, 21 (37.5%) patients had low frequency migraine (LFEM) on ≤7 migraine days per month, 2 (3.6%) patients had Chronic Migraine, 2 (3.6%) patients had Vestibular migraine and 4 (7.1%) had unreported frequency. 37 (66%) patients were hospital referrals and 19 (34%) GP referrals. 11 (57.9%) of GP referred patients had HFEM and 8 (42.1%) had LFEM compared with 16 with HFEM (43.2%) and 13 with LFEM (35.1%) of hospital patients. 18 patients (32.1%) could be contacted 3 months after the session to complete outcome measures, of which 9 (50%) were referred by GPs (table 1). For the whole group the HIT6 scores differed significantly between pre (mean 65.3, SD 4.37) and post (mean 59.6, SD 7.18) group, two tailed t=2.89, df=34, CI 95% 1.7-9.75. The within person change was greater than the 2.5 points clinically relevant for the HIT6 [3]. Patients were asked immediately after the group to rate a statement saying that the session would help them manage their migraines more effectively. 48 (85.7%) of patient’s strongly agreed with the statement, 7 (12.5%) agreed and 1 (1.8%) did not respond.

Analysis of the comments showed important themes of attending with other migraine sufferers and how patients were able to implement changes as a result of the education through informed discussion with their GP or changes to lifestyle and medicines.

e.g. “It was very useful to make a working plan how to help myself to manage the migraines better”.

Conclusion: This pilot study of patients attending a self–management education group for episodic migraine experienced clinically meaningful reduction in disability and was highly rated for effectiveness by the patients who attended.

**THE OPIOID USE IN TURKISH PATIENTS WITH EPISODIC AND CHRONIC MIGRAINE**

D. H. Ertem 1,*, I. Basarir 1, G. B. eryigit 1, N. kocabiyik 1, F. ilik 2

1Neurology, Sisli Hamidiye Etfal Training and Research Hospital, University of Health Sciences, Istanbul, Turkey., istanbul, 2Neurology, KTO Karatay University, Medicana Faculty of Medicine, konya, Turkey

**Introduction:** Despite the inadequate evidence of efficacy and safety of the use of opioids for treatment of migraine, it has been reported that patients with severe migraine headaches are prescribed for opioids for pain relief. Drug interactions, abuse, and tolerance are some disadvantages of opioid therapy in migraine. There are studies evaluating opiophobia, prejudice against the use of opioid analgesics by patients and physicians, and the use of opioids for the management of cancer pain in Turkey. However, the opioid use in Turkish migraineurs has not been well documented.

**Objectives:** The aim of this study was to assess the opioid therapy knowledge and use frequency among patients with episodic and chronic migraine.

**Methods:** In this prospective cohort study, we enrolled consecutive migraine patients in our headache clinic during the study period. The diagnosis of migraine was made according to the International Classification of Headache Disorders 3rd edition beta version. The socio-demographic and clinical characteristics were recorded for all patients. Furthermore, patients were asked about the knowledge and use of opioids for migraine headache pain.

**Results:** One hundred patients were enrolled, of which 69 were episodic migraine and 31 were chronic migraine. The mean age of patients was 41.41±12.14, 82 % were female. The duration of migraine was 12.3±10.37 years in episodic migraine and14.2±9.2 years in chronic migraine. Eighty-eight per cent of patients with chronic migraine were treated with at least one preventive treatment. For acute migraine attack treatment, paracetamol, nonsteroidal anti-inflammatory drugs, triptans, and antiemetics were taken in frequency order. All subjects reported that any kind of opioids was not offered or prescribed by general practitioners and neurologists for their headache pain. Besides this, only 8 (8%) patients declared that they heard the use of opioids for the treatment of migraine but they never consulted their doctors.

**Conclusion:** Our results show that opioids are not preferred as an option for acute or preventive migraine treatment by Turkish migraineurs and their physicians.

**References:**
SMARTPHONE OVERUSE AS A TRIGGER FACTOR FOR MIGRAINE ATTACKS
F. Ilik 1, H. Buyukgol 1, D. H. Ertem 2,*, M. uyar 3
1 Neurology, Karatay University, Medicana Faculty of Medicine, konya, 2 Neurology, Sisli Hamidiye Etfal Training and Research Hospital, University of Health Sciences, istanbul, 3 Public Health , Necmettin Erbakan University Meram Faculty of Medicine, konya, Turkey

Introduction: Trigger factors for migraine attacks are usually identified such as hunger, dehydration, changes in weather, stress, hormonal changes, dietary factors, and bright light. The importance of the knowledge of trigger factors is that it can be helpful to predict migraine attacks and decrease the probability of an attack. It has been reported that high levels of screen time exposure are associated with migraine in young adults. Smartphone addiction has been defined as the overuse of smartphones to the extent that it disturbs the users’ daily lives.

Objectives: Some of our patients with migraine had reported that long and continuous smartphone use triggered their migraine attacks. In this study, we aimed to evaluate the impact of smartphone overuse on frequency and severity of attacks in patients with migraine without aura and to assess whether the use of excessive smartphone use could trigger migraine.

Methods: Three hundred and one consecutive newly diagnosed patients within normal physical and neurological examinations, who fulfil criteria of migraine without aura of The International Classification of Headache Disorders (2013 ICHD-III beta version), were enrolled in this study. Socio-demographical characteristics of patients were recorded. To evaluate the disability and severity of migraine, the Migraine Disability Assessment Questionnaire (MIDAS) and Visual Analogue Scale (VAS) were used. Smartphone overuse was assessed by smartphone addiction scale (SAS). Patients were assigned into two groups according to smartphone use: low smartphone users (median SAS score <69) and high smartphone users (median SAS score ≥69). All the results were analysed by Statistical Package for the Social Sciences software version 22.0.

Results: Mean age of patients was 32.98 ± 6.19, 77.7 % were female. Mean duration of headache was 4.32 ± 3.15 years. The number of high smartphone users was 151 (50.16%). Among them, 60 high smartphone users (39.7%) reported that smartphone use was related to trigger their migraine attacks and 92.7% of these patients suffered from light sensitivity. Only 12 low smartphone users (8%) reported that smartphone use triggered their migraine attacks. The number of migraineurs whose attacks were triggered by smartphone use in high smartphone use group was significantly higher than the number of lower smartphone user group (p=0.00). Moreover, VAS and MIDAS scores were significantly higher in patients using the smartphone more frequently than lower smartphone users (p=0.01, p=0.00, respectively).

Conclusion: Our results show that smartphone use is associated with migraine attacks. Patients with migraine without aura who were smartphone overusers had significantly higher pain intensity and disability scores. Our results support that smartphone overuse may be considered as a trigger factor for migraine attacks.

THE ASSOCIATION BETWEEN CHRONICITY OF MIGRAINE AND COMPLEMENTARY AND ALTERNATIVE MEDICATION USE

D. H. Ertem 1,*, I. Basarir 1, G. B. eriyigit 1, N. kocabiyik 1, F. Ilik 2
1Neurology, Sisli Hamidiye Etfal Training and Research Hospital, University of Health Sciences, Istanbul, Turkey.
2Neurology, KTO Karatay University, Medicana Faculty of Medicine, konya, Turkey

Introduction: The term of Comlementary and Alternative Medication (CAM) is described by patients as all types of practices to prevent or treat illnesses which are not currently considered as a part of conventional medicine. Although the advance in medical and interventional treatment modalities for migraine, it is reported that some patients seek for CAM therapies due to their concerns about potential side effects of these therapies.

Objectives: We aimed to investigate the use of CAM therapies among patients with episodic and chronic migraine and to evaluate association between chronicity of migraine, demographic and clinical characteristics.

Methods: A questionnaire of a list of CAM modalities including traditional therapies specific to Turkish culture which was constructed by researchers through a literature review was given to all patients. Patterns of CAM treatment, patients` reluctance to share CAM use with their doctors were evaluated.

Results: One hundred patients were enrolled, of which 69 were episodic migraine and 31 were chronic migraine. The mean age of patients was 41.41±12.14, 82 % were female. Twenty-four patients with chronic migraine had medication overuse headache. Fifty patients reported that they had heard about CAM treatment for migraine and 36 of them had tried CAM at least once in their lives. Magnesium and Coenzyme Q10 pills (39%), hijama (blood drawing by local suction from small skin incisions) (%30.6), phytotherapy (medical herbalism, namely mint, sesame seed oil, black seed oil, rosemary) (%27.8), acupuncture (22%), vitamin supplements (22%), hypnose therapy (13.9%), and the others (massage, exercise, leeches, cupping, neural therapy, praying, amulet were used in frequency order. Homeopathic treatments were not used. Types of CAM use and number of patients did not differ between episodic and chronic migraine groups. There was no relationship between CAM use and medication overuse headache and demographic characteristics. However, duration of migraine and CAM use showed a moderate correlation regardless of chronicity (p=0.017, r=0.238). 77.7 % of patients who used CAM stated that they preferred not to tell their physicians about CAM use if not asked and paid an average of 125.34±213.28 € (range 0-874.12 €) for these treatments.

Conclusion: Our results show that both episodic and chronic migraineurs use different types of CAM modalities. CAM use is not related to chronicity of migraine and medication overused headache. Patterns of CAM treatment for migraine in Turkey differ from western practices. We observed that due to fear of disapproval, patients tended to hide CAM use from their doctors. Exploring the CAM use among migraineurs is essential for doctors regarding potential interactions and side effects of CAM therapies with conventional treatments.

General aspects of headache care

MTIS2018-162

THE WORKLOAD, VALUE AND COMPLEXITY OF THE HEADACHE SPECIALIST NURSE

R. Bhola \(^1\), A. Bahra \(^2\), P. Goadsby \(^3\)

\(^1\)NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College Hospital, London, \(^2\)Barts Health and The National Hospital for Neurology and Neurosurgery, \(^3\)NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College London, London, United Kingdom

Introduction: Due to its high prevalence and impact, headache is burdensome and costly to the sufferer, society and healthcare services. Multidisciplinary care is increasingly regarded as an efficient mode of service delivery (1). Professional nurses who have acquired the necessary education, skills and expertise increasingly meet patient needs in the UK. However, managing frequent and disabling primary headache, together with co-morbidities, present challenges and complexities.

Objectives: We aim to provide an overview of the workload, complexity and value of the specialist headache nurse.

Methods: We have evaluated patient needs within headache services and the service demands facing the team in practice. The broad aspects of the specialist nurse’s role, its complexity and the required skills will be illustrated.

Results: Our results will provide a representation of how complex care is delivered by the specialist nurse. These professional aspects will include: the nurse’s professional expertise in promoting patient safety, improving quality through audit and research (2), optimising the use of time and costs within the service, meeting the education needs of patients and others involved in patient care and treatment delivery e.g. ward based staff (3) and developing the service. A level of competence is achieved which is adapted to the needs of the organisation and service users and done within resource-constraints.

Conclusion: Patients in headache centres will typically present with complex needs and often co-morbidities. The specialist nurse has a key role within UK healthcare. To be effective and efficient the nurse will acquire the necessary education, skills and expertise to manage care and develop their services. The role of the specialist nurse could be extended with more nurses trained to provide the care and support for patients with headache between primary, secondary and tertiary care. Headache services can thus be optimised by the addition of specialist nurses, wherever they may be located in the world (4).

References:


3 Patient satisfaction with hospital management in a referral setting in the UK. Bhola R, Kaube H and Goadsby PJ. Cephalalgia 2004; 24: 1097


Disclosure of Interest: R. Bhola Conflict with: former clinical consultant with eNeura Inc; patent pending with eNeura for preventive treatment of migraine with sTMS., A. Bahra Conflict with: Advisory groups and satellite symposiums for Novartis., P. Goadsby Conflict with: declared for this meeting already, Conflict with: declared for this meeting already
 POTENTIAL CANDIDATE GENES FOR CLUSTER HEADACHE INVOLVED IN CA2+ SIGNALING AND T-CELL DIFFERENTIATION
C. Ran 1,*, C. Fourier 1, A. Steinberg 2, C. Sjöstrand 2, E. Waldenlind 2, A. C. Belin 1
1Neuroscience, Karolinska Institutet, 2Clinical Neuroscience, Karolinska University Hospital, Stockholm, Sweden

Introduction: Genetic variants in PCDHB6, PLCE1, ANO3 and ITGAL have been suggested to associate with a positive response to verapamil in migraine patients. Verapamil is a voltage-dependent calcium channel blocker and a potent vasodilating agent commonly used as a preventive treatment also for cluster headache (CH).

Objectives: We are currently investigating these four genes as potential new candidate genes for CH.

Methods: We used TaqMan SNP genotyping to screen four genetic variants in a Swedish CH case-control material consisting of 630 CH patients and 586 controls. 31,9 % of the CH patients were female, the average age of CH patients was 52 years and 10,6 % had a chronic version of the disorder. Around 30% of the patients used Verapamil as a prophylactic treatment. Most of the controls were anonymous blood donors, 39,4% were female. Genotyping was performed on an Applied Biosystems 7500 Fast system, using the recommended TaqMan reagents and genotyping SNP assays: C__32960006_10 for rs17844444, C___1946626_10 for rs10882386, C__1616984_10 for rs1531394 and C__11789692_10 for rs2230433.

Results: Preliminary data indicates that rs1531394 in ANO3 and rs2230433 in ITGAL might be associated with CH in Sweden. The less common genotype of rs1531394 (AA) is more common in the disease group. This difference in genotype distribution is more pronounced when only patients using verapamil are analyzed. The rs1531394 variant is located in the 5'UTR of ANO3 and constitutes an eQTL according to the gtex portal (http://www.gtexportal.org). Also rs2230433, a missense mutation in ITGAL, potentially affects gene expression. rs17844444 which is located in the PCDHB6 gene and rs10882386 in PLCE1 are not associated with CH in the Swedish cohort.

Conclusion: Our data points to ANO3 and ITGAL as two new candidate genes for CH, these genes might provide new insight to the pathophysiological mechanisms of the disorder. ANO3 encodes a Ca2+ activated Cl– channel and ITGAL is membrane protein involved in T-cell differentiation and signaling. We are currently performing more genotyping experiments to verify these data in the entire case-control material. In a later stage we will analyze at the expression of these genes in patient and control derived cell lines and test gene expression correlation with disease and/or genotype.
Genetics and biomarkers of headache disorders

MTIS2018-030

MICRONA EXPRESSION PROFILE IN MIGRAINE: THE MICROMIG STUDY

V. J. Gallardo 1,*, J. B. Gómez Galván 1, M. Torres-Ferrús 12, A. Alpuente 12, L. Asskour 1, P. Pozo-Rosich 12

1Headache Research Group, Vall d’Hebron Research Institute, 2Neurology, Vall d’Hebron University Hospital, Barcelona, Spain

Introduction: MicroRNAs (miRNAs) are short, non-coding RNAs that modulate gene expression post-transcriptionally. miRNAs have been shown to play crucial roles in human diseases including mental disorders and pain syndromes.

Objectives: To analyze the differential expression of miRNAs in peripheral blood mononuclear cells (PBMC) in migraine.

Methods: Exploratory case control study. Patients diagnosed with migraine with or without aura (ICHD-3 beta), confirmed by a neurologist, and healthy volunteers, who did not have past or first-degree family histories of migraine, were included. To eliminate confounding factors, participants completed a wide-range questionnaire and structured-interview to collect demographic and clinical data. From peripheral blood samples we extracted miRNAs using specific miRNA GenechipTM (Affymetrix) and we used “R” packages and libraries for their analysis. We validated the selected miRNAs predictors using logistic regression (LR) and support vector machine (SVM). We performed a ROC to define the area under this curve (AUC) as a measure of goodness for the previously shaped predictive models.

Results: We recruited 62 (CM 18, EM 22, controls 22) participants. We did not find significant differences between groups except: disability (MIDAS), impact (HIT-6), stress (PSS), anxiety (STAI), depression (BDI-II) and age (controls 33.5±9.7, migraine 41.1±11.1, p-value < 0.05). We used these variables as covariates in the differential expression (DE) analysis. We found 41 miRNA DE between control-migraineurs, 35 control-CM and 24 controls-EM. We built predictive models for each comparison (Controls-Migraine, Controls-CM, Controls-EM) to validated DE candidates. The best model obtained was composed of four-miRNA in the control-migraineurs group computed by a LR with leave-one-out cross-validation with accuracy rate of 70%. The global performance (AUC) of this four-miRNA signature in distinguishing migraineurs from controls was estimated to be 0.94 in the learning set and 0.96 in the testing set.

Conclusion: This analysis proves the existence of a specific miRNAs expression profile which indicates the presence epigenetic mechanisms in migraine. These results will be validated in a larger and more heterogeneous cohort.
Involvement of CGRP receptor RAMP1 in Cluster Headache – A Swedish Case-Control Study

J. Michalska 1, C. Fourier 1, A. Steinberg 2, C. Sjöstrand 2, E. Waldenlind 2, C. Ran 1, A. Carmine Belin 1,*
1Neuroscience, 2Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Introduction: Cluster headache (CH) is a severe neurovascular disorder characterized by recurring headache attacks and vasodilation of cranial arteries. Increased levels of the potent brain vasodilator calcitonin gene-related peptide (CGRP) have been found during the active phase of primary headaches and are hypothesized to be causative for the distinctive vasodilation. The receptor activity-modifying protein 1 (RAMP1) is part of the CGRP receptor complex responsible for ligand binding and specificity and therefore constitutes a promising candidate gene for CH.

Objectives: The aim of this study was to investigate the possible genetic association of RAMP1 with CH in a Swedish CH case-control cohort, with focus on two RAMP1 single nucleotide polymorphisms (SNPs) and quantify RAMP1 mRNA expression levels in biological tissue from CH patients and controls.

Methods: The RAMP1 variants rs3754701 (A>T) and rs7590387 (C>G) were genotyped in 518 CH patients and 585 control subjects. DNA was analysed by quantitative real-time polymerase chain reaction (qPCR). RAMP1 mRNA expression was determined by reverse transcription qPCR in primary fibroblasts from 12 CH patients and 12 neurologically healthy controls.

Results: We identified a significant difference between the CH patient and control group for the allelic distribution of rs3754701 (p=0.0138). In addition, RAMP1 mRNA expression was enhanced in primary fibroblasts from CH patients compared to controls (p=0.0073).

Conclusion: This is the first reported genetic link between the CGRP receptor complex and CH. Based on our results we suggest that the rs3754701 T allele is a susceptibility factor for CH in Sweden. The association between this SNP and CH as well as the enhanced RAMP1 mRNA expression in CH patients strongly support the hypothesis that CGRP and its receptor component RAMP1 are involved in CH pathophysiology.
**Genetics and biomarkers of headache disorders**

**MTIS2018-032**

**SERUM LEVELS OF ACTH, ADH, AND SEROTONIN IN PATIENTS WITH CYCLIC VOMITING SYNDROME VS. MIGRAINE**

T. Hikita 1,*

1Hikita Pediatric Clinic, Kiryu Gunma, Japan

**Introduction:** Cyclic vomiting syndrome (CVS) is included in the subgroup "Episodic syndromes that may be associated with migraine" (Sec. 1.6) in ICHD-3. Previous studies have shown increases of serum adrenocorticotropic hormone (ACTH) and antidiuretic hormone (ADH) levels in some CVS patients, and of ADH level in migraine patients.

**Objectives:** I investigated serum levels of ACTH, ADH, and serotonin in CVS and migraine patients.

**Methods:** Blood samples were taken from patients who visited Hikita Pediatric Clinic and were diagnosed with CVS or migraine during a study period from September 2013 to June 2017. ACTH, ADH, serotonin, and platelet levels were examined, after informed consent was obtained. Abnormally high levels were defined as ACTH > 63.3 pg/ml, ADH > 2.8 pg/ml, serotonin > 200 ng/ml, and platelet count > 35 x 10^4/µl. Frequencies (proportions) of abnormally high levels of these four parameters in CVS vs. migraine patients were compared by Fisher’s exact test.

**Results:** For a group of 25 migraine cases and a group of 12 CVS cases for which blood samples were analyzed following patient reports of headache or vomiting, age ranges were 8-52 and 2-53 years, ACTH ranges were 7.3-103 and 3.9-848 pg/ml, ADH ranges were 0.4-22.6 and 1.3-29.1 pg/ml, serotonin ranges were 84.1-323 and 99.7-452 ng/ml, and platelet count ranges were 14.7-38.4 x 10^4/µl and 23.2-76.7 x 10^4/µl, respectively. For the migraine and CVS groups, abnormally high levels were observed for ACTH in 2 and 5 cases, for ADH in 6 and 7 cases, for serotonin in 8 and 6 cases, and for platelet count in 3 and 2 cases, respectively. Proportion of abnormally high ACTH was higher for the CVS group (5/12) than for the migraine group (2/25) (p= 0.025).

For a group of 11 migraine cases and a group of 9 CVS cases for which blood samples were analyzed even though patients did not report headache or vomiting, age ranges were 9-45 and 2-53 years, ACTH ranges were 8.7-31.9 and 4.4-114 pg/ml, ADH ranges were 0.8-19.4 and 0.9-12.5 pg/ml, serotonin ranges were 41.8-441 and 105-372, and platelet count ranges were 17.9-41.6 x 10^4/µl and 22-42 x 10^4/µl, respectively. For the migraine and CVS groups, abnormally high levels were observed for ACTH in 0 and 1 cases, for ADH in 1 and 2 cases, for serotonin in 8 and 3 cases, and for platelet count in 1 and 3 cases, respectively.

**Conclusion:** For ACTH, abnormally high levels were observed in both the CVS and migraine groups when symptoms (headache, vomiting) were present, and the proportion was significantly higher for the CVS group. For the other clinical parameters, the two groups did not differ significantly in proportion of abnormally high levels.
Genetics and biomarkers of headache disorders

**Abstracts**

**MIGRAINE GENETIC SUSCEPTIBILITY: THE HIDDEN WORLD OF NEUREXIN (NRXN2) AND OTHER COMPONENTS OF THE SYNAPTIC VESICLE MACHINERY**


1UnIGENe, IBMC / I3S, University of Porto, 2ICBAS - University of Porto, Porto, Portugal

**Introduction:** In the last years, we have centered our attention to the synaptic vesicles’ molecular machinery and life cycle, with a central role in neurotransmitter release and its regulation. One example is neurexin (NRXN2), a component of the synaptic vesicle machinery, forming connections between the fusion proteins of intracellular and synaptic vesicles, interacting with other important components of this mechanism as synaptotagmin, GABAA-R or CASK.

**Objectives:** Our aim is to further explore the role and interaction of these proteins involved in the regulatory mechanisms of neurotransmitter release, in migraine susceptibility.

**Methods:** Four tagging single nucleotide polymorphisms (SNPs) of NRXN2 were analyzed in 183 cases and 265 controls. To evaluate association between NRXN2 SNPs and migraine, a multivariable-logistic regression was performed. Allelic and haplotypic frequencies were estimated. Interaction between NRXN2-SYT, NRXN2-GABRE and NRXN2-CASK was assessed by a multivariable-logistic regression and confirmed by a multifactor dimensionality reduction analysis.

**Results:** We found two strong and significant synergistic interactions between migraine liability and the following gene pairs: NRXN2-GABRE and NRXN2-CASK that remained significant after 1000-fold permutation-based correction.

**Conclusion:** For the first time a genetic interaction was found among NRXN2, one of GABA$_A$-receptors and CASK genes showing a synergetic effect of interaction between these genes in migraine susceptibility. These genes interactions may be a small part of a higher network of genes, allowing us to better understand migraine etiology and leading to the development of new therapeutic approaches.
Abstracts

Genetics and biomarkers of headache disorders

MTIS2018-034

GENE EXPRESSION OF THE ENDOCANNABINOID SYSTEM COMPONENTS IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF SUBJECTS WITH MIGRAINE

M. Allena 1,*, R. Greco 1, C. Demartini 1 2, A. M. Zanaboni 1 2, M. Viana 1, D. Piomelli 3, G. Sances 1, C. Tassorelli 1 2

1Laboratory of Neurophysiology of Integrative Autonomic System- Headache Science Center of Pavia, IRCCS Mondino Foundation Pavia, 2Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy, 3Department of Anatomy and Neurobiology, University of California, California, United States

Introduction: Among the mediators involved in the modulation of the trigeminovascular system, the endocannabinoid system (ES) has recently attracted considerable attention. The ES interacts with the serotonergic system, NO synthesis and neuropeptides release, all of which are involved in migraine pain. Increasing experimental and clinical evidence suggests a link between dysregulation of this system and migraine. In particular, patients with chronic migraine had reduced activities of fatty acid amide hydrolase (FAAH) and anandamide (AEA) membrane transporter in platelets when compared to either controls (CT) or episodic migraine.

Objectives: To investigate the possible changes in ES tone in episodic and chronic migraine.

Methods: The gene expression status of some ES components was evaluated by rtPCR in peripheral blood mononuclear cells (PBMCs) of patients with episodic migraine, chronic migraine and age-matched healthy controls.

Results: We detected an increase in cannabinoid2 (CB2) gene expression in PBMCs of migraine subjects, compared to controls. Subjects with chronic migraine showed higher levels of CB2 mRNA when compared to either episodic migraine and controls. CB1 and N-Acyl Phosphatidylethanolamine Phospholipase D (NAPE-PLD) gene expression increased only in chronic migraine patients. A significant decrease in FAAH gene expression was found in all migraineurs compared to controls, with significantly lower levels in chronic migraine patients.

Conclusion: The present findings show significant transcriptional changes in ES components in PBMCs of patients suffering from migraine. These changes are more marked in the chronic subtype of migraine and, for their characteristics, they are likely to reflect ongoing compensatory mechanisms aimed at maintaining AEA levels. Further studies are needed to investigate the epigenetic processes involved in modulating gene expression.

References: -
**Genetics and biomarkers of headache disorders**

**MTIS2018-035**

**GENOME-WIDE ASSOCIATION STUDY IDENTIFIES NOVEL SUSCEPTIBILITY LOCI FOR RESTLESS LEGS SYNDROME IN MIGRAINEURS**


**Introduction:** Migraine and restless legs syndrome (RLS) are comorbid with each other and have bidirectional triggering effects. Genetic variants to explain the comorbidity of RLS and migraine have not been explored using genome-wide association study (GWAS).

**Objectives:** We aimed to explore the susceptibility genes of RLS in patients with migraine.

**Methods:** We conducted a two-stage case-control GWAS to identify susceptibility genes for RLS in patients with migraine. In the discovery stage, we genotyped 115 migraine patients with RLS and 635 migraine patients without RLS using Axiom Genome-Wide CHB Array. In the replication stage, we genotyped 12 single-nucleotide polymorphisms (in \( \text{CCDC141} \), \( \text{VSTM2L} \), \( \text{RUFY3} \) and \( \text{FAM155A} \)) in 149 migraine patients with RLS and 748 migraine patients without RLS using Sequenom. We used morpholino translational knockdown in one-cell stage embryos of zebrafish to study the function of the identified genes, and CRISPR/dCas9 transcriptional knockdown to cross-validate the findings of morpholino. Morphological, cytochemical, and behavioral phenotypes of the morphants were analyzed, and gene rescues were performed to evaluate whether the phenotypes are gene-specific.

**Results:** We identified two novel susceptibility loci rs6021854 (in \( \text{VSTM2L} \)) \((P = 2.73 \times 10^{-7}, \text{OR} = 1.84)\) and rs79823654 (in \( \text{CCDC141} \)) \((P = 3.27 \times 10^{-6}, \text{OR} = 2.04)\) to be associated with increased risk of RLS in migraine patients. Two different morpholinos of \( \text{VSTM2L} \) and \( \text{CCDC141} \) respectively in zebrafish demonstrated hyperkinetic movements of pectoral fins and altered expression of dopaminergic amacrine cells, which could be partially reversed with gene rescue. Transcriptional CRISPR/dCas9 knockdown replicated the findings observed in translationally-knocked down morphants.

**Conclusion:** \( \text{VSTM2L} \) and \( \text{CCDC141} \) are associated with increased risk of RLS in migraine patients. The RLS-relevant phenotypes in zefrafish demonstrated by interrogating these two genes suggest their possible pathogenic roles in RLS.

**References:**


Genetics and biomarkers of headache disorders

MTIS2018-163

RVCL-S, A HEREDITARY SMALL BLOOD VESSEL MODEL FOR MIGRAINE, STROKE AND VASCULAR DEMENTIA: SEARCHING FOR A PREDICTIVE BIOMARKER

I. de Boer 1,*, N. Pelzer 1, E. S. Hoogeveen 1, S. R. Steenmeijer 3, I. C. Notting 3, H. A. Middelkoop 1, M. C. Kruit 2, G. M. Terwindt 1

1Neurology, 2Radiology, 3Ophthalmology, Leiden University Medical Center, Leiden, Netherlands

Introduction: Migraine, stroke and subsequent vascular dementia are the most prevalent neurological disorders causing disability at younger age (migraine) and severe disability and death at later age (stroke and dementia). New preventive therapies are urgently needed for these small vessel disorders. Retinal Vasculopathy with Cerebral Leukoencephalopathy and Systemic manifestations (RVCL-S) is an autosomal dominant neurovascular syndrome caused by mutations in the TREX1 gene for which no curative treatment is available. It manifests as a microangiopathy with retinopathy, migraine, stroke, and vascular dementia and serves as a monogenetic model for these common vascular disorders.

Objectives: We aim to find predictive biomarkers for disease progression in RVCL-S and to further dissect the disease mechanism by studying the natural history of the disease.

Methods: We are conducting a large follow up study on RVCL-S. Data from patients with a proven TREX1 mutation who participated in previous studies on RVCL-S in our centre (Terwindt et al, Brain 1998; Stam et al, Brain 2016) or visited our clinic for Cerebral Hereditary Angiopathies will be collected. This natural follow up will have a duration of at least 5 years. Mutation carriers will be assessed at least yearly, but based on clinical and radiological findings up to every 3 months, with a neurological, ophthalmological, and cognitive evaluation of disease activity, as well as a broad laboratory panel to assess systemic activity. Furthermore, non-invasive state of the art ophthalmological and radiological techniques will be used to study microcirculation in vivo.

Image:

Results: We aim to include 30 presymptomatic and 30 symptomatic patients in a our follow up study. Currently, n=33 patients are included with follow up data for n=21 patients (6 presymptomatic and 15 symptomatic, current follow up <= 4 years). Our first data show migraine without aura to occur at a relative late age and subcortical cognitive impairment in the domains of global and executive functioning at an early age. Imaging shows the known MRI described signs with impressive pseudo-tumours (figure 1) during the first years of follow up in n=3 patients.
Conclusion: This is the first large prospective natural follow up study in RVCL-S. We aim to identify predictive biomarkers for RVCL-S, a monogenic model for common neurovascular disorders, such as migraine and stroke.


Disclosure of Interest: I. de Boer: None Declared, N. Pelzer: None Declared, E. Hoogeveen: None Declared, S. Steenmeijer: None Declared, I. Notting: None Declared, H. Middelkoop: None Declared, M. Kruit: None Declared, G. Terwindt Conflict with: independent support from Netherlands Organization for Scientific Research (NWO), European Community, the Dutch Heart Foundation, and the Dutch Brain Foundation.
Abstracts

Headache pathophysiology: basic science

MTIS2018-036

COMBINATION THERAPY IN A MOUSE MODEL OF MEDICATION OVERUSE HEADACHE.
C. Saengjaroentham 1,*, P. J. Goadsby 1, P. R. Holland 1
1Basic and Clinical Neuroscience, King’s College London, London, United Kingdom

Introduction: Triptans and non-steroidal anti-inflammatory drugs (NSAIDs) are widely used as migraine therapies. Not all patients respond to triptan monotherapy, and it has been shown that using both triptans and NSAIDs together increase response rates. However, these drugs may be a risk factor for medication overuse headache (MOH) in migraine patients.

Objectives: Therefore, this study aimed to investigate the impact of combination therapy (sumatriptan and ibuprofen) in a preclinical mouse model of MOH.

Methods: Male C57BL/6J mice (N=38) were injected intraperitoneally with ibuprofen (80 mg/kg), sumatriptan (0.6 mg/kg), sumatriptan and ibuprofen in combination or vehicle control daily for 15 days. Hind paw mechanical withdrawal thresholds were measured every second day using von Frey filaments. On the testing day, mice received one of the four drugs intraperitoneally prior to habituation to the testing apparatus for 30 minutes. The left hind paw was tested in a blinded manner by application of filaments perpendicularly to the plantar surface, starting with a force of 0.4g using the up and down method until a positive response was noted. The mechanical threshold was calculated using the Claplan analysis method and analysed over time via an ANOVA. All animal testing occurred in low-light conditions, between 09:00 and 15:00 to avoid circadian variations.

Table:

Results: Repeated exposure to either sumatriptan (maximally at day 15 by 97.8 ± 0.83%; F[1, 17] = 272.9, P ≤ 0.0001) or ibuprofen (maximally at day 7 by 48.3 ± 7.85%; F[1, 17] = 13.08, P=0.0021) decreased mechanical thresholds. The combination of sumatriptan and ibuprofen reduced mechanical thresholds (maximally at day 15 by 54.7 ±10.43; F[1, 18] = 7.304 P=0.0146); however, the thresholds were significantly greater than the sumatriptan alone group (F (1, 17) = 31.44, P ≤ 0.0001).

Conclusion: Repeated exposure to either sumatriptan or ibuprofen daily for 15 days can induce mechanical hypersensitivity in mice indicative of a MOH-like phenotype. However, ibuprofen has an acute effect to reduce the mechanical thresholds of sumatriptan when tested 30 mins post ibuprofen. The combination of sumatriptan and ibuprofen had comparable effects to ibuprofen alone that resulted in modestly reduced mechanical thresholds compared to sumatriptan alone. It remains to be confirmed if repetitive ibuprofen impacts basal hyperalgesia independent of its acute analgesic activity.

This study is 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.
**Headache pathophysiology: basic science**

**MTIS2018-037**

**CHARACTERISATION OF AN OROFACIAL PAIN ASSESSMENT DEVICE (OPAD) TO MEASURE FACIAL ALLODYNA IN MICE**

P. Sureda Gibert\(^1\)^*, P. J. Goadsby\(^1\), P. R. Holland\(^1\)

\(^1\)Basic and Clinical Neuroscience, King’s College London, London, United Kingdom

**Introduction:** The Orofacial Pain Assessment Device (OPAD) is a behavioural test that measures changes in orofacial nociceptive behaviour (trigeminal nociceptive processing). It is a reward/conflict assay that allows the animal to choose between receiving a reward or avoiding a modifiable thermal stimulus. A decrease in the amount of licking suggests an avoidance behaviour, potentially due to an increased sensitivity to an aversive thermal stimuli. The nature of this method offers a more accurate and robust measure of the complex behaviour of choosing whether to withstand an aversive stimulus or not in freely-behaving mice, with the aim to complement this with other more subjective reflex based testing methods.

**Objectives:** To establish the utility of a novel orofacial pain assessment device (OPAD) as a sensitive tool to measure facial alldynia in freely behaving mice.

**Methods:** The effects of acute nitroglycerin (NTG) administration on thermal orofacial nociceptive withdrawal thresholds were studied. Mice were habituated to the OPAD for two weeks following acute (12 hour) food restriction. Following the demonstration of a stable baseline contact/licking profile mice were tested 10 minutes after intraperitoneal injection of NTG (10 mg/kg) or vehicle control at 30° and 55°. The total contact time and number of licks was recorded as a readout of orofacial thermal withdrawal thresholds. The difference between treatment groups was compared using an unpaired non-parametric Mann-Whitney test via GraphPad Prism 7.01 software (La Jolla, CA). P<0.05 was considered significant.

**Results:** NTG-treated mice (n=10) showed a significantly lower orofacial thermal nociceptive withdrawal threshold compared to Saline-treated mice (n=10) at nociceptive temperatures (55°C), with a median amount of licking of 19 (9.17-29.42) and 73.5 (35-113.3), respectively (p=0.0185). There were no significant differences at non-aversive temperatures (30°C), with a median licking number of 155.5 (84.25-205.5) for the saline-treated (n=10), compared to 143 (108.3-165.8) for the NTG-treated mice (n=10) (p=0.8132).

**Conclusion:** Our data demonstrate that the OPAD is a viable behavioural model of orofacial thermal nociceptive thresholds. As such, we propose to use the OPAD as a sensitive method that can be used to test orofacial sensitivity in conscious freely-behaving mice that is not dependent on reflex behaviours. This will enable the determination of orofacial pain sensitivity in transgenic mice exposed to modulation of specific genetically defined neural-networks using novel chemogenetic approaches.
Headache pathophysiology: basic science

MTIS2018-038

EFFECT OF ACUTE CRANIAL AND EXTRACRANIAL NOCICEPTIVE STIMULATION ON CORTICAL SPREADING DEPRESSION AND NMDA RECEPTOR PHOSPHORYLATION

W. Supronsinchai* and Anan Srikiatkhachorn

Introduction: Episodic nature of migraine implies that threshold for migraine attack can be varied. Several factors, endogenous and environmental, can alter the migraine threshold. Taken that, CSD is a primary event of migraine attack, it is possible that intense sensory stimuli may trigger the CSD or alter the threshold for CSD development. However, the direct evidence demonstrating the effect of strong sensory stimulation on CSD is still not available.

Objectives: To compare the effect of acute cranial and extracranial nociception on cortical spreading depression (CSD) and CSD-induced NMDA receptor phosphorylation in cortical neurons

Methods: Formalin (4%) or saline was injected subcutaneously into the forehead and forepaw of adult male Wistar rats. One hour after injection, CSD was induced by application of potassium chloride to the parietal cortex. The direct current depolarization shift (DC shift) and cortical blood flow were recorded for one hour. Two hours after injection, phosphorylated NR1 was identified by Western blot analysis.

Results: Nociceptive activation induced by formalin injection into forehead and forepaw significantly increased the development of CSD and CSD-evoked cortical hyperemia. There was no difference in pattern of CSD and CSD-evoked hyperemia between cranial and extracranial nociception groups. The phosphorylation NR1 was also increased in cerebral cortex in both nociception groups.

Conclusion: These results showed that nociception can evoke cortical hyperexcitability regardless of the site of stimulation. The mechanism underlying the enhancement may involve modification of the central modulating system.
LAMOTRIGINE EFFECTIVENESS IN A PRECLINICAL MODEL OF TRIGEMINAL AUTONOMIC CEPHALALGIAS

M. Vila-Pueyo 1, P. J. Goadsby 1, P. R. Holland 1,*
1Basic and clinical Neuroscience, King’s College London, London, United Kingdom

Introduction: Trigeminal autonomic cephalalgias (TACs) include cluster headache (CH), paroxysmal hemicrania (PH), hemicrania continua (HC), short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)/short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA). We have previously developed a preclinical model of TACs, where the superior salivatory nucleus (SuS) is stimulated and its parasympathetic outflow is recorded, and have validated the effect of abortive and preventive treatments used in CH and PH, such as triptans, oxygen and indomethacin.

Objectives: To further explore the validity of this preclinical model in SUNCT, we assessed the efficacy of lamotrigine.

Methods: Male Sprague-Dawley rats (n = 24) were anesthetized with isoflurane and maintained with propofol infusion (33-50 mg/kg/h). A small burr hole was drilled in the occipital bone and a tungsten electrode was placed at SuS coordinates for electrical stimulation. A laser Doppler probe was positioned on the ipsilateral anterior choroidal region of the eye to record changes in choroidal blood flow due to parasympathetic outflow during SuS stimulation. Following baseline responses to SuS stimulation, animals were either exposed to 100% oxygen or air during 15 minutes or were intravenously given saline or lamotrigine (5mg/kg) and responses were recorded for 30min or 1 hour, respectively.

Results: As previously reported, treatment with 100% oxygen significantly inhibited the choroidal blood flow responses to SuS stimulation when compared to 100% air-treated animals ($\chi^2 (6) = 16.581, p = 0.011$). Interestingly, the intravenous injection of lamotrigine significantly inhibited the choroidal blood flow responses when compared to saline-treated animals ($\chi^2 (6) = 6.43, p = 0.003$), showing a maximum decrease of 49.6% at 1-hour post injection.

Conclusion: The results demonstrate a clear effect of lamotrigine in the preclinical model of TACs, showing for the first time the efficacy of a treatment used in SUNCT in this model, and suggest that lamotrigine might be acting in the cranial parasympathetic pathway.

Disclosure of Interest: M. Vila-Pueyo: None Declared, P. Goadsby Conflict with: Grants and personal fees from Allergan, Amgen, and Eli-Lilly and Company; and personal fees from Akita Biomedical, Alder Biopharmaceuticals, Cipla Ltd, Dr Reddy’s Laboratories, eNeura, Electrocore LLC, Novartis, Pfizer Inc, Quest Diagnostics, Scion, Teva Pharmaceuticals, Trigema Inc., Scion; and personal fees from MedicoLegal work, Journal Watch, Up-to-Date, Massachusetts Medical Society, Oxford University Press; and in addition, Dr. Goadsby has a patent Magnetic stimulation for headache assigned to eNeura., P. Holland Conflict with: Honoraria for educational and advisory purposes from Allergan, Novartis and TEVA as well as research funding from Amgen.
Abstracts

Headache pathophysiology: basic science

MTIS2018-040

THE EFFECT OF CALCITONIN GENE-RELATED PEPTIDE IN ELECTRICAL PROPERTY OF TRIGEMINAL GANGLION NEURONS

M. Saleeon 1,*, S. Sanguanrangsirikul 2, A. Srikiatkhachorn 3

1MAHIDOL UNIVERSITY, 2Physiology, Chulalongorn University, 3King Mongkut’s Institute of technology ladkrabang, Bangkok, Thailand

Introduction: Calcitonin gene-related peptide (CGRP) is a neuropeptide and expressed in both central and peripheral nervous systems, and is especially enrich in dorsal root ganglion (DRG), trigeminal ganglion neurons(TG). This has the effect of extending the blood vessels of the cerebral nerve and inflammation. Trigeminal system is the most important pathway in the process of craniofacial pain perception. TG neurons can be divided into as small-sized, medium-size and large-sized neurons. Small cells are a nociceptive. Large cells are a non-nociceptive. In previous study showed that CGRP is secreted from small cells that act to recognize pain, but not from large cells. Anatomical studies showed that small cell do not express any CGRP receptor. On the contrary, it is expressed in large cells and satellite glia cell. These findings imply that CGRP does not directly affect small trigeminal fibers. Therefore, indicates that small to medium cells indirectly play a role in peripheral sensitization.

Objectives: In this study purpose the effect of CGRP on the electrical physiology of small TG neurons.

Methods: This experiment remove trigeminal ganglion and culture in primary culture. We used whole-cell patch-clamp recording techniques to estimate the electrophysiological properties of small TG neurons.

Results: The results showed that the small TG neurons in CGRP-treated group is sensitivity more than normal group. Step of action potential, rheobase, threshold of CGRP-treated group was significantly lower than normal group. Total spike of CGRP-treated group was significantly higher than normal group.

Conclusion: Thus, it can be concluded that CGRP indirect affects small cells function, although there is no CGRP receptor. This may be due to large cells secrete chemicals to stimulate small cells


**Headache pathophysiology: basic science**

**MTIS2018-041**

PHARMACOLOGICAL SELECTIVITY OF INHIBITION OF CGRP-INDUCED RELAXATIONS BY ERENUMAB STUDIED IN HUMAN ISOLATED INTERNAL MAMMARY ARTERY

A. E. R. Beltrán 1*, A. L. Ramírez 1, A. J. Bogers 2, A. J. Danser 1, C. Xu 3, J. Snellman 4, A. M. V. D. Brink 1

1Div. of Vascular Medicine and Pharmacology, Dept. of Internal Medicine, 2Dept of Thoracic Surgery, Erasmus MC, Rotterdam, Netherlands, 3Amgen Inc., , Thousand Oaks, CA, United States, 4Novartis Pharma AG, Basel, Switzerland

**Introduction:** Calcitonin gene-related peptide (CGRP) is a potent vasodilator and a key molecule in the pathophysiology of migraine. Currently, the fully human monoclonal antibody, erenumab is being studied for the preventative treatment of migraine. We have previously demonstrated that the anti-CGRP receptor monoclonal antibody erenumab antagonizes relaxations to CGRP in human isolated coronary and internal mammary arteries, has no contractile effect per se and does not affect contractions to sumatriptan.

**Objectives:** To assess the pharmacological specificity of erenumab by investigating whether the vascular responses to ligands other than CGRP are affected by erenumab.

**Methods:** Segments of internal mammary arteries were perioperatively obtained from 7 male patients (age 74±1 years) undergoing coronary artery bypass surgery. Segments were immediately brought to the laboratory and were mounted in Mulvany myographs for isometric tension measurements. Concentration response curves to the vasodilators CGRP (calcitonin gene-related peptide), acetylcholine, sodium nitroprusside, PACAP (pituitary adenylate cyclase-activating peptide), VIP (vasoactive intestinal polypeptide), nicardipine and the vasoconstrictor dihydroergotamine were constructed in a cumulative manner in the absence or presence of 1 µM erenumab.

**Results:** As expected, relaxant responses to CGRP (pEC50 7.75±0.17; n=5) were inhibited (pEC50 5.66±0.81; n=5) in the presence of erenumab. Acetylcholine, sodium nitroprusside, PACAP, VIP and nicardipine all induced concentration-dependent relaxations, while dihydroergotamine induced a concentration-dependent contraction. These responses were all unaffected by the presence of erenumab (in all cases, n=5-6).

**Conclusion:** We have demonstrated the functional specificity of the effect of erenumab on CGRP-mediated responses. The lack of interaction with other vasodilatory peptides (PACAP, VIP), or nitric oxide-mediated endothelium-dependent (acetylcholine) or –independent (sodium nitroprusside) responses is expected, but clinically relevant, particularly in patients who may take a nitrate, calcium channel blocker or dihydro-ergotamine, in addition to erenumab.

**Disclosure of Interest:** A. E. Beltrán: None Declared, A. Ramírez: None Declared, A. J. Bogers: None Declared, A. J. Danser: None Declared, C. Xu Conflict with: Employee of Amgen, J. Snellman Conflict with: Employee of Novartis, A. Brink Conflict with: Research support from Amgen/Novartis and CoLucid/Lilly, Conflict with: Personal compensation from any commercial entity (for-profit business) as an employee, for consulting, serving on a scientific advisory board, speaking, or other activities from Lilly, Teva and Novartis
ERENUMAB (AMG334) AN ANTAGONIST TO CANONICAL CGRP-RECEPTOR DOES NOT IMPAIR VASODILATORY OR CONTRACTILE RESPONSES TO OTHER AGENTS IN HUMAN ISOLATED CEREBRAL ARTERIES

L. Ohlsson 1, E. Kronvall 2, C. Xu 3, J. Snellman 4, L. Edvinsson 1,*

1Departments of Internal Medicine, 2Departments of Internal Medicine and Neurosurgery, Lund University Hospital, Lund, Sweden, 3Amgen Inc., Thousand Oaks, CA, United States, 4Novartis Pharma AG, Basel, Switzerland

Introduction: Calcitonin gene-related peptide (CGRP) is a neuronal transmitter involved in migraine pathophysiology and in other biological functions. Recently, a monoclonal antibody to the canonical CGRP receptor, erenumab (AMG334), showed significant prophylactic efficacy and favourable safety in phase II and III clinical trials for migraine.

Objectives: Given that CGRP can mediate vasodilation, we investigated the effect of erenumab on vasoactive agent responses to CGRP and other mediators using isolated human cerebral and meningeal arteries in the presence/absence of various vasodilatory (e.g. CGRP) and of several vasocontractile mediators.

Methods: Ring segments of human isolated cerebral and meningeal arteries were mounted in a sensitive myograph. Functional responses were studied by first inducing pre-contraction with 30 mM potassium chloride (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, and relaxant responses to substance-P and nicardipine were examined.

Results: 30 mM KCl showed stable contraction and CGRP induced a concentration-dependent relaxation. We observed that (i) erenumab had no direct contractile or relaxant effects, (ii) pre-treatment with erenumab antagonized CGRP-induced relaxation in a competitive manner, (iii) relaxant responses to substance-P and nicardipine were unaffected in the presence of erenumab and (iv) the contraction induced by sumatriptan or dihydroergotamine were unmodified by erenumab.

Conclusion: Our findings demonstrate the specific inhibitory effect of erenumab of CGRP-induced relaxation, while it is not associated with vasoconstrictive effect and does not impact vasorelaxant or contractile responses of other relevant vasoactive agents in human biology.

Disclosure of Interest: L. Ohlsson: None Declared, E. Kronvall : None Declared, C. Xu Conflict with: Employee of Amgen, J. Snellman Conflict with: Employee of Novartis, L. Edvinsson Conflict with: from Novartis
THE NOVEL TRPA1 ANTAGONIST ADM-12 IS A POTENTIAL MEDIATOR OF MIGRAINE PAIN

C. Demartini 1, R. Greco 1, A. Zanaboni 2, G. Tonsi 1, C. Nativi 3, C. Tassorelli 1,4,*

1Headache Science Centre, IRCCS C. Mondino Foundation, 2Headache Science Centre, Dept. of Brain and Behavioral Science, University of Pavia, Pavia, 3Department of Chemistry ‘Ugo Schiff’ and FiorGen, University of Florence, Florence, 4Headache Science Centre, IRCCS C. Mondino Foundation and Dept of Brain and Behavioral Sciences of the University of Pavia, Pavia, Italy

**Introduction:** To date, the pharmacological treatment of migraine remains somewhat unsatisfactory, partly because the pathophysiology of this disabling disease is still poorly understood. Clinical and experimental studies have pointed to the possible involvement of the transient receptor potential ankyrin type-1 (TRPA1) channels in migraine pain.

**Objectives:** To further investigate the role of TRPA1 in the pathophysiology of migraine pain in an animal model using a novel TRPA1 antagonist (ADM_12) as a probe.

**Methods:** The effect of ADM_12 was tested on nitroglycerin-induced hyperalgesia at the trigeminal level were investigated in male rats using the quantification of nocifensive behavior in the orofacial formalin test. The expression levels of the genes coding for c-Fos, TRPA1, calcitonin gene-related peptide (CGRP) and substance P (SP) was evaluated in peripheral and central neuronal areas relevant for migraine pain. In a subset of animals we also analysed CGRP and SP protein immunoreactivity in nucleus trigeminalis caudalis (NTC), one of the main relay station in the transmission of pain originating in the cranial district.

**Results:** ADM_12 reduced the nocifensive behavior (face rubbing) induced by orofacial formalin test in rat made hyperalgesic by nitroglycerin administration. This effect was associated to a significant inhibition of nitroglycerin-induced increase in c-Fos, TRPA1 and neuropeptides mRNA levels in medulla-pons area, cervical spinal cord and in the trigeminal ganglion. No changes were instead observed as regards CGRP and SP protein expression in the NTC.

**Conclusion:** The present findings support a critical involvement of TRPA1 channels in the pathophysiology of migraine and show their active role in counteracting hyperalgesia at the trigeminal level.

**Acknowledgements**

We are grateful to Barbara Richichi and Oscar Francesconi from the Department of Chemistry ‘Ugo Schiff’ of the University of Florence (Italy), University of Florence (Italy).


**Headache pathophysiology: basic science**

**MTIS2018-044**

**EFFECTS OF CALCITONIN GENE-RELATED PEPTIDE ON THE ARTERIAL VASODILATION IN THE EYE AND IMPLICATIONS FOR RETINAL FUNCTION.**

K. A. Haanes 1,*, V. Fedulov 1, F. W. Blixt 2, M. Sheykhzade 3, K. Warfvinge 1, L. Edvinsson 1

1Clinical Experimental Research, Rigshospitalet - Glostrup, Copenhagen, Denmark, 2Division of Experimental Vascular Research, Lund University, Lund, Sweden, 3Drug Design and Development, Copenhagen University, Copenhagen, Denmark

**Introduction:** CGRP is a peptide with strong vasoactive effects. Retinal vasculature is known to be important in retinal ischemia, where vasodilating peptides could be a potential treatment. In addition, CGRP is known to be involved in migraine, a disease with vascular symptoms such as photosensitivity and aura, although they are hypothesized to also involve changes in the CNS.

**Objectives:** We therefore set out to investigate the potential effect of CGRP on the retinal vasculature, and if the retinal and its vasculature could have sensory innervation.

**Methods:** We studied the porcine retinal vasculature and the porcine/rat ophthalmic artery using a wire myograph. The in vivo effect of subconjunctival CGRP on the ciliary arteries was investigated using fundus imaging in male Sprague Dawley rats. To investigate the vasoactive effect of CGRP on retina function, electroretinogram (ERG) was performed. We further applied immunohistochemistry to visualize the innervation of the ciliary and ophthalmic artery. Retrograde tracer experiments, were performed using the dye Dil, injected intravitreally, where we traced the marker back to the trigeminal ganglion.

**Results:** CGRP was shown to be a strong vasodilator in vitro on the porcine ophthalmic artery (Emax dilation 83 ± 5 %), rat ophthalmic artery (Emax dilation 68 ± 6 %) and porcine retinal arteries CGRP (Emax dilation 29 ± 9 %). Furthermore, CGRP caused a rapid and large vasodilation in vivo of the rat ciliary arteries following subconjunctival application. The functional consequence of ciliary artery vasodilation resulting from CGRP application under the conjunctiva of the eyeball was further investigated in dark-adapted rats. CGRP-induced vasodilation of the ciliary artery had a significant effect on the ERG. The ERG data showed an average of 22 ± 9 % increase in B wave and 25 ± 5 % increase in A wave amplitudes compared to the control eye. Our immunohistochemistry confirmed that CGRP fibres are found along both the ophthalmic and ciliary artery. Finally, our retrograde tracing experiment showed that sensory neurons originating in the trigeminal ganglion, innervate the retina

**Conclusion:** CGRP induced vasodilation on the specific arteries tested. We show that nerves originating from the trigeminal ganglion innervate the rat retina, and could therefore be the source of the sensory and vasoactive peptides. Interestingly, subconjunctival addition of CGRP to the rat eye resulted in dilation of ciliary artery and increased amplitudes of both the A-wave and the B-wave measured with ERG. These findings have a big potential for increasing the understanding of functional consequences of modulating the vasculature of the eye. On one hand, increases in A-wave and B-wave amplitude could explain the increased photosensitivity observed in migraine patients. On the other hand, several ischemic eye disorders result from vasoconstriction of vasculature in the eye, and application of exogenous CGRP in these patients could be used as a treatment to improve function.
**Headache pathophysiology: basic science**

**MTIS2018-045**

**BRAIN NETWORKS IN MIGRAINE: CONTINUOUS RESTINGSTATE FMRI OVER 30 DAYS**

L. Schulte*, M. Menz¹, J. Haaker¹, A. May¹

¹Department of Systems Neuroscience, University Medical Center Eppendorf, Hamburg, Germany

**Introduction:** Recent evidence in migraine pathophysiology suggests that certain changes in brain activity take place long before headache onset. Identifying neuronal changes occurring in different stages of the migraine cycle are thus of vast importance in understanding migraine pathophysiology.

**Objectives:** To identify typical changes in resting state connectivity within different stages of the migraine cycle and to thus explore task-free neuronal mechanisms of headache attack generation in migraineurs.

**Methods:** Nine episodic migraineurs underwent daily resting-state functional magnetic resonance imaging for a minimum period of 30 consecutive days, leading to a cumulative number of 282 total days scanned. 15 spontaneous headache attacks preceded by at least 4 consecutive pain-free days were acquired allowing not only for analysis not only of the ictal and the interictal phase of migraine but also the preictal phase. We computed ROI-to-ROI and ROI-to-voxel connectivity for Harvard-Oxford ROIs plus two custom designed ROIs of specific interest (Dorsal Pons and Hypothalamus) over the migraine cycle.

**Results:** Within the ROI-to-ROI analysis, the right nucleus accumbens showed enhanced functional connectivity to the left Amygdala, Hippocampus and gyrus parahippocampalis in the preictal phase compared to the interictal phase. ROI-to-voxel connectivity of the right accumbens with the dorsal rostral pons was enhanced during the preictal phase compared to interictally. Regarding custom defined ROIs, the dorsal pons was ictally functionally stronger coupled to the hypothalamic area than interictally.

**Conclusion:** Using this unique data set it was possible to identify typical changes in functional connectivity involved in the preictal and ictal phase of migraine. Our data suggest that connectivity changes in dopaminergic centers and between the dorsal pons and the hypothalamus might play a role in migraine attack generation and sustainment of migraine pain.
**Headache pathophysiology: basic science**

**MTIS2018-164**

**ENDOTHELUM-DEPENDENT MICROVASCULAR VASODILATATION IN MIGRAINE/STROKE WOMEN: DEVELOPMENT OF A SEX-SPECIFIC METHOD**


1Department of Neurology, Leiden University Medical Centre, Leiden, 2Division of Vascular Medicine and Pharmacology, Department of Internal Medicine, Erasmus University Medical Center, Rotterdam, Netherlands

**Introduction:** Migraine is associated with an increased risk of stroke, especially in women, possibly due to microvascular endothelial dysfunction. Recently, the assessment of microvascular endothelial function by measuring dermal blood flow (DBF) with laser Doppler perfusion imaging after local thermal hyperaemia (LTH), with and without iontophoretic administration of the nitric oxide synthase inhibitor L-NMMA, was validated in healthy men. In a large study aimed to identify female specific risk factors for cardiovascular disease with a special focus on migraine and stroke (CREW: CaRdiovascular hEalthy ageing in Women) we used this method in stroke/migraine women. However, ‘current-induced vasodilation’, an artefact caused by iontophoresis, was observed, inhibiting proper functional LTH assessment.

**Objectives:** The objective of the current study was to develop a more suitable protocol to reduce the current-induced vasodilation effect for assessment in women.

**Methods:** Different iontophoresis protocols were assessed in twelve young, healthy female subjects (18-40 years old). Current intensities were 40, 60 and 80 µA, during 15 min. Time to occurrence of current-induced vasodilation, which was defined as 200% of the baseline DBF values, was recorded. NO inhibition with the adjusted protocol was assessed. Based on these results, an adjusted protocol is now being validated in healthy, middle-aged (40-60 years old) female subjects.

**Results:** In 31 of the 36 measurements iontophoresis resulted in current-induced vasodilation. Time to current-induced vasodilation was not significantly different between the three different currents ($p>0.05$). Based on the time until current-induced vasodilation, the protocol was adjusted from 15 to 7 min of iontophoresis, where 60 µA seemed to be the highest current possible with least subjects showing current-induced vasodilation. This adjusted protocol sufficiently inhibited NO-mediated vasodilation. Validation of the adjusted protocol in five healthy, middle-aged female subjects is being assessed and results will be presented at the congress.

**Conclusion:** The iontophoresis protocol using 60 µA during 7 min seems more reliable to assess NO-dependent DBF response during LTH than 100 µA during 15 min in women. Thus, the method for measuring microvasculature should be adapted when applied to women as sex-differences play a role in the mechanism of current-induced vasodilation.
MODULATION OF THE TRIGEMINAL AUTONOMIC REFLEX BY NONINVASIVE VAGAL NERVE STIMULATION (NVNS): AN FMRI STUDY

M. Moeller 1,*, C. F. Schroeder 1, A. May 1
1Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Introduction: The trigeminal autonomic reflex plays an important role in trigeminal autonomic cephalalgias (TACs). Even though this reflex is quite well understood we still do not know which structures have a modulating effect on the reflex. Recent studies suggest that noninvasive vagal nerve stimulation is effective in cluster headache and further has an inhibitory effect on the trigeminal autonomic reflex. These findings suggest a modulating function of the vagal nerve. However, the mechanisms underlying this effect are still under debate.

Objectives: The aim of the present study was therefore to investigate the effect of nVNS on the reflex with a new high resolution fmri brain stem protocol.

Methods: All together 22 healthy participants (11 female, 11 male, mean age 25.64±3.81) were included into the study, who were free from any headache or psychiatric diseases. The trigeminal autonomic reflex was activated by stimulation of the nasal mucosa with kinetic oscillation stimulation (KOS) during the fmri procedure. For KOS a balloon catheter with an inflatable tip was placed into the participants left nostril, which oscillated during stimulation (40 mbar/50 Hz). In general, this activates the reflex and leads to an increase in lacrimation.

A two-day within-subject design was used and the participants received either nVNS of the left cervical vagal nerve or sham stimulation of the left dorsal neck in a pseudorandomized order. For the fmri procedure each day consisted of 4 sessions, two sessions prior to the nVNS or sham and two sessions post stimulation. The fmri block design included 8 s of stimulation interleaved with 52 s of rest. For the general linear model analysis we performed a physiological noise correction. In order to investigate the lower brain stem and the medulla we used a specific segmentation developed by Blaiotta and colleagues instead of the standard procedure for our SPM analysis.

Results: For the main effect we observed an increased bilateral activation of the insulae and the right SII area and a region in the right basal ganglia during intranasal stimulation (p<0.001, uncorrected, minimum cluster extend of 10 voxel).

The comparison between nVNS and sham showed a decreased activation of brainstem networks including distinct nuclei at the level of the lower and mid pons after stimulation of the left cervical vagal nerve with nVNS during intranasal stimulation (p<0.005, uncorrected, minimum cluster extend of 10 voxel).

Conclusion: In the present study we were able to replicate the results for the main effect from a previous study, where the same paradigm was used in order to activate the trigeminal autonomic reflex and to provoke lacrimation. Furthermore our preliminary data suggests an inhibitory effect on brain stem networks after nVNS. The inhibited regions are located in the region medial to the facial nerve in a region that could be interpreted as the superior salivatory nucleus, which is involved in the trigeminal autonomic reflex.

Disclosure of Interest: M. Moeller Conflict with: travel grant to the the american headache society 60th annual scientific meeting in san francisco by electrocore, Conflict with: talk at the electrocore industrial symposium at the american headache society 60th annual scientific meeting in san francisco, C. Schroeder Conflict with: none, Conflict with: none, A. May Conflict with: unrestricted scientific grant to the university medical center by electrocore
Introduction: Migraine with cranial autonomic symptoms (CAS) has been reported in 26.9% of migraine patients in a population-based study, and in 37.4% in patients presenting at tertiary headache centers. However, there have so far been no reports on migraine with CAS in Japan.

Objectives: To clarify the prevalence of migraine with CAS (CAS+) and without CAS (CAS-) in patients presenting at a tertiary headache center in Japan, and to investigate the clinical phenotype.

Methods: We studied 373 consecutive episodic and chronic migraineurs who presented at the Tominaga Hospital Headache Center with face-to-face interviews, while carefully noting the detailed migraine characteristics as well as using semi-structured questionnaire from August 2016 until January 2018.

Results: According to our findings, 158 out of 373 cases (42.4%) had CAS. The CAS+ cases had more severe headache pain compared to the CAS- cases (NRS 8.25 vs 7.82, p=0.016), more frequent cutaneous allodynia (CA) (31.6% vs 17.2%, p=0.001), osmophobia (53.2% vs 37.2%, p=0.002), and phonophobia (75.9% vs 66.5%, p=0.048).

Conclusion: Migraine with CAS is common at a tertiary headache center in Japan. CAS+ cases are characterized by severe headache, more frequent CA and osmophobia. CA is the most evident clinical manifestation of central sensitization (CS), and osmophobia is reported to be related to CA. It is also reported that inhalation of certain odors may cause severe attacks of headache by stimulation of TRPA1 and the activation of TRPA1 may lead to CS and CA. These findings suggest that the hyperactivity of the trigemino-autonomic reflex due to CS plays a role in CAS+ cases.
CRANIAL AUTONOMIC SYMPTOMS IN CLUSTER HEADACHE INDUCED BY NITROGLYCERIN

D. Y. Wei1 2*, P. J. Goadsby1 3

1Headache Group, Department of Basic and Clinical Neuroscience, Institute of Psychiatry, Psychology and Neuroscience, King’s College London, 2 NIHR-Wellcome Trust Clinical Research Facility, 3NIHR-Wellcome Trust Clinical Research Facility, King’s College Hospital, London, United Kingdom

Introduction: Cluster headache (CH) is characterised by attacks of unilateral excruciating headache, ipsilateral cranial autonomic symptoms (CAS) and/or agitation. Studying CAS can further our understanding of CH pathophysiology, but is limited by the episodic nature of the disease. Nitroglycerin (NTG) is known to induce CH.

Objectives: The aim of this study is to characterise CAS induced by NTG.

Methods: CH patients received intravenous NTG 0.5mcg/kg/min over 20 minutes. CAS and headache phenotype were recorded. The study was approved by the NHS Research Ethics Committee.

Results: Twenty-three patients participated: 83% male and 61% episodic cluster headache. The most common spontaneous CAS reported were lacrimation, nasal congestion and conjunctival injection. Agitation was reported in 96%. Nitroglycerin induced ipsilateral CAS in 91% of the patients, with 74% with ipsilateral pain. Most commonly induced CAS were nasal congestion, lacrimation and periorbital swelling. Agitation was reported in 61%. The majority of the CAS (80%) induced by NTG presented before the onset of severe pain.

Conclusion: We demonstrate that NTG effectively triggers ipsilateral cranial autonomic symptoms in CH patients and that they often present in a phase before the onset of pain reflecting the underlying pathways during a cluster headache attack.
Headache pathophysiology: clinical
MTIS2018-048
ALTERED OCCIPITAL POLE CONNECTIVITY IN CHRONIC VS. EPISODIC MIGRAINE: WHOLE BRAIN REGION-OF-INTEREST ANALYSIS OF RESTING-STATE FUNCTIONAL CONNECTIVITY
N. Imai1,*, A. Moriya1
1Department of Neurology, Japanese Red Cross Shizuoka Hospital, Shizuoka, Japan

Introduction: Resting-state functional magnetic resonance imaging has demonstrated altered resting-state functional connectivity of several regions that participate in pain processing in individuals suffering from episodic migraines.

Objectives: To explore migraine chronification, we investigated differences in whole brain resting-state functional connectivity between patients with chronic and episodic migraine.

Methods: Thirty-one women with chronic migraine and 31 age-matched women with episodic migraine underwent resting-state functional magnetic resonance imaging scanning during the interictal phase. Resting-state functional connectivity was assessed using region-of-interest to region-of-interest analysis with 91 cortical, 15 subcortical, and 26 cerebellar areas.

Image:

Results: Analyses revealed that patients with chronic migraine showed a higher connectivity between the anterior cingulate cortex (AC) and bilateral occipital pole (OP I, OP r) and between the right occipital pole (OP r) and right supramarginal gyrus, anterior division (aSMG r), bilateral planum polare (PP I, PP r), right planum temporale (PT r), and right supplementary motor cortex (SMA r) than patients with episodic migraine.

Conclusion: Our results suggest that the occipital pole plays a key role in migraine chronification.
THE NEURAL SIGNATURE OF CHRONIC MIGRAINE: A RESTING-STATE FUNCTIONAL CONNECTIVITY STUDY OF CHRONIC MIGRAINE

M. J. Lee 1,*, B.-Y. Park 2, C. Lee 1, H. Park 2,3, C.-S. Chung 1
1Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul,
2Department of Electronic, Electrical and Computer Engineering, Sungkyunkwan University, 3Center for
Neuroscience Imaging Research, Institute for Basic Science (IBS), Suwon, Korea, Republic Of

Introduction: Although risk factors promoting conversion to CM have been identified, it is unknown whether interictal brain networks differ between patients with EM and CM.

Objectives: In this study, we aimed to investigate the resting-state functional connectivity in patients with EM and CM with a data-driven method.

Methods: We prospectively recruited patients with migraine aged 18 – 60 visiting the headache clinic of Samsung Medical Center from July 2016 to December 2017. All patients underwent a thorough clinical evaluation and 3T MR imaging using an identical scanner. Patients were considered interictal if they did not have a migraine headache at the day and ± 1 days of fMRI acquisition. Using the group independent component analysis (ICA), connectivity analysis with weighted and undirected network model was performed. The between-group differences in DC values were assessed using permutation tests.

Results: A total of 62 patients (44 EM and 18 CM) were included for this study. Among seven functionally interpretable ICs were identified, patients with CM showed stronger connectivity between anterior cingulate cortex, precuneus, dorsolateral prefrontal cortex, and anterior insula than those with EM (p=0.0130, permutation test corrected). This association remained significant after adjusting age, sex, MWA, allodynia, depression and anxiety (p=0.0051, permutation test corrected). Headache days, depression, anxiety, allodynia, and disease duration was not associated with the alleged connectivity. Depression, anxiety, or the presence of mild non-migrainous headache at the day of fMRI acquisition did not modify the effect of CM on the strength of network connectivity (P for interaction = 0.425, 0.479, and 0.372, respectively).

Conclusion: CM patients have stronger connectivity between areas of pain attention, pain expectation, and pain catastrophizing. These findings suggest that a unique interictal neural network of CM may exist.

Disclosure of Interest: M. J. Lee Conflict with: National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIP) (No. 2017R1A2B4007254)., B.-Y. Park Conflict with: National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIP) (No. 2017R1A2B2009086), C. Lee: None Declared, H. Park: None Declared, C.-S. Chung Conflict with: National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIP) (No. 2017R1A2B2009086)
MTIS2018-051
ALTERATIONS IN CEREBRAL BLOOD FLOW ASSOCIATED WITH THE PREMONITORY PHASE OF MIGRAINE
N. Karsan*, P. Bose, F. O. Zelaya, P. J. Goadsby

Introduction:
The premonitory phase of migraine is an area of increased research interest, because of the insights it can offer into understanding the neurobiology of the disorder (1,2).

Objectives: We aimed to study the phenotype and imaging characteristics of the premonitory stage using nitroglycerin-triggered attacks.

Methods:
Subjects (n=25) were recruited following screening and informed consent and exposed to either a 0.5mcg/kg/min NTG infusion over 20 minutes or placebo. Each subject was randomised to receive both infusions on two different visits and was blinded to which treatment was being administered. Following the infusion, the timeline and phenotype to development of migraine symptoms was documented. Pseudocontinuous arterial spin labelled (pCASL) imaging as a measure of cerebral blood flow (CBF), was acquired at baseline, during the premonitory stage, during migraine headache and following headache resolution with treatment.

Table:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Tiredness</th>
<th>Neck stiffness</th>
<th>Yawning</th>
<th>Mood change</th>
<th>Thirst</th>
<th>Concentration change</th>
<th>Photophobia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohen’s kappa coefficient</td>
<td>0.51</td>
<td>0.4</td>
<td>0.3</td>
<td>0.075</td>
<td>0.4</td>
<td>0.2</td>
<td>0.14</td>
</tr>
<tr>
<td>Percentage of agreement between spontaneous and triggered attacks (%)</td>
<td>85% (45/53)</td>
<td>70% (37/53)</td>
<td>64% (34/53)</td>
<td>47% (25/53)</td>
<td>72% (38/53)</td>
<td>66% (35/53)</td>
<td>51% (27/53)</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>0.006</td>
<td>0.028</td>
<td>0.468</td>
<td>0.004</td>
<td>0.117</td>
<td>0.177</td>
</tr>
</tbody>
</table>
Abstracts

Image:

**Results:**
There was a significant difference in increases in CBF with NTG relative to placebo during the premonitory phase compared to baseline in a large cluster that included the frontal and cingulate cortices, thalamus, amygdala, head of caudate, putamen and pallidum ($p<0.001$, FWE-corrected for multiple comparisons at the cluster level). Small volume correction revealed significant increases in blood flow in the hypothalamus ($p=0.026$, peak-level FWE corrected). Post-hoc paired $t$-tests revealed significantly increased CBF in the region of the substantia nigra ($p=0.041$, peak-level FWE corrected) and significant decreases in CBF in a cluster including the occipital and posterior parietal cortices ($p<0.001$, FWE-corrected for multiple comparisons at the cluster level).

**Conclusion:** The premonitory stage of migraine is associated with significant alterations in CBF in brain areas of interest in migraine, in particular in areas with functional correlation with the clinical symptomatology displayed during this phase.

**References:**
Headache pathophysiology: clinical
MTIS2018-052
DYSFUNCTIONAL CEREBELLO-THALAMO-CORTICAL INHIBITORY PATHWAY IN CHRONIC MIGRAINE
G. Coppola*, C. Centurioni 1, C. Abagnale 1, V. M. Parisi 2, M. Serrao 1, C. Di Lorenzo 3, F. Pierelli 4
1Department of Medico-surgical Sciences and Biotechnologies, Sapienza University of Rome Polo Pontino, Latina,
2Research Unit of Neurophysiology of Vision and Neuroophthalmology, G.B. Bietti Foundation IRCCS, Rome,
3Neurology section, Don Carlo Gnocchi Onlus Foundation, Milan, 4Headache Clinic, IRCCS Neuromed, Pozzilli, Italy

Introduction: Previous structural neuroimaging studies suggest that patients with chronic migraine (CM) with and without medication overuse have abnormal structural changes within the cerebellum. In healthy humans, the cerebellum exerts a suppressive effect on the contralateral motor cortical response, through a cerebello-thalamo-cortical pathway.

Objectives: Here, we investigate the functional correlates of the structural abnormalities previously observed within the cerebellum in CM patients.

Methods: We recruited 19 patients affected from CM (11 without and 8 with medication overuse), and we compared them to a group of 18 healthy volunteers (HVs). After a conditioning single pulse high-voltage electrical stimulation delivered over the posterior surface of the mastoid processes (anode placed on the right side, and the cathode on the left), a TMS pulse was delivered over the contralateral motor cortex with 5, 7, 10, and 15 ms interstimulus interval (ISI) in random order. Five stimuli were delivered at each ISI. Motor cortical excitability changes were evaluated by amplitude changes of EMG responses from the first dorsal interosseous muscle to motor cortical stimulation.

Results: In HVs, suppression occurs at an ISI of 5 ms (-19.4%) and lasts a few milliseconds. In CM patients, conditioning electric stimulation over the cerebellum did not reduce the size of MEPs to test TMS of the motor cortex at conditioning-test intervals of 5 ms (+3.0%, p=0.022). In CM patients, the percentage of MEP suppression at 5 ms ISI negatively correlated with number of tablets taken per month (r= -0.473, p= 0.04).

Conclusion: We found neurophysiological evidence for dysfunctional cerebello-thalamo-cortical inhibitory pathway in CM, a chronic head pain condition where abnormal structure of the cerebellum had been previously reported. Overall, we reason that abnormal macrostructural and functional patterns in the cerebellum might be involved in cue-elicited acute medication craving. Whether these functional abnormalities are due to primary abnormal cerebellar inhibitory dysfunction or are secondary to a disrupted cerebellar-thalamic-cortical connectivity, remains to be determined.
**Headache pathophysiology: clinical**

**MTIS2018-053**

**CEPHALIC AND EXTRACEPHALIC NEUROPHYSIOLOGICAL EFFECTS OF BOTULINUM TOXIN TYPE A IN CHRONIC MIGRAINE**

G. Coppola*, F. Cortese 1, D. Di Lenola 1, V. M. Parisi 2, M. Serrao 1, C. Di Lorenzo 3, F. Pierelli 4

1Department of Medico-surgical Sciences and Biotechnologies, Sapienza University of Rome Polo Pontino, Latina, 2Research Unit of Neurophysiology of Vision and Neurophthalmology, G.B. Bietti Foundation IRCCS, Rome, 3Neurology section, Don Carlo Gnocchi Onlus Foundation, Milan, 4Headache Clinic, IRCCS Neuromed, Pozzilli, Italy

**Introduction:** Injection botulinum toxin type A (BTX-A) has been approved for the treatment of chronic migraine (CM). Although different studies have shown that this treatment is highly effective and safe, the neurophysiological mechanisms underlying its clinical efficacy are still debated widely.

**Objectives:** This study assessed the segmental, suprasegmental, cephalic, and extra-cephalic effects of BTX-A injection in a group of patients with CM.

**Methods:** We assessed the excitability of the trigeminal system in a group of 13 CM patients (11 with and 2 without medication overuse), by simultaneously recording the blink reflex (nBR), the trigemino-cervical reflex (nTCR), and the pain-related evoked potential (PREP), following stimulation of the right supraorbital nerve with a nociception specific concentric electrode. Further, we recorded the non-noxious somatosensory evoked potentials (SSEPs) amplitude and habituation to verify the influence of BTX-A prophylaxis on the cortical excitability in extracephalic sensory areas. Neurophysiological measurements were recorded before (T0), and 1 month (T1) and 3 months (T3) after BTX-A injections.

**Results:** At month 3, BTX-A significantly reduced the mean monthly headache days, severity of headache (1-3), and the mean monthly tablet intake (all p<=0.001). A significant increase in pain threshold, but not in perception threshold was noted 3 months after treatment compared to baseline (T0=8.3 mA, T2=12.0 mA; p=0.04). Despite a non-significant variation of the 1st nBR and nTCR amplitude blocks, we found that the initial nBR and nTCR lack of habitation was replaced by normal habituating response at 3 months after treatment (p=0.005 for nBR, p<0.05 for nTCR). There were no variations in the initial PREP and SSEP after BTX-A, despite a trend for an increased habituation for PREP and lack of SSEP amplitudes.

**Conclusion:** This is the first study to show that the clinical improvement induced by a single session of BTX-A injection in CM patients may be attributed to the neurophysiological changes that occur at the brainstem and that BTX-A may have an active in modulating the habituation of subcortical trigemino-cervical circuits. Further, our findings suggest that the responsiveness of nociceptive neurons in the dorsal horn, without an evident involvement of cortical circuitries.
**Headache pathophysiology: clinical**

**MTIS2018-054**

**SHORT-TERM PAIRED ASSOCIATIVE STIMULATIONS DO NOT CHANGE CORTICAL VISUAL HYPERRESPONSIVITY OF MIGRAINE PATIENTS BETWEEN ATTACKS**

G. Coppola 1,*, C. Abagnale 1, F. Ranieri 2, C. Centurioni 1, G. Musumeci 2, F. Capone 2, G. Di Pino 2, V. M. Parisi 3, V. Di Lazzaro 2, F. Pierelli 4

1Department of Medico-surgical Sciences and Biotechnologies, Sapienza University of Rome Polo Pontino, Latina, 2Research Unit of Neurology, Neurophysiology, Neurobiology, Department of Medicine, Università Campus Bio-Medico, Rome, 3Research Unit of Neurophysiology of Vision and Neurophthalmology, G.B. Bietti Foundation IRCCS, Rome, 4Headache Clinic, IRCCS Neuromed, Pozzilli, Italy

**Introduction:** In healthy controls (HCs), we recently observed that the same time-dependent paired-associative plasticity rules found within the sensorimotor system are valid for the visual system.

**Objectives:** With the same paradigm of stimulation, here, we have verified whether dysfunctioning associative plasticity might characterize the visual system of episodic migraine without aura patients (MO) where abnormalities in both inhibitory and excitatory paired-associative sensorimotor plasticity have been previously observed in between attacks (1).

**Methods:** In 15 HCs and in 12 MO patients between attacks, we performed a visual paired associative stimulation (vPAS) protocol by coupling 90 black-and-white checkerboard pattern reversals with low-frequency TMS pulses over the occipital cortex at 2 interstimulus intervals in separate sessions by subtracting or adding 25ms to the visual evoked potential (VEP) P100 latency. We recorded VEPs (600 sweeps) before, after, and 10-min later each vPAS session. VEPs were partitioned in 6 blocks of 100 sweeps. We analysed VEP N1-P1 first block amplitude and delayed habituation.

**Results:** While vPAS-25 significantly enhanced and vPAS+25 reduced VEP amplitude habituation in HCs, they both did not significantly changed VEP amplitude habituation in MO between attacks.

**Conclusion:** We provide for the first time evidence for lack of excitability depressing and enhancing short-term associative plasticity mechanisms within the visual system in migraine between attacks.

**Headache pathophysiology: clinical**

MTIS2018-055

**TRANSVERSE SINUS STENOSIS IN REFRACTORY CHRONIC HEADACHE PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY**

V. Favoni*, G. Pierangeli¹², F. Toni³, L. Cirillo³, C. La Morgia¹, S. Abu-Rumeileh¹², M. Messia³, R. Agati³, P. Cortelli¹², S. Cevoli³

¹Department of Biomedical and NeuroMotor Sciences (DiBiNeM), University of Bologna, ²IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy, ³Neuroradiology Department, IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy

**Introduction:** A diagnosis of idiopathic intracranial hypertension without papilledema (IIHWOP) should be considered in chronic headache (CH) patients refractory to preventive therapy. The role of transverse sinus stenosis (TSS) at magnetic resonance venography (MRV) is still unclear.

**Objectives:** To clarify the clinical/diagnostic significance of TSS at MRV in a series of consecutive refractory CH patients.

**Methods:** This is a prospective observational study. Forty patients without evidence of papilledema at fundoscopic examination underwent MRV and a lumbar puncture (LP) with opening pressure (OP) measurement to rule out idiopathic intracranial hypertension without papilledema (IIHWOP). CSF withdrawal was performed in patients with CSF OP>200 mmH2O. TSS was determined using the combined conduit score (CCS) previously proposed by Farb. Effect of CSF withdrawal was evaluated with a MRV study at 1 month.

**Results:** Nineteen cases (47.5%) had MRV evidence of TSS: bilateral (BTSS) in 7 patients (17.5%); unilateral (UTSS) in 12 cases (30%). Nine cases (22.5%) had OP greater than 200 mmH2O and underwent CSF withdrawal. No statistical significant differences were found regarding TSS between patients with OP<200 mmH2O and those with OP>200 mmH2O. In particular, BTSS were found in 3 (42.9%) patients with OP<200 mmH2O, 3 (42.9%) patients with OP between 200 and 250 mmH2O and 1 (14.3%) patient with OP >250 mmH2O. Among patients with UTSS, 10 (83.3%) had OP had OP<200 mmH2O and 2 (16.7%) patients had OP between 200 and 250 mmH2O. Among patients with no TSS evidence 18 (85.7%) patients had OP<200 mmH2O, 2 (9.5%) patients had OP between 200 and 250 mmH2O and 1 (4.8%) patient had OP >250 mmH2O. At Spearman bivariate test, there was no effect of OP on CCS score. All the 9 patients with OP>200 mmH2O repeated MRV one month after CSF withdrawal. No changes of CCS scores were found.

**Conclusion:** In our study, we found a high prevalence (47.5%) of TSS in CH patients refractory to medical treatments. Our result suggest that the isolated TSS finding is not suggestive of intracranial hypertension. However, we confirm that the diagnosis of IIHWOP should be based on the combination of neuroradiological findings and CSF OP.
**Headache pathophysiology: clinical**

**MTIS2018-056**

**ALTERED RESTING-STATE BETWEEN-NETWORKS FUNCTIONAL CONNECTIVITY IN PATIENTS WITH CHRONIC MIGRAINE**

G. Coppola*, B. Petolicchio¹, A. Di Renzo², E. Tinelli¹, C. Di Lorenzo³, V. M. Parisi², M. Serrao⁴, V. Calisti⁵, S. Tardioli³, G. Cartocci⁵, F. Caramia⁶, V. Di Piero⁵, F. Pierelli⁶

¹Department of Neurology and Psychiatry, Sapienza University of Rome, ²Research Unit of Neurophysiology of Vision and Neuroophthalmology, G.B. Bietti Foundation IRCCS, Rome, ³Neurology section, Don Carlo Gnocchi Onlus Foundation, Milan, ⁴Department of Medico-surgical Sciences and Biotechnologies, Sapienza University of Rome Polo Pontino, Latina, ⁵Neurology section, Sapienza University of Rome, Rome, ⁶Headache Clinic, IRCCS Neuromed, Pozzilli, Italy

**Introduction:** In episodic migraine patients, we previously observed evidence for changes in functional connectivity (FC) between various independent networks using resting state functional magnetic resonance imaging (RS-fMRI) depending on attacks frequency and migraine phase (ictal/interictal).

**Objectives:** Here, we investigated RS-fMRI using independent component analysis (ICA) to determine the functional connectivity between networks in chronic migraine (CM) patients.

**Methods:** Twenty patients with untreated chronic migraine (CM) without medication overuse underwent 3T MRI scans and were compared to a group of 20 healthy volunteers (HV). We used MRI to collect resting state data among three selected resting state networks, identified using group ICA: the default mode network (DMN), the executive control network (ECN), and the dorsal attention system (DAS).

**Results:** Compared to HVs, CM patients showed significant reduced functional connectivity between the DMN and the ECN. Moreover, in patients, the DAS showed significant stronger FC with the DMN and weaker FC with the ECN. The severity of headache attacks was correlated positively with the strength of DAS connectivity, and negatively with the strength of ECN connectivity.

**Conclusion:** These results provide evidence for large-scale reorganization at the level of the functional networks during chronic migraine. They further suggest that the severity of migraine pain is associated with proportional inverse pattern of frontal executive and dorsal attentive networks connectivity.
**Headache pathophysiology: clinical**

**MTIS2018-057**

**INTERICTAL INCREASES IN CEREBRAL BLOOD FLOW IN PATIENTS WITH EPISODIC MIGRAINE**


---

**Introduction:** Migraine pathophysiology is complex and its neuronal pathways are not fully understood. In patients with migraine with aura (MwA), it has been shown that the source of cortical spreading depression (CSD) is located in the motion-processing area V3A (Hadjikhani et al., 2001) and it overlaps with cortical thickening of the same and other visual brain regions (Granziera et al., 2006). Arterial spin labelling magnetic resonance imaging (ASL-MRI) is a non-invasive imaging method to assess changes in cerebral blood flow (CBF).

**Objectives:** It has not been examined if interictal changes in CBF in episodic migraine are detectable in MwA and migraine without aura (MwoA). We hypothesize that in episodic migraine (EM) increased CBF may be shown in the higher visual cortex due cortical hyperexcitability.

**Methods:** We assessed interictal CBF using 2D pseudo-continuous ASL-MRI with two background suppression pulses. The sample consisted of 17 EM patients (mean age: 32.7 ± 9.9 years, 13 females) according to International Headache Society Criteria, and 19 healthy controls (HC, mean age: 31.3 ± 9.3 years, 10 females). Depression and anxiety was assessed by HADS questionnaire. Headache days were recorded retrospectively based on the MIDAS questionnaire. On the whole-brain level, between-group comparisons were performed with two-tailed unpaired t-tests. A statistical voxel threshold of \( p < 0.001 \) (uncorrected, \( t > 3.3 \)) with an additional cluster correction of \( k > 44 \) voxels was applied to achieve a \( p < 0.05 \) (cluster-corrected). Results were corrected for age, gender, and global CBF. Data analysis was performed with SPM12 (Wellcome Trust, UK) and ASLtoolbox.

**Image:**

---

**Results:** EM patients had a mean of 3.98 migraine days per month (± 3.85, range 0-12.3 days) and showed moderate signs of anxiety (5.29 ± 3.90) and depression (3.24 ± 2.73). Compared to HC they exclusively demonstrated hyperperfusion in the right middle temporal gyrus (MTG), located at V3A (Fig. 1A). This hyperperfusion was also seen when comparing MwA (\( N = 12 \)) with HC (Fig. 1B), but not MwoA with HC. No CBF differences were seen comparing MWA to MwoA. In EM, anxiety was positively associated (\( p < 0.001 \), corrected) with CBF in the left parietal operculum and right angular gyrus.

**Conclusion:** In the interictal state, hyperperfusion was found in the supposed region of CSD onset, located occipito-temporally. We conclude that ASL-MRI is a sensitive method to identify local abnormalities in CBF in episodic migraine with aura. This furthermore points to different underlying pathomechanisms for MwA and MwoA.
Headache pathophysiology: clinical
MTIS2018-166
MIGRAINE AND CLUSTER HEADACHE CLASSIFICATION USING A SUPERVISED MACHINE LEARNING APPROACH: A MULTIMODAL MRI STUDY
R. Messina 1 2,*, R. Leech 3, F. Zelaya 3, O. Dipasquale 3, D. Wei 4, M. Filippi 1, P. J. Goadsby 4
1 Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy, 2 Headache Group, Department of Basic and Clinical Neuroscience, King’s College London, NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College Hospital, London, 3 Centre for Neuroimaging Science, Institute of Psychiatry, King’s College London, 4 Headache Group, Department of Basic and Clinical Neuroscience, King’s College London, NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College Hospital, London, United Kingdom

Introduction: Neuroimaging studies have shown widespread structural and functional abnormalities in cortical and subcortical areas involved in multisensory processing, including pain, in migraine and cluster headache patients.

Objectives: The aim of our study was to identify a magnetic resonance imaging (MRI) pattern that best discriminate controls, migraine and cluster headache patients.

Methods: Functional, pulsed continuous arterial spin labelled and resting state (RS) functional MRI, and structural, diffusion tensor and 3D T1-weighted images, MR modalities were acquired from 20 migraineurs, 20 cluster headache patients and 15 controls. A dual regression analysis was used to study voxel-wise functional connectivity (FC) within brain regions involved in headache pathophysiology (thalamus, hypothalamus, dorsal pons and spinal trigeminal nucleus). Feature selection was performed using a probabilistic spatial independent components analysis. Support vector machine algorithms and a 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 the entire group of headache patients from controls was 82%. The best classification accuracy for discrimination between migraine and controls was 83%, and for cluster headache patients and controls it was 80%. The best classifier yielded an accuracy of 73% in distinguishing cluster headache patients from migraineurs. Distinct functional and structural MRI features contributed to the different classification models. The right thalamic RS FC was the most useful feature between headache and control groups. The right hypothalamic RS FC and the RS FC of the left pons had the highest feature importance when classifying migraineurs from controls. The right hypothalamic RS FC was also the most important MRI feature in migraine and cluster headache classification.

Conclusion: The combination of multiple functional and structural MRI patterns can accurately classify patients with primary headaches from a group of controls. Among the different brain networks involved in primary headaches, the thalamus, hypothalamus and pons play a central role in migraine and cluster headache pathophysiology.
**Headache pathophysiology: clinical**

**MTIS2018-167**

**HIPPOCAMPAL VOLUME IS NORMAL IN CHRONIC MIGRAINE WITH MEDICATION OVERUSE**

F. Riederer 1,*, A. R. Gantenbein 2, L. Michels 3, S. Kollias 3, C. Baumgartner 1, P. S. Sandor 2

1Neurological Center Rosenhuegel and Karl Landsteiner Institute for Epilepsy Research and Cognitive Neurology, Vienna, Austria, 2RehaClinic, Bad Zurzach, 3Neuroradiology, University Hospital Zurich, Zurich, Switzerland

**Introduction:** In recent years temporal lobe structures have been suggested to be of importance in migraine pathophysiology. The hippocampus is considered to be involved in pain processing, pain-related anxiety and stress response. Studies on hippocampal volume in migraine have shown mixed results to date.

**Objectives:** To investigate hippocampal volumes in patients with chronic migraine and medication overuse in comparison to a large normal database.

**Methods:** Hippocampal volumes of 58 patients with chronic migraine and medication overuse (42 women, mean age 43±12 years) according to International Headache Society criteria were estimated based on high resolution MRI of the brain and compared against a normal database (58 matched controls, 42 women, mean age 42±12 years, and controls from previous studies, in total N=110).

**Results:** Hippocampal volumes did not differ significantly between chronic migraine patients with medication overuse and healthy controls. Voxel-based analyses showed a small cluster of increased grey matter volume in the right hippocampus, not significant after correction for multiple comparisons. At an uncorrected threshold (p<0.001), grey matter increases were found in regions including basal ganglia, hypothalamus, periaqueductal grey and cerebellum.

**Conclusion:** The present study does not support findings of volume change in the hippocampus in chronic migraine. Basal ganglia and periaqueductal grey matter abnormalities are in line with previous work, changes in the hypothalamus merit further study.

**References:**
Headache pathophysiology: clinical
MTIS2018-168

SELF-REPORTED PREVALENCE OF MIGRAINE TRIGGER FACTORS AND PATIENTS WILLINGNESS TO PARTICIPATE IN FUTURE TRIGGER RESEARCH

I. E. Verhagen\textsuperscript{1,2,*}, G. L. J. Onderwater \textsuperscript{1}, D. S. van Casteren \textsuperscript{1,2}, A. MaassenVanDenBrink \textsuperscript{2}, G. M. Terwindt \textsuperscript{1}
\textsuperscript{1}Department of Neurology, Leiden University Medical Center, Leiden, \textsuperscript{2}Division of Vascular Medicine and Pharmacology, Department of Internal Medicine, Erasmus University Medical Center, Rotterdam, Netherlands

Introduction: Migraine is a multifactorial brain disorder characterised by recurring attacks of severe headache with neurological features. Exactly how attacks are initiated is unknown. Experimental administration of specific substances may provoke attacks. Many patients and physicians are convinced that attacks are provoked by external triggers such as food-items, alcohol, stress, and internal threshold-modulating factors such as hormones. However, evidence supporting this conviction is lacking.

Objectives: The aim of this study was to investigate the self-reported prevalence of several frequently reported migraine trigger factors and to assess patients willingness to participate in future research.

Methods: A survey concerning trigger factors in migraine was performed among 4032 migraine patients from the Leiden University Medical Centre Migraine Neuro Analysis programme (LUMINA) database. The prevalence of several frequently reported trigger factors was assessed. In addition, two separate groups of patients visiting our outpatient headache clinic were included. The first group comprised 53 male and female migraine patients who were asked about multiple trigger factors and willingness to participate in a prospective study. The second group included 48 female migraineurs who were asked about the influence of sex-hormonal changes on migraine and their willingness to participate in a clinical trial regarding hormonal treatment.

Results: In the LUMINA cohort 3785 patients (85% women) participated in the survey. Of these 38% had migraine with aura and 62% migraine without aura. The top three most reported trigger factors were stress (89%), followed by sleep deprivation (81%) and menstruation in women (78%). At our outpatient headache clinic 92% of male and female migraineurs indicated that more research needs to be performed addressing trigger factors in migraine, 64% was willing to participate in a trigger-diary study and 70% in a clinical trial. In the second group, 85% of women stated that the role of sex hormones in migraine should be further investigated, 77% of patients with sex-hormonal related migraine was willing to participate in a diary study and 58% in a clinical trial with hormonal treatment.

Conclusion: Stress, sleep deprivation and menstruation are the top three most patient-reported trigger factors in migraine. Our results indicate the need among migraine patients for research concerning trigger factors and they are promising when it comes to future inclusion of participants.
Abstracts

Migraine - acute therapy
MTIS2018-058

PARTIAL REBREATHING AS MIGRAINE TREATMENT: THE PHYSIOLOGY OF REVERSING CEREBRAL VASOCONSTRICTION

T. Johansen 1 2 *
1School of Engineering, Aarhus University, Aarhus, 2BalancAir, Kongens Lyngby, Denmark

Introduction: A recent randomized, controlled pilot study investigated the use of a partial rebreathing device (PRD) for early treatment of migraine-with-aura attacks (1), with promising results. The PRD elicits steady-state normoxic hypercapnia (NH) and is compact and light-weight. NH markedly increases oxygen brain delivery (DO2brain), and it is hypothesized that NH achieves its effect on migraine by reversing early-attack cerebral vasoconstriction and resulting cerebral hypoxia, hypoxia being known to trigger migraine attacks in patients (2,3) as well as triggering and propagating spreading depressions in brain slices (4).

Objectives: We aimed to estimate which parameters are likely to be most influential on the effect and safety of the device, informing the design of future clinical studies.

Methods: In a modelling and simulation study we investigated the device’s effect on cerebral blood flow, DO2brain, and arterial CO2 - and oxygen tensions (Paco2 and Paco2), taking into account device parameters, ventilatory response level, metabolic rate, altitude above sea level and cardiopulmonary health.

Results: The simulation results indicated that:
- DO2brain can be increased significantly by the use of a PRD, without incurring hypoxemia, e.g. an increase of Paco2 from 38 to 48 mmHg would in a typical healthy young person increase DO2brain by approx. 75%, SaO2 decreasing only by two percentage points. These predictions of PaO2 and SaO2 fit well with experimental data obtained in 18 migraine patients.
- The effect of a given PRD on Paco2 and DO2brain decreases with the user’s ventilatory response level and increases with the metabolic rate.
- PRDs are safe to use in healthy individuals, though a pulse oximeter should always be used in case of unknown acute or chronic lung disease. In addition, PRDs must be used with caution in cases of anaemia or at high altitudes, due to the risk of hypoxemia.

Conclusion: Partial rebreathing devices show promise as a drug-free alternative/adjunctive migraine treatment, simulations concurring with experimental data that the intended state of normoxic hypercapnia is achievable in healthy individuals at low to moderate altitudes.


Disclosure of Interest: T. Johansen Conflict with: is a share holder in BalancAir
PRACTICAL AND CLINICAL UTILITY OF NON-INVASIVE VAGUS NERVE STIMULATION (NVNS) FOR THE ACUTE TREATMENT OF MIGRAINE: POST HOC ASSESSMENT OF THE RANDOMIZED, SHAM–CONTROLLED, DOUBLE-BLIND PRESTO TRIAL

L. Grazzi 1,*, C. Tassorelli 2,3, M. de Tommaso 4, G. Pierangeli 5, P. Martelletti 6, I. Rainero 7, P. Geppetti 8, A. Ambrosini 9, P. Sarchielli 10, E. Liebler 11, P. Barbanti 12 and the PRESTO Study Group

1Headache Center, Carlo Besta Neurological Institute and Foundation, Milano, 2Headache Science Centre, National Neurological Institute C. Mondino Foundation, 3University of Pavia, Pavia, 4Neurophysiology and Pain Unit, University of Bari Aldo Moro, Bari, 5Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Istituto delle Scienze Neurologiche di Bologna, Bologna, 6Department of Clinical and Molecular Medicine, Sapienza University, Rome, 7Department of Neuroscience, University of Turin, Turin, 8Headache Centre, University Hospital of Careggi, Florence, 9IRCCS Neuromed, Pozzilli (IS), 10Neurologic Clinic, Santa Maria della Misericordia Hospital, Perugia, Italy, 11ElectroCore, LLC, Basking Ridge, New Jersey, United States, 12Headache and Pain Unit, IRCCS San Raffaele Pisana, Rome, Italy

Introduction: The efficacy of non-invasive vagus nerve stimulation (nVNS; gammaCore®) for the acute treatment of migraine has been demonstrated in multiple trials using standard end points recommended by the International Headache Society. Here, we examine patient-centric data from the multicentre, double-blind, randomised, sham-controlled PRESTO study.

Objectives: Our aim was to reveal further insights into the practical and clinical utility of nVNS as an acute treatment for migraine by evaluating the ability of this therapy to provide clinically meaningful improvements in pain intensity while reducing the need for rescue medication.

Methods: In the PRESTO study, patients maintained their individualised treatment regimens during a 4-week run-in period. Eligible patients entered a 4-week double-blind period and were randomly assigned to receive nVNS or sham treatment. The double-blind period was followed by a 4-week open-label period, wherein all patients received nVNS. Patients recorded pain intensity for each of their attacks on a 4-point scale (0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain) in electronic diaries at 30, 60, and 120 minutes. In this post hoc assessment of the double-blind period, data from the intent-to-treat population were examined to compare nVNS and sham with regard to the percentage of patients who benefited by at least 1 point in pain intensity during their first treated attack and for all attacks. The percentage of attacks in the double-blind period that required rescue medication at any time point during the attack was also assessed.

Table:

Results: Acute nVNS treatment (n=120) resulted in a significantly higher percentage of patients with a ≥1-point decrease in pain intensity than sham (n=123) for the first treated migraine attack at 30 minutes (nVNS, 32.2%; sham, 18.5%; p=0.020), 60 minutes (nVNS, 38.8%; sham, 24.0%; p=0.017), and 120 minutes (nVNS, 46.8%; sham, 26.2%; p=0.002). These results for the first treated attack were similar to results using the percentage of all treated attacks. The need for rescue medication at any time during an attack was significantly lower with nVNS than with sham treatment for the first attack (nVNS, 40.7%; sham, 58.2%; p=0.013) and all attacks (nVNS, 47.7%; sham, 62.7%; p=0.008).

Conclusion: This post hoc analysis demonstrates that acute nVNS treatment quickly and consistently reduced pain intensity by ≥1 point on a 4-point scale while decreasing the need for rescue medication. These clinical benefits highlight the flexibility and practical utility of nVNS in everyday practice. nVNS offers the possibility to treat multiple attacks without increasing exposure to acute medications and pharmacologic adverse events.
Disclosure of Interest: L. Grazzi Conflict with: Consultancy and advisory fees from Allergan S.p.A. and electroCore, LLC., C. Tassorelli Conflict with: Consultancy fees from Allergan S.p.A.; electroCore, LLC; Eli Lilly and Company; 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 Company; and Teva Pharmaceutical Industries Ltd., M. de Tommaso Conflict with: Advisory fees from Allergan S.p.A.; Neopharmed; and Pfizer Inc., G. Pierangeli: None Declared, P. Martelletti Conflict with: Research grants, advisory board fees, or travel fees from ACRAF; Allergan S.p.A.; Amgen Inc.; electroCore, LLC; Novartis AG; and Teva Pharmaceutical Industries Ltd., I. Rainero Conflict with: Consultancy fees from electroCore, LLC, and Mylan N.V. and research grants from the European Commission – Horizon 2020. He is also a principal investigator for RCTs sponsored by Axovant Sciences Ltd. and TauRx Pharmaceuticals Ltd., P. Geppetti Conflict with: Consultancy fees from Allergan S.p.A., electroCore, LLC, Evidera, Novartis AG, Pfizer Inc., and Sanofi S.p.A. and research grants from Chiesi Farmaceutici S.p.A. He is also a principal investigator for RCTs sponsored by Eli Lilly and Company, Novartis AG, and Teva Pharmaceutical Industries Ltd., A. Ambrosini Conflict with: Consultancy fees from Almirall, S.A., and travel grants from Allergan S.p.A. and Almirall, S.A., P. Sarchielli Conflict with: Clinical study fees from Allergan S.p.A., E. Liebler Conflict with: Employee of electroCore, LLC, and receives stock ownership., P. Barbanti Conflict with: Consultancy fees from Allergan S.p.A.; electroCore, LLC; Janssen Pharmaceuticals, Inc.; Lusofarmaco; and Visufarma and advisory fees from Abbott Laboratories; Merck & Co., Inc.; Novartis AG; and Teva Pharmaceutical Industries Ltd. He is also a principal investigator for RCTs sponsored by Alder BioPharmaceuticals Inc.; Eli Lilly and Company; GlaxoSmithKline Pharmaceuticals Ltd.; and Teva Pharmaceutical Industries Ltd.
**Migraine - acute therapy**

**MTIS2018-060**

ADDITIONAL FINDINGS FROM THE RANDOMISED, SHAM-CONTROLLED, DOUBLE-BLIND PRESTO STUDY OF NON-INVASIVE VAGUS NERVE STIMULATION (NVNS) FOR THE ACUTE TREATMENT OF EPISODIC MIGRAINE

P. Martelletti 1, L. Grazzi 2, G. Pierangeli 3, I. Rainero 4, P. Geppetti 5, A. Ambrosini 6, P. Sarchielli 7, P. Barbanti 8, C. Tassorelli 9, 10, E. Liebler 11, M. de Tommaso 12, and the PRESTO Study Group

1 Department of Clinical and Molecular Medicine, Sapienza University, Rome, 2 Headache Center, Carlo Besta Neurological Institute and Foundation, Milano, 3 Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Istituto delle Scienze Neurologiche di Bologna, Bologna, 4 Department of Neuroscience, University of Turin, Turin, 5 Headache Centre, University Hospital of Careggi, Florence, 6 IRCCS Neuromed, Pozzilli (IS), 7 Neurologic Clinic, Santa Maria della Misericordia Hospital, Perugia, 8 Headache and Pain Unit, IRCCS San Raffaele Pisana, Rome, 9 Headache Science Centre, National Neurological Institute C. Mondino Foundation, 10 University of Pavia, Pavia, Italy, 11 electroCore, LLC, Basking Ridge, New Jersey, United States, 12 Neurophysiology and Pain Unit, University of Bari Aldo Moro, Bari, Italy

**Introduction:** Non-invasive vagus nerve stimulation (nVNS; gammaCore*) is a practical therapeutic option for the acute treatment of migraine. The multicentre, randomised, double-blind, sham-controlled PRESTO trial provided Class I evidence that for patients with an episodic migraine, nVNS significantly increases the probability of having mild pain or being pain-free 2 hours post stimulation.

**Objectives:** We evaluated the consistency and durability of the efficacy of nVNS in PRESTO using a range of end points beyond those previously reported.

**Methods:** The PRESTO trial consisted of 3 study periods: a 4-week run-in period wherein patients treated their attacks with individualised standard medications, a 4-week double-blind period of randomised treatment with nVNS or sham, and a 4-week open-label period of nVNS. Patients treated up to 5 attacks in the double-blind period and up to 5 more in the open-label period; only 1 attack could be treated in 48 hours. Additional end points reported here include the percentages of all attacks that were aborted and of those with pain relief at 30, 60, and 120 minutes, mean change in pain score at 30, 60, and 120 minutes, sustained response rates through 24 and 48 hours, and acute medication use.

**Table:**

**Results:** Percentages of attacks that were aborted and of those that achieved pain relief at 120 minutes were significantly higher with nVNS (pain-free: 22.9%; pain relief: 35.2%) than with sham (pain-free: 14.8%, p=0.026; pain relief: 24.4%, p=0.018). Results also showed superiority of nVNS vs sham at 60 minutes. The mean change in pain score from baseline to 120 minutes was −0.62 (nVNS) vs −0.23 (sham) for the first attack (p=0.011) and −0.50 (nVNS) vs −0.28 (sham) for all attacks (p=0.057), with similar results seen at 60 minutes. Sustained pain-free and pain relief response rates were high in both the nVNS and sham groups (24 h: ≥75%; 48 h, ≥58%) for both the first attack and all attacks. Patients decreased their acute medications per attack from the run-in period (0.86) to the double-blind period (nVNS, 0.45; sham, 0.55; p=0.054). Across these end points, findings from the nVNS group in the double-blind period were consistent with findings from the open-label period.

**Conclusion:** These additional findings from the randomised sham-controlled PRESTO trial further support the efficacy and reliability of nVNS for the acute treatment of migraine. Therapeutic benefits of this therapy were observed regardless of whether the first attack or all attacks were evaluated. The consistency of response suggests that nVNS is an attractive option for treating multiple attacks while reducing the need for current acute medications and consequently decreasing any drug-related adverse events and risk of medication overuse.
Disclosure of Interest: P. Martelletti Conflict with: Research grants, advisory board fees, or travel fees from ACRAF; Allergan S.p.A.; Amgen Inc.; electroCore, LLC; Novartis AG; and Teva Pharmaceutical Industries Ltd, L. Grazzi Conflict with: Consultancy and advisory fees from Allergan S.p.A. and electroCore, LLC., G. Pierangeli: None Declared, I. Rainero Conflict with: Consultancy fees from electroCore, LLC, and Mylan N.V. and research grants from the European Commission – Horizon 2020. He is also a principal investigator for RCTs sponsored by Axovant Sciences Ltd. and TaurRx Pharmaceuticals Ltd., P. Geppetti Conflict with: Consultancy fees from Allergan S.p.A., electroCore, LLC, Evidera, Novartis AG, Pfizer Inc., and Sanofi S.p.A. and research grants from Chiesi Farmaceutici S.p.A. He is also a principal investigator for RCTs sponsored by Eli Lilly and Company, Novartis AG, and Teva Pharmaceutical Industries Ltd., A. Ambrosini Conflict with: Consultancy fees from Almirall, S.A., and travel grants from Allergan S.p.A. and Almirall, S.A., P. Sarchielli Conflict with: Consultancy fees from Allergan S.p.A.; electroCore, LLC; Janssen Pharmaceuticals, Inc.; Lusofarmaco; and Visufarma and advisory fees from Abbott Laboratories; Merck & Co., Inc.; Novartis AG; and Teva Pharmaceutical Industries Ltd. He is also a principal investigator for RCTs sponsored by Alder BioPharmaceuticals Inc.; Eli Lilly and Company; GlaxoSmithKline Pharmaceuticals Ltd.; and Teva Pharmaceutical Industries Ltd., C. Tassorelli Conflict with: Consultancy fees from Allergan S.p.A.; electroCore, LLC; Eli Lilly and Company; 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 Company; and Teva Pharmaceutical Industries Ltd., E. Liebler Conflict with: Employee of electroCore, LLC, and receives stock ownership., M. de Tommaso Conflict with: Advisory fees from Allergan S.p.A.; Neopharmed; and Pfizer Inc.
**Migraine - acute therapy**

**MTIS2018-061**

**EFFECTS OF NON-INVASIVE VAGUS NERVE STIMULATION (NVNS) ON RESTING-STATE EEG AND LASER-EVOKED POTENTIALS IN MIGRAINE: FINDINGS FROM A SUBGROUP OF PATIENTS ENROLLED IN THE RANDOMISED, SHAM-CONTROLLED, DOUBLE-BLIND PRESTO STUDY**

E. Vecchio 1,*, I. Bassez 2, K. Ricci 3, C. Tassorelli 3,4, E. Liebler 5, M. de Tommaso 1

1Applied Neurophysiology and Pain Unit, SMBNOS Department, Polyclinic General Hospital, University of Bari Aldo Moro, Bari, Italy, 2Department of Data Analysis, Ghent University, Ghent, Belgium, 3Headache Science Centre, National Neurological Institute C. Mondino Foundation, 4Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy, 5electroCore, LLC, Basking Ridge, New Jersey, United States

Introduction: The randomised, double-blind, sham-controlled PRESTO study of non-invasive vagus nerve stimulation (nVNS; gammaCore) provided Class I evidence that for patients with an episodic migraine, nVNS significantly increases the probability of having mild pain or being pain-free 2 hours post stimulation. The mechanism of action of these effects may involve inhibition of the trigeminovascular pathway and suppression of extracellular glutamate in the central nervous system but is likely multifactorial.

Objectives: We evaluated resting-state electroencephalography (EEG) and trigeminal laser-evoked potentials (LEPs) in a subgroup of patients from the PRESTO trial to identify further potential mechanistic actions of nVNS.

Methods: The methods for PRESTO were previously reported. Patients from our site who were enrolled in the trial and agreed to participate in this sub-study underwent EEG and LEP recordings on the day of randomisation (T0) and during (T1) and after (T2) bilateral nVNS or sham stimulations. The EEG was recorded in the third minute of a resting-state condition; 30-ms laser stimulations were then applied to the right and left supraorbital zones for the LEP recordings. Power values for frequencies between 2 and 100 Hz in the resting-state condition; the LEP amplitudes and latencies for N1, N2, and P2 components; and laser pain ratings were measured.

Table:

Results: Of 42 patients enrolled in PRESTO at our study site, 22 agreed to participate in this EEG and LEP sub-study, and 20 had evaluable data (nVNS, n=10; sham, n=10). nVNS induced an increase in the slow delta-theta and alpha bands and, for the left vagal nerve, a slight increase in delta-theta and gamma power. In the nVNS group, the P2 amplitudes for the right and left trigeminal branches were smaller at T1 than at T0. In the sham group, the P2 amplitude for the left trigeminal branch was attenuated at both T1 and T2, but these attenuations did not reach significance. The N2 amplitude was slightly reduced after both nVNS and sham stimulation. Neither nVNS nor sham affected N1 amplitude, latencies (N1, N2, P2), or laser pain ratings.

Conclusion: These EEG and LEP findings suggest that nVNS acts on cortical areas that are responsible for trigeminal pain control. Further studies are warranted to identify potential correlations between these findings and clinical outcomes known to be associated with trigeminal pain processing and modulation.

Disclosure of Interest: E. Vecchio: None Declared, I. Bassez: None Declared, K. Ricci: None Declared, C. Tassorelli Conflict with: Consultancy fees from Allergan S.p.A.; electroCore, LLC; Eli Lilly and Company; 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 Company; and Teva Pharmaceutical Industries Ltd., E. Liebler Conflict with: Employee of electroCore, LLC, and receives stock ownership., M. de Tommaso Conflict with: Advisory fees from Allergan S.p.A.; Neopharmed; and Pfizer Inc.
Migraine - acute therapy

MTIS2018-062

LASMIDITAN INHIBITS DURAL CGRP RELEASE FROM THE RAT TRIGEMINOVASCULAR SYSTEM

A. Labastida-Ramírez 1*, E. Rubio-Beltrán 1, K. A. Haanes 1, J. Danser 1, J. Kovalchin 2, K. W. Johnson 2, C. M. Villalón 3, A. MaassenvandenBrink 4

1 Division of Vascular Medicine and Pharmacology, Erasmus University Medical Center, Rotterdam, Netherlands, 2 Eli Lilly and Company, Lilly Corporate Center, Indianapolis, United States, 3 Dept. of Pharmacobiology, Cinvestav-Coapa, Mexico City, Mexico, 4 Division of Vascular Medicine and Pharmacology, Erasmus MC Rotterdam, Rotterdam, Netherlands

Introduction: Migraine is associated with activation of the trigeminovascular system, resulting in release of calcitonin gene-related peptide (CGRP) and dysfunctional nociceptive transmission. Intravital microscopy of a closed cranial window in rats is a well-established model to study activation of the trigeminovascular system and neurogenic dural inflammation. Lasmiditan is a novel, selective 5-HT1F receptor agonist recently developed for the acute treatment of migraine. While lasmiditan has been efficacious in clinical trials, the exact mechanism of action has not been completely elucidated. Previous ex-vivo studies have shown that lasmiditan can inhibit CGRP release from mouse dura, trigeminal ganglion and trigeminal nucleus caudalis.

Objectives: The present study investigated the effects of lasmiditan (and thus the role of 5-HT1F receptor agonism) in the modulation of peripheral trigeminal CGRP release from trigeminal afferents in the dura of anesthetized rats.

Methods: Male Sprague-Dawley rats (n=54) were anesthetized and the parietal bone was thinned to visualize and measure the middle meningeal artery diameter using intravital microscopy. Vasodilator responses to endogenous (released by 10 µg/kg i.v. capsaicin or 150-250 µA periarterial electrical stimulation) or exogenous (1 µg/kg i.v. bolus) CGRP were elicited in the absence or presence of intravenous vehicle, sumatriptan or lasmiditan (0.3, 1, 3 and 10 mg/kg).

Results: The administration of lasmiditan (0.3-10 mg/kg), as well as the higher doses of sumatriptan (3-10 mg/kg) significantly and dose-dependently attenuated (P<0.05) endogenous CGRP release, but not the effects of exogenous CGRP. Additionally, in contrast to sumatriptan, lasmiditan did not affect blood pressure effects per se at any of the doses tested.

Conclusion: In addition to peripheral and central antinociceptive mechanisms (since lasmiditan can cross the blood-brain barrier), inhibition of dural CGRP release from peripheral trigeminal afferents may contribute to lasmiditan’s efficacy for the treatment of migraine attacks.
Efficacy of M207 (intracutaneous zolmitriptan) for the acute treatment of difficult to treat migraine

S. Tepper 1,*, P. Schmidt 2, D. Kellerman 3, J. Engels 4

1Professor of Neurology+, Geisel School of Medicine at Dartmouth, Hanover, 2Clinical Development and Medical Affairs, 3Clinical Development, Zosano Pharma, Fremont, 4Biostatistical Consultant, Zosano Pharma, Minneapolis, United States

Introduction: Oral triptans have historically not been very effective for certain types of migraines. Typically, these are migraines: 1) associated with rapid onset of nausea and/or vomiting 2) present on awakening 3) that reach peak intensity rapidly or are severe at the time of treatment 4) that have been present for an extended period, and 5) prolonged duration (due to recurrence). M207 is a new intracutaneous formulation of zolmitriptan in development for the acute treatment of migraine. We hypothesized that the very different pharmacokinetic profile seen after application of M207, (more rapid and higher plasma zolmitriptan levels than seen after oral doses of 2.5 to 5 mg of oral zolmitriptan), may be associated with a higher level of efficacy in subjects with difficult to treat migraines.

Objectives: To assess the efficacy of M207 in patients with migraines that historically have been difficult to treat. The methods recently we reported overall study results of a multicenter trial where M207 3.8 mg was superior to placebo for pain freedom (PF) and most bothersome symptom freedom (MBSF) at 2 hours post-dose. Here, we present results of post-hoc analyses for these 2 co-primary endpoints focusing on subgroups of subjects with specific, definable, migraine characteristics at the time of treatment, that are often associated with poor response to treatment. PF and MBSF were analyzed for subgroups in the placebo and M207 3.8 mg treatment groups who 1) had nausea at the time of treatment 2) woke up with migraine 3) had severe migraine pain at the time of treatment 4) treated more than 2 hours after the onset of migraine.

Overall, there were 77 subjects in the placebo group and 82 subjects in M207 3.8 mg group evaluated for efficacy. PF was observed in 14% of placebo and 42% of M207 3.8 mg, MBSF was seen in 42% of placebo and 68% of M207 3.8 mg. The results for PF and MBSF for the definable subgroups are shown below:

Table:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PF 2 Hour</th>
<th>MBSF 2 Hour</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>M207 3.8</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>mg</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>n (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n (%)</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>51</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>7 (14%)</td>
<td>26 (44%)</td>
</tr>
<tr>
<td></td>
<td>0.0005</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>23 (45%)</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>0.0090</td>
<td>40 (68%)</td>
</tr>
<tr>
<td>On Awakening</td>
<td>44</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>7 (16%)</td>
<td>16 (44%)</td>
</tr>
<tr>
<td></td>
<td>0.0056</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>17 (39%)</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>0.0031</td>
<td>26 (72%)</td>
</tr>
<tr>
<td>Severe Pain</td>
<td>33</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>5 (15%)</td>
<td>10 (26%)</td>
</tr>
<tr>
<td></td>
<td>0.2489</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>14 (42%)</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>0.0376</td>
<td>25 (64%)</td>
</tr>
<tr>
<td>Time to Treat ≥ 2hr</td>
<td>39</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>4 (10%)</td>
<td>12 (33%)</td>
</tr>
<tr>
<td></td>
<td>0.0169</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>16 (41%)</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>0.0137</td>
<td>25 (69%)</td>
</tr>
</tbody>
</table>
Note: p-values obtained via CMH test controlling for randomization stratification by Most Bothersome Other Symptom. N=total number of subjects in subgroup, n=number of subjects PF or MBSF.

**Results:** As shown in the table, M207 was superior to placebo for most subgroups evaluated. **Conclusion:** For 3 of the 4 subgroups of difficult to treat migraines, higher response rates were seen with M207 than Placebo (p<0.05). There was a trend for severe migraine pain subjects to respond better to M207, but the p-value was less than 0.05 only for MBSF. M207 3.8 mg may be an effective alternative for the types of migraines that have historically been difficult to treat.

**Disclosure of Interest:** S. Tepper Conflict with: Zosano Pharma, Conflict with: Advisor, P. Schmidt Conflict with: Zosano Pharma, Conflict with: Employee, D. Kellerman: None Declared, J. Engels: None Declared
PERIPHERAL VAGAL NERVE STIMULATION ATTENUATES MIGRAINE AURA: A CASE REPORT

D. Martinelli 1 2*, G. Sances 1, V. Bitetto 1, E. J. Liebler 3, R. De Icco 1 2, C. Tassorelli 1 2
1Headache Science Center, Mondino Institute of Neurology, 2Dept. of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy, 3electroCore LLC, Basking Ridge, United States

Introduction: Non-invasive neuromodulation techniques promise efficacy in the treatment of migraine [1]. Interestingly, Ayata et al. have recently reported that non-invasive direct vagus nerve stimulation (nVNS) significantly suppresses spreading depression susceptibility in the occipital cortex in rats [2].

Objectives: Here we describe a case of a female patient whose aura was repeatedly and consistently shortened by peripheral vagal nerve stimulation using the gammaCore device.

Methods: The subject is a 38-year-old female patient with both migraine with (MA) and without aura (MwA), diagnosed according to the ICHD-3 criteria [3] The reported mean frequency of MwA days per month was 7-8, while the frequency of MA attacks was 4-5 per year. Usual aura consisted in monolateral negative scotoma with gradual onset, progressively evolving into homonymous hemianopia (either left or right), followed by unilateral paresthesia progressively spreading to the arm and hemiface. The full aura duration was usually 60-120 minutes, being followed almost immediately by severe unilateral migraine (either left or right) resistant to triptans. Neuroimaging studies showed only a paraphysiological vascular variation of the anterior communicating artery. The patient was treated with cinnarizine, 25 mg daily, for migraine prevention. She was also on combined oral contraception since 2013, without any worsening effect of hormonal treatment on either MA or MwA.

Results: The patient first used the gammaCore device during a clinical trial [4]. She was trained to deliver one 120” stimulation per side of the neck at the beginning of the attack, regardless of the location of the pain. During the open label phase of the study, she had the chance to treat 3 MA attacks, which she recorded on an electronic diary. She experienced a consistent effect of nVNS in terms of i) a marked reduction of the duration of the visual symptoms (which was down to no more than 1-2 minutes), ii) the complete prevention of the somatosensory aura and iii) the prevention and/or marked attenuation of the painful phase.

Conclusion: Previous data from the literature clearly show that, in animal studies, nVNS modulates multiple pain pathways and decreases cortical spreading depression. VNS activates nucleus tractus solitarius, locus ceruleus and dorsal raphe nuclei, all of which can modulate CSD susceptibility [2]. To the best of our knowledge this is the first documented report on the effectiveness of nVNS using gammaCore on aura symptoms and, together with the experimental data cited above, it provides a rationale for assessing the potential effect of nVNS in the acute treatment of MA.


Disclosure of Interest: D. Martinelli: None Declared, G. Sances: None Declared, V. Bitetto: None Declared, E. Liebler Conflict with: Employee of electroCore, R. De Icco: None Declared, C. Tassorelli Conflict with: CT was PI in the RCT sponsored by electroCore, LLC and participated in an advisory board organized by electroCore, LLC
**Migraine - acute therapy**

**MTIS2018-169**

**DISABILITY IMPROVEMENTS OVER 12 MONTHS WITH LASMIDITAN FOR ACUTE TREATMENT OF MIGRAINE: INTERIM ANALYSIS OF MIGRAINE DISABILITY ASSESSMENT (MIDAS) SCALE CHANGES IN THE GLADIATOR STUDY**

R. B. Lipton 1,*, L. Lombard 2, D. D. Ruff 2, R. M. Nichols 2, J. H. Kuge 2

1Department of Neurology, Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, 2Eli Lilly and Company, Indianapolis, IN, United States

**Introduction:** Lasmiditan is a novel, selective 5-hydroxytryptamine1F receptor agonist under investigation for the acute treatment of migraine in adults. The Phase 3 studies SAMURAI (NCT02439320) and SPARTAN (NCT02605174) evaluated three doses of lasmiditan (50mg [SPARTAN only], 100mg and 200mg). In comparison with placebo, all doses of lasmiditan showed significantly higher rates of freedom from pain two hours post dose. GLADIATOR (NCT02565186) is a prospective randomised open-label Phase 3 study to evaluate long-term intermittent use of lasmiditan for acute treatment of migraine.

**Objectives:** Interim analysis of the effects of lasmiditan on migraine disability assessed with the Migraine Disability Assessment (MIDAS) scale in GLADIATOR.

**Methods:** Patients eligible for SAMURAI or SPARTAN had at least moderate migraine disability (MIDAS score ≥11).1,2 Patients who completed these studies were offered participation in GLADIATOR with randomisation to lasmiditan 100mg or lasmiditan 200mg (1:1). Patients were to use lasmiditan as first treatment for each new migraine attack (with a second dose permitted between 2 and 24 hours for rescue or recurrence of migraine) for up to 12 months. The analysis is based on the MIDAS questionnaire administered at baseline and at months 3, 6, 9 and 12. MIDAS measures lost time due to migraine in days over 3 months in the domains of activity limitations at work, household work or family, social and leisure activity.3,4 MIDAS has demonstrated reliability and validity; scores correlate with clinical judgement on the need for medical care.3,4 This interim analysis includes patients with MIDAS data at baseline and post-baseline; changes were modelled using a mixed model repeated measures analysis.

**Table:**

<table>
<thead>
<tr>
<th>Time of measurement</th>
<th>Mean MIDAS total score for 3 months preceding the assessment (SD)</th>
<th>Least squares mean change from baseline (SE)</th>
<th>Mean MIDAS total score for 3 months preceding the assessment (SD)</th>
<th>Least squares mean change from baseline (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>29.4 (22.4)</td>
<td>—</td>
<td>28.9 (21.1)</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>n=972</td>
<td></td>
<td>n=1063</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>21.2 (20.4)</td>
<td>7.7* (0.7)</td>
<td>21.1 (21.7)</td>
<td>7.0* (0.7)</td>
</tr>
<tr>
<td></td>
<td>n=818</td>
<td></td>
<td>n=884</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>19.1 (20.2)</td>
<td>9.8* (0.7)</td>
<td>18.1 (19.5)</td>
<td>9.2* (0.7)</td>
</tr>
<tr>
<td></td>
<td>n=672</td>
<td></td>
<td>n=719</td>
<td></td>
</tr>
<tr>
<td>9 months</td>
<td>17.3 (17.0)</td>
<td>11.0* (0.9)</td>
<td>16.1 (21.4)</td>
<td>10.1* (0.8)</td>
</tr>
<tr>
<td></td>
<td>n=541</td>
<td></td>
<td>n=581</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>15.3 (16.1)</td>
<td>12.5* (0.9)</td>
<td>13.4 (18.1)</td>
<td>12.2* (0.8)</td>
</tr>
<tr>
<td></td>
<td>n=429</td>
<td></td>
<td>n=418</td>
<td></td>
</tr>
</tbody>
</table>

MIDAS, Migraine Disability Assessment; SD, standard deviation; SE, standard error

*P value <0.001 vs baseline (mixed model for repeated measures)

There were no significant differences between the lasmiditan doses.
Results: Total MIDAS scores are shown in Table 1. At baseline, patients randomised to lasmiditan 100mg had a mean score of 29.4 and patients randomised to lasmiditan 200mg had a mean score of 28.9. Improvements from baseline increased over time for both doses and were statistically significant at all timepoints. At 12 months, improvements in MIDAS score reached 12.5 for lasmiditan 100mg and 12.2 for lasmiditan 200mg. Mean days with headache in past 3 months decreased from 15.5 at baseline to 8.8 at 12 months and from 15.5 to 8.2 at 12 months (both P<0.001) in the lasmiditan 100mg and 200mg groups, respectively. There were no significant differences between the lasmiditan doses.

Conclusion: In this uncontrolled, open-label study, patients randomised to lasmiditan 100mg or lasmiditan 200mg had, on average, severe migraine disability at baseline (mean MIDAS score 21+) and showed a large, clinically meaningful improvement over 12 months of treatment. Migraine disability and headache days improved over time with both doses. These results warrant further investigation in a controlled study.


Disclosure of Interest: R. Lipton Conflict with: RBL 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: 2P01 AG003949 (Program Director), 5U10 NS077308 (PI), RO1 NS082432 (Investigator), 1RF1 AG057531 (Site PI), RF1 AG054548 (Investigator), 1RO1 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, and is senior advisor to Headache, and associate editor to Cephalalgia. He has reviewed for the National Institute on Aging (NIA) and National Institute of Neurological Disorders and Stroke (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, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy’s, Electrocore, Eli Lilly and Company, eNeura Therapeutics, GlaxoSmithKline, Merck, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. He receives royalties from Wolff’s Headache 7th and 8th Edition, Oxford Press University, 2009, Wiley and Informa., L. Lombard Conflict with: Employee and minor shareholder of Eli Lilly and Company, D. Ruff Conflict with: Employee and minor shareholder of Eli Lilly and Company, R. Nichols Conflict with: Employee and minor shareholder of Eli Lilly and Company, J. Krege Conflict with: Employee and minor shareholder of Eli Lilly and Company.
Migraine - acute therapy

MTIS2018-170

A PHASE 1 STUDY TO EVALUATE THE BIOEQUIVALENCE OF ORAL TABLET AND ORALLY DISSOLVING TABLET FORMULATIONS OF RIMEGEPANT, A SMALL MOLECULE CGRP RECEPTOR ANTAGONIST

R. Croop 1,*, A. Ivans 1, D. Stock 1, J. Hould 1, B. A. Morris 1, J. Stringfellow 1, C. M. Jensen 1, J.-A. Moulin 2, R. Larouche 2, M. Tanguay 2, V. Coric 1, R. B. Lipton 3

1Biohaven Pharmaceuticals, New Haven, United States, 2Syneos Health, Quebec, Canada, 3Albert Einstein College of Medicine, New York, United States

Introduction: Rimegepant is an orally administered small molecule calcitonin gene-related peptide (CGRP) receptor antagonist in development for the acute treatment of migraine.

Objectives: This study compared the rate and extent of absorption of rimegepant ODT administered sublingually with rimegepant oral tablet in healthy fasted volunteers.

Methods: This was a single center, randomized, 4-period, 2-sequence, fully replicated, crossover bioequivalence study. Two treatments were given twice: 75 mg rimegepant ODT administered sublingually until fully dissolved then swallowed without water, and 75 mg rimegepant oral tablet swallowed with water. Eligible subjects included adult nonsmokers, aged 18 to 55 years, with BMI between 18.5 and 30.0 kg/m² and weight of at least 50.0 kg for males and 45.0 kg for females. Pharmacokinetic parameters included Cmax, AUC0-t, AUC0-inf, and Tmax. The formulations were considered bioequivalent if, after analyses of primary pharmacokinetic endpoints Cmax, AUC0-t, AUC0-inf, and AUC0-t of the 90% CIs for the ratio of geometric means for all primary endpoints were within 80% to 125%.

Results: In total, 35 subjects were enrolled, and 34 (97.1%) completed the study. The population was 80% male and 80% White; and had a mean age of 37.7 years, BMI of 25.9 kg/m² and weight of 76.6 kg. Statistical comparisons of the log-transformed Cmax, AUC0-t, and AUC0-inf of rimegepant ODT administered sublingually with rimegepant tablet showed that all 90% CIs of geometric mean ratios were within the predefined range of 80% to 125% for bioequivalence. Median Tmax was 1.5 hours for rimegepant ODT administered sublingually versus 2 hours for rimegepant oral tablet. A statistical comparison, using Proc Mixed, found the least-squares means (standard errors) for the ODT and tablet to be 1.48 (0.098) hours and 1.92 (0.163) hours, respectively. The difference in Tmax, 0.44 hours (26 minutes), was statistically significant (P=0.0021). Adverse events (AEs) were reported by 17 subjects; 88.2% of these AEs were mild. One subject withdrew from the study due to a moderate AE of external otitis that was considered unrelated to treatment. No severe or serious AEs were reported.

Conclusion: Rimegepant ODT administered sublingually and rimegepant oral tablet were bioequivalent, and both formulations were well tolerated. The earlier Tmax seen with rimegepant ODT might result in an earlier onset of action for this fast dissolving formulation.
**Migraine - acute therapy**

**MTIS2018-171**

RIMEGEPANT 75 MG, AN ORAL CALCITONIN GENE-RELATED PEPTIDE ANTAGONIST, FOR THE ACUTE TREATMENT OF MIGRAINE: TWO PHASE 3, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIALS

R. B. Lipton 1*, V. Coric 2, E. G. Stock 2, D. A. Stock 2, B. A. Morris 2, T. J. McCormack 2, M. Frost 2, K. Gentile 2, C. M. Jensen 2, G. M. Dubowchik 2, C. M. Conway 2, R. Croop 2, P. J. Goadsby 2

1 Albert Einstein College of Medicine, New York, 2 Biohaven Pharmaceuticals, New Haven, United States

**Introduction:** A previous Phase 2 study of rimegepant — a novel, small molecule CGRP receptor antagonist — found that a 75 mg dose was safe and effective for the acute treatment of migraine.

**Objectives:** Herein we present the results of 2 methodologically identical Phase 3 studies comparing rimegepant 75 mg with placebo in the acute treatment of migraine.

**Methods:** Two double-blind, randomized, placebo-controlled, multicenter studies were conducted (Study 301, NCT03235479; Study 302, NCT03237845). Adults aged ≥18 years with ≥1-year history of ICHD 3-beta migraine could participate. Coprimary endpoints were pain freedom and freedom from the most bothersome symptom (MBS) at 2 h postdose. Subjects received rimegepant or matching placebo and treated a single migraine attack of at least moderate pain intensity. Secondary endpoints were tested using a prespecified hierarchical approach.

**Table:**

<table>
<thead>
<tr>
<th></th>
<th>301 (N=1084)</th>
<th></th>
<th>302 (N=1072)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rimegepant</td>
<td>Placebo</td>
<td>P-value</td>
<td>Rimegepant</td>
</tr>
<tr>
<td>2 h postdose (%)</td>
<td>n=543</td>
<td>n=541</td>
<td></td>
<td>n=537</td>
</tr>
<tr>
<td>Pain-free</td>
<td>19.2</td>
<td>14.2</td>
<td>.03</td>
<td>19.6</td>
</tr>
<tr>
<td>MBS-free</td>
<td>36.6</td>
<td>27.7</td>
<td>.002</td>
<td>37.6</td>
</tr>
<tr>
<td>Photophobia-free</td>
<td>34.9</td>
<td>24.8</td>
<td>&lt;.001</td>
<td>37.4</td>
</tr>
<tr>
<td>Phonophobia-free</td>
<td>38.6</td>
<td>30.9</td>
<td>.03a</td>
<td>36.7</td>
</tr>
<tr>
<td>Pain relief</td>
<td>56.0</td>
<td>45.7</td>
<td>&lt;.001</td>
<td>58.1</td>
</tr>
<tr>
<td>Nausea-free</td>
<td>46.9</td>
<td>41.6</td>
<td>.182</td>
<td>48.1</td>
</tr>
</tbody>
</table>

a Rimegepant n=470 and placebo n=483
b Rimegepant n=345 and placebo n=366
c Rimegepant n=318 and placebo n=322
d Rimegepant n=489 and placebo n=477
e Rimegepant n=362 and placebo n=374
f Rimegepant n=355 and placebo n=336

**Results:** In both studies more than 85% of subjects were women, the mean age was about 41 years, and subjects had ~5 attacks per month. Rimegepant was superior to placebo at 2 h postdose for pain freedom, freedom from the MBS, and pain relief in both studies (P<.03). Durable efficacy versus placebo was also observed at later timepoints, including use of rescue medication within 24 h (301: 20.4% vs 31.8%; 302: 21.0% vs 37.0%); sustained pain freedom 2-48 h (301: 11.6% vs 7.2%; 302: 9.9% vs 6.0%); sustained pain relief 2-48 h (301: 33.7% vs 23.9%; 302: 36.3% vs 22.6%); and normal function at 2 h (301: 33.3% vs 21.8%; 302: 32.6% vs 23.4%). The overall safety of rimegepant was favorable and similar to placebo on tests of liver function.

**Conclusion:** In adults with migraine, a single 75 mg dose of rimegepant oral tablet was significantly more effective than placebo, with comparable safety. These findings complement the positive results seen in previous research.
Disclosure of Interest: R. Lipton Conflict with: receives grant support from the National Institutes of Health, the National Headache Foundation, and the Migraine Research Fund; serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, American Headache Society, Biohaven Pharmaceuticals, Boston Scientific, Bristol Myers Squibb, Cognimed, Dr. Reddy’s Laboratories/Promius Pharma, Eli Lilly and Company, eNeura Therapeutics, Merck, Novartis, Pfizer, and Teva, Inc; holds stock options in Biohaven Pharmaceuticals and eNeura Therapeutics; receives royalties from Wolff’s Headache, 8th Edition., V. Coric Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals, E. Stock Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals, D. Stock Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals., B. Morris Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals., T. McCormack Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals., M. Frost Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals, K. Gentile Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals, C. Jensen Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals., G. Dubowchik Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals, C. Conway Conflict with: Employed by and holds stock/stock options in Biohaven Pharmaceuticals., R. Goadsby Conflict with: personal compensation for consulting, serving on a scientific advisory board, speaking, or other activities with Alder Biopharmaceuticals, Allergan, Amgen, Electrocore, Eli-Lilly, eNeura, Novartis, and Teva; personal compensation in an editorial capacity for Journal Watch, Up-to-Date, Oxford University Press, Massachusetts Medical Society, and Walters Kluwer; compensation for serving on the Board of Directors of Trigemina Inc.; research support from Amgen.
**Migraine - acute therapy**

**MTIS2018-172**

**ASSESSMENT OF MEDICATION OVERUSE HEADACHE (MOH) BY GENERAL PHYSICIANS, PHARMACISTS AND PHARMACY ASSISTANTS: AN INTERNET-BASED SURVEY**

C. Gaul 1*, T. Weiser 2, H. Graeter 2

1 MIGRAINE AND HEADACHE CLINIC, Koenigstein im Taunus, 2 Medical Affairs, Sanofi, Frankfurt, Germany

**Introduction:** Tension-type headache and migraine are frequently treated with over-the-counter (OTC) analgesics like ibuprofen (IBU), paracetamol (PARA), acetylsalicylic acid (ASA) or the combination of PARA, ASA and caffeine (APC). The efficacy and safety of these drugs has been proven. However, overuse may result in medication overuse headache (MOH).

**Objectives:** The aim of this study was to collect data on health care providers’ understanding of MOH.

**Methods:** In June/July 2017, general physicians (n=150), pharmacists (n=151), and pharmacy assistants (PAs) (n=154) answered an internet-based survey on MOH performed by DocCheck Research, Köln, Germany. Herein we present the results on IBU, PARA, ASA and APC.

**Results:** 88% of the HCPs rated the topic MOH as very important. 34% of the participants thought that for IBU, PARA, or ASA the critical maximum duration of daily intake to avoid MOH is 2 weeks. This was estimated by 55% of the participants for APC. Moreover, 15% set the upper limit for the combination at 4 days. In total, the risk for MOH was estimated as “very high” by 50% of the participants for the mono-analgesics compared to 86% for the combinations with caffeine.

Furthermore, the perceived benefit and risk for the various preparations varied greatly. For example, 53% of HCPs rated the efficacy of IBU in migraine as “very high/high”, 47% the tolerability and 27% the risk for MOH, for APC 21%, 15% and 64%, i.e. the benefits were assessed lower and the risks higher.

**Conclusion:** MOH was regarded as a very important topic by the interviewed HCPs. Interestingly, the risk of MOH was overestimated according to the criteria of the International Classification of Headache Disorders. Mono-preparations were assessed differently compared to analgesics containing caffeine, although according to current scientific knowledge both do not have a different risk for MOH (Bigal et al, 2008). There were also discrepancies between the perceptions and current data of efficacy in migraine: APC was rated worse than IBU, although the superiority of the combination was shown in a comparative study and meta-analysis (Goldstein et al., 2006; Petersen, 2017). For the patients, an evidence-based assessment of the benefits and risks of acute pain analgesics for the treatment of tension-type headache and migraine would be desirable.

**References:**

**Disclosure of Interest:** C. Gaul Conflict with: Consulting fees from Sanofi., T. Weiser Conflict with: Employee of Sanofi, H. Graeter Conflict with: Employee of Sanofi
**Introduction:** There is a high unmet need for new prophylactic treatments for migraine, especially for patients who have failed existing migraine therapies or have contraindications. In the STRIVE study (NCT02456740), erenumab 70 mg and 140 mg monthly led to significant improvement of patient-reported outcomes (PROs) in patients with episodic migraine (EM).

**Objectives:** We report STRIVE results from a post hoc subgroup analysis assessing the effect of erenumab (70 mg and 140 mg) vs placebo on PROs in patients with ≥1 prior prophylactic treatment failure (TF) due to lack of efficacy and/or poor tolerability.

**Methods:** Patient-reported outcome endpoints were change from baseline in mean monthly scores over Months 4–6 for the Headache Impact Test (HIT-6), the modified monthly Migraine Disability Assessment Questionnaire (MIDAS; total score, absenteeism, and presenteeism), and the Migraine-Specific Quality of Life Questionnaire (MSQ; -role function restrictive, -role function preventive, and -emotional function), based on eDiary calculations. P-values comparing erenumab versus placebo are nominal without multiplicity adjustment.
### Table: Change from baseline in PROs over Months 4–6 in the subgroup of patients with ≥1 prior prophylactic TF

<table>
<thead>
<tr>
<th>PRO</th>
<th>Placebo N=126</th>
<th>Erenumab 70 mg N=127</th>
<th>Erenumab 140 mg N=116</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIT-6 total score*</td>
<td>-2.8 (-4.0,-1.5)</td>
<td>-5.7 (-6.9,-4.5) TD: -2.9, p&lt;0.001</td>
<td>-6.6 (-7.9,-5.3) TD: -3.8, p&lt;0.001</td>
</tr>
<tr>
<td>MIDAS total score*</td>
<td>-3.2 (-4.9,-1.5)</td>
<td>-6.5 (-8.2,-4.8) TD: -3.3, p&lt;0.001</td>
<td>-6.7 (-8.5,-4.9) TD: -3.5, p&lt;0.001</td>
</tr>
<tr>
<td>MIDAS absenteeism score*</td>
<td>-1.9 (-2.9,-0.9)</td>
<td>-3.3 (-4.4,-2.3) TD: -1.4, p=0.016</td>
<td>-3.6 (-4.7,-2.5) TD: -1.7, p=0.006</td>
</tr>
<tr>
<td>MIDAS presenteeism score*</td>
<td>-1.3 (-2.2,-0.4)</td>
<td>-3.1 (-4.1,-2.2) TD: -1.9, p&lt;0.001</td>
<td>-3.1 (-4.1,-2.2) TD: -1.9, p&lt;0.001</td>
</tr>
<tr>
<td>MSQ-RFR score‡</td>
<td>7.7 (4.9,10.7)</td>
<td>14.4 (11.5,17.4) TD: 6.7, p&lt;0.001</td>
<td>15.3 (12.3,18.4) TD: 7.6, p&lt;0.001</td>
</tr>
<tr>
<td>MSQ-RFP score‡</td>
<td>5.7 (3.1,8.3)</td>
<td>11.0 (8.4,13.6) TD: 5.4, p&lt;0.001</td>
<td>11.2 (8.5,13.9) TD: 5.5, p&lt;0.001</td>
</tr>
<tr>
<td>MSQ-EF score‡</td>
<td>5.1 (2.0,8.2)</td>
<td>12.8 (9.7,16.0) TD: 7.7, p&lt;0.001</td>
<td>13.5 (10.3,16.8) TD: 8.4, p&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as least squares means (95% CI). P-value: erenumab versus placebo. P-value for pairwise comparisons are nominal without multiplicity adjustment

*Reduction in scores indicate improvement; ‡Increase in scores indicate improvement

CI, confidence interval; HIT-6, Headache Impact Test-6; MIDAS, Migraine Disability Assessment Questionnaire; MSQ, Migraine-Specific Quality of Life Questionnaire; MSQ-EF, MSQ-emotional function; MSQ-RFP, MSQ-role function preventive; MSQ-RFR, MSQ-role function restrictive; N, number of participants included in the subgroup analysis; PROs, patient-reported outcomes; TD, treatment difference; TF, treatment failure
**Results:** At baseline, mean values for all measures were similar between treatment subgroups. Significant improvements were observed in HIT-6 (greater reduction; \( p<0.001 \)), total MIDAS (greater reduction; \( p<0.001 \)) and MSQ scores (greater increase; \( p<0.001 \)) in patients treated with erenumab (70 mg and 140 mg) versus placebo (Table).

**Conclusion:** Erenumab 70 mg and 140 mg showed robust treatment effects on migraine-related disability, functional impact and quality of life in EM patients with \( \geq 1 \) prior prophylactic TF showing the benefit of treatment with erenumab in this subgroup of patients. Numerically better or equal scores were observed for the 140 mg dose compared with 70 mg for all PROs.

**References:** Disclosure: This study was supported by Amgen Inc., Thousand Oaks, California, USA and Novartis Pharma AG, Basel, Switzerland.

Migraine - preventive therapy
MTIS2018-066

PATIENT-REPORTED OUTCOMES IN CHRONIC MIGRAINE PATIENTS WITH PRIOR PROPHYLACTIC TREATMENT FAILURE RECEIVING PLACEBO OR ERENUMAB: SUBGROUP ANALYSIS OF A PIVOTAL RANDOMISED STUDY
1Department of Pain and FHU InovPain, Côte d’Azur University, Nice, France, 2Department of Neurology, Albert Einstein College of Medicine, Bronx, 3Department of Neurology, Mayo Clinic, Scottsdale, Arizona, 4Department of Neurology, Medstar Georgetown University Hospital, Washington, 5Amgen Inc, Thousand Oaks, California, 6Novartis Pharmaceutical Corporation, East Hanover, New Jersey, United States, 7Novartis Global Services Center, Dublin, Ireland, 8Novartis Pharma AG, Basel, Switzerland

Introduction: Erenumab, a fully human monoclonal antibody, selectively targets the calcitonin gene-related peptide (CGRP) receptor. A pivotal, 12-week, randomised, double-blind study demonstrated efficacy and safety of erenumab (70 mg and 140 mg monthly) in patients with chronic migraine (CM).

Objectives: We report here the patient-reported outcomes (PROs) in subgroups of patients with prior prophylactic treatment failures (TFs) (≥1 and ≥2 medication categories) due to lack of efficacy and/or poor tolerability.

Methods: Adults with CM (N=667) were randomized (3:2:2) to receive monthly subcutaneous placebo/erenumab 70 mg/140 mg. Exploratory endpoints included the Headache Impact Test (HIT-6), Migraine Disability Assessment Test (MIDAS), and the Patient-Reported Outcome Measurement Information System (PROMIS). No formal hypothesis was tested; p-values are descriptive.
### Table: Change from baseline in PROs in patients with prior prophylactic TFs (≥1 and ≥2) at Week 12

<table>
<thead>
<tr>
<th>Patient-reported outcomes</th>
<th>Prior treatment failures</th>
<th>Placebo</th>
<th>Erenumab 70 mg</th>
<th>Erenumab 140 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HIT-6 total score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>-2.6 (−3.5, -1.7) (n=184)</td>
<td>-5.2 (-6.3, -4.1) TD: −2.6, p&lt;0.001 (n=119)</td>
<td>-5.6 (-6.7, -4.5) TD: −3.0, p&lt;0.001 (n=123)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>-1.5 (−2.6, -0.5) (n=134)</td>
<td>-5.4 (-6.7, -4.1) TD: −3.9, p&lt;0.001 (n=86)</td>
<td>-5.2 (-6.5, -4.0) TD: −3.7, p&lt;0.001 (n=91)</td>
<td></td>
</tr>
<tr>
<td><strong>MIDAS total score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>-8.2 (−14.4, -2.0) (n=176)</td>
<td>-19.3 (−26.8, -11.8) TD: -11.1, p=0.024 (n=115)</td>
<td>-18.4 (−25.7, -11.0), TD: -10.1, p=0.036 (n=121)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>-3.3 (−10.8, 4.2) (n=126)</td>
<td>-17.7 (−26.7, -8.7) TD: -14.4, p=0.014 (n=82)</td>
<td>-17.2 (−25.8, -8.5) TD: -13.9, p=0.016 (n=89)</td>
<td></td>
</tr>
<tr>
<td><strong>MIDAS absenteeism score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>-5.6 (−9.2, -1.9) (n=176)</td>
<td>-9.6 (−14.0, -5.2) TD: -4.1, p=0.126 (n=115)</td>
<td>-9.2 (−13.5, -4.8), TD: -3.6, p=0.206 (n=121)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>-4.0 (−8.5, 0.6) (n=126)</td>
<td>-9.5 (−15.0, -4.1) TD: -5.6, p=0.117 (n=82)</td>
<td>-8.0 (−13.2, -2.8) TD: -4.1, p=0.244 (n=89)</td>
<td></td>
</tr>
<tr>
<td><strong>MIDAS presenteeism score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>-2.3 (−5.7, 1.0) (n=176)</td>
<td>-9.8 (−13.9, -5.8) TD: -7.5, p=0.005 (n=115)</td>
<td>-9.8 (−13.8, -5.8) TD: -7.4, p=0.005 (n=121)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>1.0 (−2.9, 4.9) (n=126)</td>
<td>-8.7 (−13.5, -4.0) TD: -9.7, p=0.002 (n=82)</td>
<td>-9.4 (−14.0, -4.9) TD: -10.4, p&lt;0.001 (n=89)</td>
<td></td>
</tr>
</tbody>
</table>

Data reported as least squares mean (95%CI of LSM), (TD), or p value unless otherwise specified.

P-values for pairwise comparisons are nominal p-values without multiplicity adjustment.

CI, confidence interval; HIT-6, Headache Impact Test; LSM, least square mean; MIDAS, Migraine Disability Assessment Test; n, number of subjects included in the model; TD, treatment difference; TF, treatment failure.
**Results:** For both TF subgroups, treatment with erenumab resulted in greater reduction (improvement) in HIT-6 total score and MIDAS total, absenteeism and presenteeism scores versus placebo at Week 12 (Table). For both TF subgroups, erenumab resulted in greater reduction (improvement) in PROMIS scores versus placebo at Weeks 4, 8 and 12, except for erenumab 70 mg at Week 4. Treatment-corrected differences exceeded established minimal-intergroup differences where applicable (e.g. for HIT-6 of −2.3 points).

**Conclusion:** Erenumab-treated CM patients with prior TFs experienced consistent and clinically meaningful improvements in PROs (such as disability, work productivity) as compared with placebo starting from the first month of treatment. Improvement was particularly visible among patients with ≥2 TFs, a hard-to-treat population.

**References:** Disclosure: This study was supported by Amgen Inc., Thousand Oaks, California, USA and Novartis Pharma AG, Basel, Switzerland.

GALCANEZUMAB EFFECTS IN ADULT PATIENTS WITH EPISODIC OR CHRONIC MIGRAINE ARE PERSISTENT: DATA FROM THREE PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED EVOLVE-1, EVOLVE-2, AND REGAIN STUDIES

S. Aurora¹, Q. Zhang¹, V. Stauffer¹,*
¹Eli Lilly and Company, Indianapolis, United States

Introduction: Galcanezumab is a humanized monoclonal antibody that selectively binds to calcitonin gene-related peptide (CGRP) and has demonstrated efficacy in reducing migraine headache days (MHD) in patients suffering from episodic and chronic migraine headaches.

Objectives: The purpose of the present analysis was to describe the persistence of effect following galcanezumab treatment in adult patients with episodic or chronic migraine.

Methods: Data from two parallel studies of patients with episodic migraine (between 4 and 14 migraine headache days [MHD] and at least 2 migraine attacks per month during baseline) and one study of patients with chronic migraine (headache ≥15 days/month for >3 months, with features of migraine headache ≥8 days/month at baseline) were analyzed. In all three studies, patients randomized in a 1:1:2 ratio received a subcutaneous (SC) injection of galcanezumab at 120 mg/month or 240 mg/month or a SC placebo. The evaluation of persistence of effect during the double-blind phase was based on a comparison of the percentages of galcanezumab- and placebo-treated patients with maintenance of ≥50% response (defined as ≥50% reduction from baseline in monthly MHDs) for at least 3 and 6 consecutive months for the episodic studies and 3 months for the chronic study. Logistic regression analyses were used for between treatment comparisons.

Table:

Results: A total of 1773 adult patients with episodic migraine (n=444 for galcanezumab 120 mg; n=435 for galcanezumab 240 mg; n=894 for placebo for the two episodic studies pooled) and 1113 adult patients with chronic migraine (n=278 for galcanezumab 120 mg; n=277 for galcanezumab 240 mg; n=558 for placebo) were evaluated. In patients with episodic migraine, significantly higher percentages of patients maintained ≥50% response for at least 3 consecutive months in the galcanezumab 120 mg (41.5%; p<.001) and 240 mg (41.1%; p<.001) groups or for 6 consecutive months (19.0% and 20.8%, respectively; p<.001) compared with the placebo group (21.4% at 3 months and 8.0% at 6 months). In patients with chronic migraine, significantly higher percentages of patients in the galcanezumab 120 mg (16.8%) and 240 mg (14.6%) groups maintained ≥50% response for all 3 months of the double-blind treatment phase compared with placebo (6.3%; all p<.001).

Conclusion: Treatment with galcanezumab 120 mg or 240 mg demonstrated statistically significant and clinically meaningful persistence of effect in patients with episodic migraine (at least 3 and 6 consecutive months) and in patients with chronic migraine (for 3 months).

TREATMENT OF CHRONIC MIGRAINE USING A SPECIALIZED ORAL DEVICE TO REDUCE TRIGEMINAL NOCIOCEPTION: A SINGLE-BLANDED, PLACEBO-CONTROLLED CROSSOVER STUDY

A. Blumenfeld, J. Boyd

Introduction: The [NTI] (Nocioceptive Trigeminal Inhibition) is an FDA approved intraoral device for prophylaxis of migraine pain, hypothesized to reduce trigeminal nociception through reduction of nocturnal jaw-clenching intensity and the resulting complications of TemporoMandibular Disorders. The [NTI] minimizes jaw-clenching intensity by providing an anterior point contact for incisors only (while traditional "full coverage" mouthpieces provide a posterior biting surfaces that can provide for an increase of clenching intensity).

Objectives: To assess the efficacy of the [NTI] compared to placebo using the Headache Impact Test (HIT-6). The HIT-6 has been underutilized in acquiring a more accurate picture of a patient’s suffering. The HIT-6 asks the patient to rank the extent to which headache/migraine pain interrupts a host of activities of daily life on a scale from one to five. For the Chronic Migraine patient, a positive one-level shift to a lesser category is considered highly significant.

The HIT-6 results ranks of the degree of negative impact:
- Little or no impact;
- Some impact with considerable pain;
- Substantial impact with severe pain;
- Sever impact with disabling pain.

Methods: 30 consecutive intractable Chronic Migraine (CM) patients were diagnosed at a Neurology Headache Center, whose conditions had been non-responsive to all prior therapies and were considered “unmanageable”. 25 consented and completed a baseline HIT-6 questionnaire, then treated with either an [NTI] device, or a placebo intraoral device that had no influence on nocturnal jaw muscle activity. After 30 days, patients completed another HIT-6, then fitted with the alternate device. After 30 days, patients completed another HIT-6.

Table:

<table>
<thead>
<tr>
<th>Degree of Improvement</th>
<th>[NTI]</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 catagory</td>
<td>89%</td>
<td>16%</td>
</tr>
<tr>
<td>2 catagory</td>
<td>47%</td>
<td>0%</td>
</tr>
<tr>
<td>% improvement in numerical score</td>
<td>62%</td>
<td>14%</td>
</tr>
</tbody>
</table>

Results: 19 of the 25 patients completed the 3 month trial with post treatment HIT-6 data. The initial average baseline HIT-6 was Category 4: "Severe impact, disabling pain". (see table for treatment outcomes)

Conclusion: The considerable improvement of the majority of patients produced by the [NTI] device, with nearly half experiencing a profound 2-catagory improvement, suggests that Chronic Migraine sufferers may have intense nocturnal jaw clenching as a contributing factor, which typically goes unnoticed and undetected by both physician and dentist. The production of nociceptive input by the affected teeth, bone, TMJs and muscles to the trigeminal sensory nucleus caused by intense nocturnal jaw clenching should be considered as a perpetuating and confounding co-factor of CM. An [NTI] device and its therapeutic protocol provided by a knowledgeable dental practitioner should be considered as an important rule-out of intense jaw-clenching and then to improve the quality of life of the migraine sufferer

Disclosure of Interest: A. Blumenfeld: None Declared, J. Boyd Conflict with: vested interest
Efficacy of Galcanezumab in Patients Who Failed to Respond to Preventives Previously: Results from Evolve-1, Evolve-2 and Regain Studies

Q. Zhang¹, D. D. Ruff¹, E. M. Pearlman², S. Govindan³, S. Aurora⁴,*  
¹Statistics-Neuroscience (LTC), ²Migraine/Headache, Eli Lilly and Company, Indianapolis, ³Medical Writing, LCCI Biometrics, Eli Lilly and Company, Bangalore, ⁴Medical Fellow-Launch Leader, Galcanezumab Launch, Eli Lilly and Company, Indianapolis, United States

Introduction: Galcanezumab (GMB) is a humanized monoclonal antibody against calcitonin gene-related peptide under development for prevention of migraine.

Objectives: To assess if there were any differential treatment effects in patients who had failed ≥2 previous preventives versus those who had not through a subgroup analysis of three Phase 3 studies of GMB.

Methods: EVOLVE-1 (NCT02614183), EVOLVE-2 (NCT02614196) and REGAIN (NCT02614261) were Phase 3, randomized, double-blind, placebo-controlled studies in patients with episodic (EVOLVE-1/2) or chronic (REGAIN) migraine. Patients were randomized 2:1:1 to receive placebo, GMB_120mg or GMB_240mg during double-blind treatment period lasting six months (EVOLVE-1/2) or three months (REGAIN). Subgroup analysis was conducted for change from baseline in number of monthly migraine headache days (MHD) and ≥50% response (reduction in number of MHD) for patients who failed ≥2 prior preventive therapies (yes vs no). Subgroup-by-treatment interactions were calculated using linear or generalized linear mixed models.

Results: In the integrated analysis of EVOLVE studies and in the REGAIN study, GMB_120mg/240mg statistically significantly improved (p<0.001) overall mean reduction of monthly MHD compared with placebo in both subgroups of patients. For the subgroup who failed prior preventives, reductions were: EVOLVE: placebo: 0.81; GMB_120mg: 3.45; GMB_240mg: 3.85; REGAIN: placebo: 1.44; GMB_120mg: 5.91; GMB_240mg: 3.30. Significant treatment-by-subgroup interactions were seen for GMB_240mg (EVOLVE studies) and for GMB_120mg (REGAIN) suggesting better efficacy compared with placebo for these doses in patients who failed prior preventives. Mean percentage of patients with ≥50% response were significantly higher, compared with placebo, for both subgroups in EVOLVE studies and REGAIN study.

Conclusion: GMB_120mg/240mg is efficacious compared with placebo in reducing monthly MHDs in both patients who failed and did not fail ≥2 prior preventives. Treatment-by-subgroup interactions may be driven by lower placebo response in patients who failed preventives previously as magnitude of change for GMB-treated patients were similar in both subgroups.
Migraine - preventive therapy

MTIS2018-070

HUMANISTIC BURDEN OF MIGRAINE IN THE EU5: A MATCHED ANALYSIS OF THE NHWS 2017
M. J. Doane 1, P. Vo 2,*, A. Bilitou 3, J. Fang 4, A. K. Laflamme 2, S. Gupta 5
1Kantar Health, Philadelphia, United States, 2Novartis Pharma AG, Basel, Switzerland, 3Novartis Global Services Centre, Dublin, Ireland, 4Novartis Pharmaceuticals Corporation, New Jersey, 5Kantar Health, New York, United States

Introduction: Migraine is a distinct neurological disease ranking among the top causes of disability globally and affecting multiple domains of life for individuals 1.

Objectives: The purpose of this study was to describe the incremental burden of migraine on health-related quality of life (HRQoL) in those suffering from migraine of >=4 monthly headache days (HDs) compared with matched controls in Europe (EU5; France, Germany, Italy, Spain, and UK).

Methods: A retrospective, cross-sectional analysis was conducted using patient-reported data from the 2017 EU5 National Health and Wellness Survey (NHWS). Outcomes from 1569 adult respondents, who self-reported a doctor diagnosis of migraine, experiencing at least one migraine in the prior month, and overall >=4 HDs during the prior month, were stratified by HD frequency (i.e. 4-7, 8-14 and >=15 HDs) and matched by propensity scores to 1569 respondents without migraine (controls) within each HD subgroup and country using sociodemographic characteristics. HRQoL was assessed via SF-36v2 and EQ-5D. Independent samples t-tests were used for the pairwise comparison of the outcomes across subgroups.

Image:

Table 1. HRQoL outcomes in NHWS respondents with migraine versus matched controls

<table>
<thead>
<tr>
<th></th>
<th>Non-migraine controls (N=1,569)</th>
<th>4-7 HDs (N=783)</th>
<th>8-14 HDs (N=429)</th>
<th>&gt;=15 HDs (N=357)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td><strong>Mental Component Score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary Score</td>
<td>45.17 (10.09)</td>
<td>41.02 (10.75)</td>
<td>40.03 (10.15)</td>
<td>36.52 (11.46)</td>
</tr>
<tr>
<td><strong>Physical Component</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary Score</td>
<td>50.87 (8.54)</td>
<td>48.11 (9.07)</td>
<td>47.15 (8.56)</td>
<td>42.89 (10.86)</td>
</tr>
<tr>
<td><strong>SF-36 Utility Score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.70 (0.13)</td>
<td>0.64 (0.11)</td>
<td>0.63 (0.11)</td>
<td>0.58 (0.12)</td>
</tr>
<tr>
<td><strong>EQ-5D Index</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.83 (0.20)</td>
<td>0.75 (0.23)</td>
<td>0.72 (0.24)</td>
<td>0.58 (0.31)</td>
</tr>
<tr>
<td><strong>Health Status, EQ VAS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>74.22 (21.75)</td>
<td>67.13 (22.29)</td>
<td>64.24 (21.75)</td>
<td>52.28 (25.61)</td>
</tr>
</tbody>
</table>

Propensity matching was conducted using patient demographic variables identified in pre-matched bivariate results (i.e., age, gender, employment status, marital status, income, education, smoking, alcohol use, body mass index, exercise and the Charlson comorbidity index). Subscripts refer to pairwise comparisons using independent samples t-tests between subgroups. Values in the same row that do not share the same subscript are significantly different at p<0.05.

Results: All HRQoL outcomes assessed, after propensity score matching in 783 respondents with 4-7 HDs, 429 respondents with 8-14 HDs and 357 respondents with >=15 HDs, were significantly lower compared with outcomes of 1569 control respondents without migraine (Table 1).

Conclusion: Individuals with migraine across migraine frequency subgroups report significantly worse HRQoL compared with those without migraine. Results highlight the burden that exists across the spectrum of migraine patients who may be eligible for preventive treatment.

Disclosure of Interest: M. Doane Conflict with: Kantar Health employee, P. Vo Conflict with: Employee of Novartis Pharma AG, Basel, Switzerland, A. Bilotou Conflict with: Novartis employee, J. Fang Conflict with: Novartis employee, A. Laflamme Conflict with: Novartis employee, S. Gupta Conflict with: Kantar Health received funding from Novartis to conduct this study
LIVING WITH MIGRAINE: A REPORT FROM THE MY MIGRAINE VOICE SURVEY

Introduction: As a pilot to the My Migraine Voice study, online bulletin boards provided insights into the impact of migraine on the lives of those affected and the coping mechanisms used.

Objectives: The objective of this worldwide study was to better understand what it is like to live with migraine, as directly reported from patients across the world.

Methods: My Migraine Voice is a worldwide cross-sectional online survey of 11,266 individuals (31 countries in Africa, America, Asia and Europe) recruited via online panels and patient organizations. Participants were adult migraine patients who reported ≥4 MMD in the 3 months preceding survey administration, with pre-specified 90% among those having reported having used preventive migraine treatment.

Results: A total of 11,266 migraine individuals participated (75% female, mean age 39 years); most were in employment/students (73%), with 9% receiving disability-related allowances due to migraines. 85% of participants reported negative aspects of living with migraine (feeling helpless, depressed, not understood), sleeping difficulties (83%); 55% lived in fear of the next attack. Migraines were associated with severe pain (85%), long-lasting headaches (lasting 4 to 72 hours) (83%), sound sensitivity (81%) light sensitivity (74%; mean=19 hours/month spent in darkness). Migraine impact on professional, private or social domains was reported by 87% of participants. Over the previous 3 months, 61% had relied on external support (family/friends/anyone else) to cope with daily tasks (mean=12.8 days). Despite the negative aspects, 57% of respondents indicated >=1 positive aspect, mainly relating to learning to cope with their disease (40%), or making them responsible for their disease (13%), and being stronger as a person (11%).

Conclusion: This study describes the daily reality of migraine individuals, especially those with frequent attacks and who have received migraine preventive treatments. While it highlights the significant challenges and unmet needs for these individuals suffering with migraine, the positive outlook on personal growth brought from coping with the disease highlights their resilience and strength.

Disclosure of Interest: A. Craven Conflict with: President of the Migraine Association of Ireland, R. Quintana Conflict with: Employee of GFK, V. Carboni Conflict with: Employee of GFK, P. Martelletti Conflict with: Consulting fees from various pharmaceutical companies, M. Lanteri-Minet Conflict with: Consulting fees from various pharmaceutical companies, T. Schwedt Conflict with: Consulting fees from various pharmaceutical companies, H.- C. Diener Conflict with: Consulting fees (Advisory board) from Novartis, A. K.-Lafiamme Conflict with: Consulting fees (advisory board) from Novartis, A. Vangaa Rasmussen Conflict with: Consulting fees (advisory board) from Novartis, E. Ruiz de la Torre Conflict with: President of the EHA, D. Walsh Conflict with: EFNA Executive Director, S. Evans Conflict with: Chief Executive of Migraine Action, P. Dumas Conflict with: CEO of Migraine Again, R. Fink Conflict with: Novartis employee, A. Fiorin Conflict with: Novartis employee, S. Ribbe Conflict with: Novartis employee, P. Vo Conflict with: Novartis employee
Migraine - preventive therapy
MTIS2018-072

EVALUATION OF INJECTION SITE RELATED ADVERSE EVENTS FROM PHASE 3 PLACEBO CONTROLLED STUDIES OF GALCANEZUMAB FOR MIGRAINE PREVENTION
V. L. Stauffer 1,*, S. Wang 1, J. N. Carter 1, K. A. Day 1, A. Camporeale 2
1Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, United States, 2Eli Lilly Italia, Sesto Fiorentino, Italy

Introduction: Galcanezumab is a humanized monoclonal antibody that selectively binds to the calcitonin gene-related peptide, and is being studied for migraine prevention.

Objectives: To evaluate injection site related adverse events (ISR-AEs) observed in galcanezumab- vs. placebo-treated patients with episodic or chronic migraine.

Methods: Data were integrated from double-blind clinical studies (EVOLVE-1=NCT02614183; EVOLVE-2=NCT02614196; REGAIN=NCT02614261) of up to 6 months duration. Patients received two subcutaneous injections (1 mL each) of either galcanezumab 120 mg (120 mg and placebo), galcanezumab 240 mg (2 injections of 120 mg) or placebo (2 injections). Incidence of ISR-AEs, discontinuation due to an ISR-AE, and duration of those events were analyzed. All events listed in the MedDRA v19.1 high-level term of ‘injection site reactions’ were analyzed.

Results: A total of 1,435 patients were treated with galcanezumab and 1,451 with placebo. ISR-AEs were reported at a higher rate in the galcanezumab 120 mg dose-group (18.2%; \( P < .001 \)) and the galcanezumab 240 mg dose-group (22.8%; \( P < .001 \)) compared with placebo (12.6%). Injection site pain was the most frequent ISR-AE reported for galcanezumab-treated patients (Table 1). Its incidence was similar to placebo, generally occurred within 60 minutes after injection, and on average resolved in 1.4 days. Other ISR-AEs occurring in 1.5% or more of galcanezumab-treated patients, and significantly more frequently than among placebo-treated patients are displayed in Table 1. Seven galcanezumab-treated patients discontinued due to an ISR-AE. None of the ISR-AEs were reported as a serious AE; the majority (90.8%) of galcanezumab-treated patients reported the events as mild or moderate in severity.

Conclusion: ISR-AEs occurred in significantly more galcanezumab-treated patients than placebo. Most patients reporting ISR-AEs had events that were mild to moderate in severity, occurred on the day of treatment, and were self-limiting. No serious AEs related to injection sites were reported, and the rate of discontinuations related to injection sites was low (< 0.5%).
Migraine - preventive therapy
MTIS2018-073
CHANGES IN PATIENT FUNCTIONING AND DISABILITY IN A PHASE 3, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL EVALUATING GALCANEZUMAB FOR CHRONIC MIGRAINE PREVENTION (REGAIN)
J. H. Ford 1, H. C. Detke 1,*, D. Ayer 1, S. Wang 1, A. Tockhorn-Heidenreich 2, R. M. Nichols 1
1Eli Lilly and Company, Indianapolis, United States, 2Eli Lilly and Company, Erl Wood Manor, United Kingdom

Introduction: Galcanezumab (GMB) is a humanized monoclonal antibody against calcitonin gene-related peptide under development for migraine prevention.

Objectives: To assess changes from baseline in patient-reported outcomes (PRO) measuring impact of chronic migraine on functioning and disability, among patients treated with galcanezumab (GMB) versus placebo (PBO) (REGAIN, NCT02614261).

Methods: Patients with chronic migraine (≥15 monthly headache days, of which at least 8 are migraine) received GMB_240mg (N=277), GMB_120mg (N=278) or placebo (N=558) as monthly subcutaneous injections during the 3-month double-blind treatment period. PRO instruments included Migraine-Specific Quality of Life Questionnaire v2.1 (MSQ) and Migraine Disability Assessment (MIDAS). MSQ measures impact of migraine on patient functioning across three domains: Role Function-Restrictive (RF-R), Role Function-Preventive (RF-P), and Emotional Function (EF), for which transformed scores (scale:0–100) were analyzed. MIDAS quantifies headache-related disability associated with missed or reduced productivity at work/home and social events (scale:0–270). Outcomes were collected at baseline and during treatment period (MSQ=monthly; MIDAS=Month 3). Changes from baseline to Month 3 in MSQ and MIDAS scores were analyzed using MMRM and ANCOVA, respectively. Higher scores on MSQ indicate better functioning, while higher scores on MIDAS indicate more disability. Patients with ≥50% reduction in total MIDAS score were defined as responding to treatment.

Results: Mean (SD) baseline total scores were 44.88 (18.02) for MSQ and 67.24 (57.31) for MIDAS, indicating significant functional impairment and very severe disability in the population. At Month 3, least squares (LS) mean change±SE from baseline to Month 3 in MSQ total scores were:14.55±1.21 (PBO), 20.51±1.49 (GMB_120mg) and 20.49±1.49 (GMB_240mg). For MSQ domains, values were:RF-R:16.76±1.18 (PBO), 21.81±1.41 (GMB_120mg), 23.05±1.63 (GMB_240); RF-P:10.98±1.15 (PBO), 17.98±1.42 (GMB_120mg), 16.07±1.41 (GMB_240mg); EF:14.07±1.55 (PBO), 21.03±1.91 (GMB_120mg), 20.70±1.90 (GMB_240mg). All differences between GMB dose groups and placebo were statistically significant (p<0.05). For MIDAS total score at Month 3, patients in GMB_120mg group had significantly (p<0.05) greater mean reduction from baseline versus PBO (LS Mean Change±SE: -20.27±4.07 [GMB_120mg], -11.53±3.38 [PBO]), and there were significant differences in proportion of patients responding for both GMB_120mg (p<0.001) and GMB_240mg (p<0.05) versus PBO.

Conclusion: In this Phase 3 study in patients with chronic migraine, treatment with GMB versus PBO led to statistically significant and clinically meaningful improvements in PRO scores. Negative impact of migraine on daily functioning and disability was reduced after 3 months.

**Migraine - preventive therapy**

**MTIS2018-074**

**EFFICACY OUTCOMES IN RESPONDER AND NON-RESPONDER PATIENTS WITH EPISODIC MIGRAINE TREATED PREVENTIVELY WITH ERENUMAB IN STRIVE**


1Headache Outpatient Clinic, Medizinische Universität Innsbruck, Innsbruck, Austria, 2Charité Universitätsmedizin Berlin, Berlin, Germany, 3Mercy Clinic Neurology and Headache Center, Saint Louis, MO, 4Mayo Clinic, Scottsdale, AZ, 5Amgen Inc., Thousand Oaks, CA, 6Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States, 7Novartis Pharma AG, Basel, Switzerland

**Introduction:** Erenumab is a fully human anti-CGRP receptor antibody recently approved in the United States and recommended for approval in Europe as a preventive treatment for migraine. STRIVE was a randomised, placebo-controlled clinical trial in which the change from baseline in mean number of monthly migraine days (MMD) in treatment month 4–6 and the proportions of patients with ≥50% reduction from baseline in MMD were −3.7, −3.2, and −1.8, and 50%, 43%, and 27% in patients with episodic migraine (EM) treated with monthly subcutaneous (SC) injections of erenumab 140 mg, 70 mg, and placebo, respectively (both doses p<0.001 compared with placebo; Goadsby et al., 2017). Since in clinical practice, patients achieving/not achieving sufficient response to treatment are likely to continue/discontinue treatment, we sought to contextualize the actual treatment benefit among patients achieving (R subgroup) or not achieving (NR subgroup) response at the ≥50% threshold.

**Objectives:** To evaluate change from baseline in MMD, migraine-specific medication treatment days (MSMD), and Migraine Physical Function Impact Diary domain scores for everyday activity (MPFID-EA) and physical impact (MPFID-PI) in R and NR subgroups in STRIVE.

**Methods:** Patients (N=955; aged 18–65 years) with ≥4 and <15 migraine days per month were randomised (1:1:1) to receive erenumab 70 mg, 140 mg, or placebo SC once monthly for 6 months. The primary endpoint was change from baseline in MMD. The proportion of ≥50% Rs and change from baseline in MSMD, MPFID-EA, and MPFID-PI were prespecified secondary endpoints. All endpoints were evaluated by averaging the monthly treatment effect over Months 4, 5, and 6 of the double-blind treatment phase.
Results: In the overall study population, the odds for being a ≥50% R on erenumab 70 mg or 140 mg were 2.13 and 2.81, respectively, compared with placebo. Baseline characteristics were similar in the R and NR subgroups (Table). In the R subgroup, there was a mean change of −6.0 to −6.1 MMD from a baseline of 8.2 to 8.3. For this and for the efficacy measures MSMD, MPFID-EA, and MPFID-PI, change from baseline was 2.7-fold to 7.5-fold greater in Rs than in NRs and 1.4-fold to 1.9-fold greater in Rs than in the overall population (Table). Mean MPFID-EA and MPFID-PI domain scores were reduced by 7–10 points in responders (differences ≥3–5 points have been shown to be clinically meaningful).

Conclusion: Among the 43% and 50% of patients with EM who achieved ≥50% reduction from baseline in MMD when treated with erenumab 70 mg and 140 mg in STRIVE, there were substantial, clinically relevant reductions in the frequency of migraine days, the acute use of migraine-specific medication, and MPFID scores compared with non-responders and with the overall patient population. These findings from STRIVE should help to provide context for setting realistic patient expectations for response to treatment with erenumab. The odds of responding were numerically greater with the 140 mg dose than with the 70 mg dose.


Table: Primary and secondary outcome measures in erenumab-treated responder and non-responder subgroups in STRIVE. Data are mean ±SD, except as indicated. Abbreviations are defined in the abstract body.
Disclosure of Interest: G. Brössner Conflict with: G. Brössner has received unrestricted grants, honoraria, personal fees, and travel grants from: Allergan, AMGEN, Menarini, Pfizer, Linde AG, AstraZeneca, St. Jude Medical, Reckitt Benkiser, Novartis, TEVA, Fresenius, Janssen Cilag, Österreichische Gesellschaft für Neurologie (ÖGN), European Headache Foundation (EHF), Österreichische Kopfschmerzgesellschaft (ÖKSG), and Österreichische Akademie der Wissenschaften (ÖAW)., U. Reuter Conflict with: Professor Reuter has served on advisory boards and consulted for Amgen, Allergan, ATI, Eli Lilly, Teva, Novartis and ElecroCore. Professor Reuter serves onspeaker’s bureaus for Amgen, Allergan, Eli Lilly, Teva,Novartis, and ElecroCore., J. Bonner Conflict with: None declared, D. Dodick Conflict with: David William Dodick, M.D., has received compensation from serving on advisory boards and/or consulting within the past 5 years for: Allergan, Amgen, Novartis, Alder, Arteaus, Pfizer, Colucid, Merck, NuPathet, Eli Lilly and Company, Autonomic Technologies, Ethicon J&J, Zogenix, Supernus, Labrys, Boston Scientific, Medtronic, St Jude, Bristol-Myers Squibb, Lundbeck, Impax, MAP, Electrocore, Tonix, Novartis, Teva, Alcobra, Zosano, Insys, Ipsen, GBS/Nocira, Acorda, eNeura, Charleston Laboratories, Gore, Biohaven, Bioventric, Magellan, Theranica, Xenon, Dr Reddy’s/Promius Pharma. Dr Dodick owns equity in Epient, Nocira, Second Opinion, Healint, and Theranica. Dr Dodick has received funding for travel, speaking, editorial activities, or royalty payments from IntraMed, SAGE Publishing, Sun Pharma, Allergan, Oxford University Press, American Academy of Neurology, American Headache Society, West Virginia University Foundation, Canadian Headache Society, Healthlogix, Universal Meeting Management, WebMD, UptoDate, Medscape, Oregon Health Science Center, Albert Einstein University, University of Toronto, Starr Clinical, Decision Resources, Synergy, MedNet LLC, Peer View Institute for Medical Education, Medicom, Chameleon Communications, Academy for Continued Healthcare Learning, Haymarket Medical Education, Global Scientific Communications, HealthLogix, Miller Medical, MeetingLogiX, Wiley Blackwell. Dr Dodick, through his employer, has consulting use agreements with NeuroAssessment Systems and Myndshft. He holds board of director positions with King-Devick Technologies, and Epien Inc. He holds the following Patent 17189376.1-1466:vTitle: ; H. Picard Conflict with: employee of Amgen Inc., S. Wen Conflict with: employee of Novartis Pharmaceuticals Corp., S. Ritter Conflict with: employee of Novartis Pharmaceuticals Corp., J. Klatt Conflict with: employee of Novartis Pharma AG, D. Mikol Conflict with: employee of Amgen Inc.
**Migraine - preventive therapy**

**MTIS2018-075**

**PHASE 3 STUDY (SPARTAN) OF LASMIDITAN COMPARED TO PLACEBO FOR ACUTE TREATMENT OF MIGRAINE**

L. A. Wietecha 1, B. Kuca 2, M. G. Case 1, K. J. Selzler 1, S. Aurora 1,*

1Eli Lilly and Company, Indianapolis, 2 CoLucid Pharmaceuticals, Inc., a wholly owned subsidiary of Eli Lilly and Company, Massachusetts, United States

**Introduction:** Lasmiditan is a selective 5HT1F receptor agonist.

**Objectives:** Efficacy on headache pain and most bothersome symptom (MBS; nausea, phonophobia, or photophobia) at 2 hours post-dose and safety following lasmiditan 200 mg, 100 mg, 50 mg, or placebo.

**Methods:** This double-blind, placebo-controlled study randomized patients with at least moderate disability (Migraine Disability Assessment Score >11), 1:1:1:1 to a first dose of lasmiditan (200 mg, 100 mg, or 50 mg) or placebo (CTgov # NCT02605174) within 4 hours of migraine attack onset (moderate severity or worse and not improving). For rescue or recurrence of migraine (2-24 hours post dose), patients were randomized to their previously assigned lasmiditan dose or placebo; patients randomized to placebo received placebo. The primary and key secondary analyses compared the proportions of patients (modified intent-to-treat population [mITT]) in the lasmiditan 200-mg group with the placebo group who were headache pain-free and MBS-free at 2 hours post-first dose. Comparisons were made via logistic regression with terms for treatment group and background migraine preventative use. Lasmiditan 100 mg and 50 mg were also compared to placebo. Safety was assessed by treatment-emergent adverse events (TEAEs).

**Results:** 3005 patients were randomized, 2156 (mITT) were evaluated in the lasmiditan 200 mg (N=528), 100 mg (N=532), 50 mg (N=556), and placebo (N=540) groups. At baseline, 36.6% had a history of migraine with aura and 79.2% had ≥1 cardiovascular risk factor in addition to migraine. The proportion of patients headache pain-free at 2 hours post-first dose was significantly greater with lasmiditan 200 mg (38.8%; p<.001), 100 mg (31.4%; p<.001), and 50 mg (28.6%; p<.01) than placebo (21.3%). Significantly more patients were MBS-free at 2 hours post-first dose with lasmiditan 200 mg (48.7%; p<.001), 100 mg (44.2%; p<.001), or 50 mg (40.8%; p<.01) than with placebo (33.5%). At 2 hours, patients in lasmiditan 200 mg (65.0%), 100 mg (64.8%), and 50 mg (59.0%) experienced headache relief (mild or no pain) compared to placebo (47.7%) (all doses p<.001). Of the lasmiditan 200mg, 100mg, 50mg and placebo groups, 26.4%, 32.7%, 41.0% and 49.8% took a second dose for rescue. After the first dose of lasmiditan 200 mg (253/649; 39.0%), lasmiditan 100 mg (229/635; 36.1%), lasmiditan 50 mg (166/654; 25.4%) and placebo (75/645; 11.6%) experienced a TEAE; the majority of TEAEs were mild or moderate severity. Most frequently reported TEAEs (≥2%) after first dose were dizziness, paresthesia, somnolence, fatigue, nausea, and lethargy.

**Conclusion:** SPARTAN, a Phase 3 trial of lasmiditan in patients with migraine, met the primary and key secondary endpoints of pain-free and MBS-free at 2 hours for lasmiditan 200 mg. The same endpoints were significant for lasmiditan 100 mg and lasmiditan 50 mg. Safety was consistent with a previous Phase 3 trial of lasmiditan, with dizziness being reported as the most frequent TEAE.

**Migraine - preventive therapy**

**MTIS2018-076**

**NON-INVASIVE VAGUS NERVE STIMULATION (NVNS) FOR THE PREVENTIVE TREATMENT OF EPISODIC MIGRAINE: THE MULTICENTRE, DOUBLE-BLIND, RANDOMISED, SHAM-CONTROLLED PREMIUM TRIAL**

H.-C. Diener 1*, P. J. Goadsby 2, M. Ashina 3, M. Al-Mahdi Al-Karagholi 3, A. Sinclair 4, D. Mitsikostas 5, D. Magis 6, P. Pozo-Rosich 7 8, P. Irinia Sieira 9, M. J. Lainez 10, C. Gaul 11, N. Silver 12, J. Hoffmann 13, E. Liebler 14, M. D. Ferrari 15 and the PREMIUM Study Group

1 Klinik für Neurologie, Universitätsklinikum Essen, Essen, Germany, 2 NIHR-Wellcome Trust King's Clinical Research Facility, King’s College London, London, United Kingdom, 3 Danish Headache Center, Rigshospitalet Glostrup, University of Copenhagen, Copenhagen, Denmark, 4 Metabolic Neurology, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom, 5 Neurology Clinic, Eginition Hospital, Athens, Greece, 6 CHR de la Citadelle, University of Liège, Liège, Belgium, 7 Headache Clinic, Neurology Department, Hospital Universitari Vall d’Hebron, 8 Headache Research Group, Vall d’Hebron Research Institute, Universitat Autonoma de Barcelona, Barcelona, 9 Clinica Universidad de Navarra, Pamplona, 10 Catholic University of Valencia, University Clinic Hospital, Valencia, Spain, 11 Migraine and Headache Clinic, Königstein, Germany, 12 The Walton Centre, Liverpool, United Kingdom, 13 Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 14 electroCore, LLC, Basking Ridge, New Jersey, United States, 15 Leiden University Center, Leiden, Netherlands

**Introduction:** Adherence to available preventive drug therapies for migraine remains low due to adverse events (AEs) and limited efficacy, demonstrating a need for additional options. Non-invasive vagus nerve stimulation (nVNS; gammaCore®) has the potential to reduce the number of migraine/headache days and acute medication use, as suggested by results from previous studies.

**Objectives:** We conducted PREMIUM, a randomised, double-blind, sham-controlled study, to evaluate the efficacy, safety, and tolerability of nVNS for the preventive treatment of episodic migraine.

**Methods:** The PREMIUM study, conducted in 22 European sites, included a 4-week observational run-in period wherein no study treatment was administered, a 12-week double-blind period of randomised treatment with nVNS or sham, and a 24-week open-label period of nVNS. Patients were instructed to administer two 120-second stimulations bilaterally to the neck 3 times daily (TID; 6-8 hours apart) for a total of 6 stimulations per day. Patients could use abortive migraine medication if needed, but add-on preventive migraine medication was not permitted until week 24. The primary analysis set for efficacy was the intent-to-treat (ITT) population, defined as enrolled patients who received ≥1 treatment in the double-blind period. Upon observation of suboptimal rates of adherence to the TID treatment protocol in the ITT population, a modified intent-to-treat (mITT) population was defined as those with >67% adherence per month for evaluation in a post hoc analysis. Safety was evaluated in all enrolled patients.

**Table:**

**Results:** Baseline characteristics in the ITT population (nVNS, n=165; sham, n=167) were typical of an episodic migraine population. The mean reduction in number of migraine days from the run-in period to the last 4 weeks of the double-blind period (primary end point) was −2.26 days with nVNS vs −1.80 days with sham (p=0.146). The proportion of patients with a ≥50% reduction in number of migraine days was 31.9% with nVNS and 25.0% with sham (p=0.186). Results were similar for headache and acute medication days. In the post hoc analysis of the mITT population, significant differences between the nVNS (n=138) and sham (n=140) groups were seen for reductions in number of migraine days (nVNS, −2.27 days; sham, −1.53 days; p=0.043), headache days (nVNS, −2.85 days; sham, −1.99 days; p=0.045), and acute medication days (nVNS, −1.94 days; sham, −1.14 days; p=0.039). Most device-related AEs for nVNS were mild, with application site pain being the most common.
Abstracts

**Conclusion:** Preventive nVNS treatment demonstrated consistent but nonsignificant benefits over sham for patients with episodic migraine, with sham providing a higher response than anticipated. Significant effects of nVNS were seen for patients with >67% adherence to treatment. Further evaluation of the role of adherence and the sham response is warranted.

**Disclosure of Interest:** H.-C. Diener Conflict with: Honoraria for participation in clinical trials and for contributions to advisory boards and oral presentations sponsored by 3M Medica; Addex Pharma; Adler; Allergan; Almirall; Amgen; AstraZeneca; Autonomic Technologies; Bayer; Berlin-Chemie; Boehringer Ingelheim; Bristol-Myers Squibb; Chordate Medical; CoLucid Pharmaceuticals; electroCore, LLC; Eli Lilly and Company; GlaxoSmithKline; Grünenthal; Janssen-Cilag; Johnson & Johnson; Labrys Biologics; La Roche; Medtronic; Menarini; Minster Pharmaceuticals; MSD; NeuroScore; Novartis; Pfizer; Pierre Fabre; Sanofi; Schaper and Brümmer; St. Jude Medical; Vital; and Weber & Weber. Prof. Diener has also received research funding from Allergan; Almirall; AstraZeneca; Bayer; electroCore, LLC; GlaxoSmithKline; Janssen-Cilag; MSD; and Pfizer. He has received additional research support from the European Union; the German Ministry of Education and Research; and the German Research Council. Prof. Diener has no ownership interests and does not own any pharmaceutical company stocks., P. Goadsby Conflict with: Grants and personal fees from Allergan; Amgen; and Eli Lilly and Company. He has also received personal fees from Akita Biomedical; Alder Biopharmaceuticals; Autonomic Technologies; Avanir Pharmaceuticals; Cipla Ltd; CoLucid Pharmaceuticals, Inc.; Dr. Reddy's Laboratories; electroCore, LLC; eNeura; Journal Watch; Medico-Legal Journal; Novartis; Oxford University Press; Pfizer Inc; Promius Pharma; Quest Diagnostics; Scion; Teva Pharmaceuticals; Trigemina, Inc.; and Up-to-Date. In addition, Prof. Goadsby has a patent for magnetic stimulation for headache pending assigned to eNeura., M. Ashina Conflict with: Honoraria for contributions to advisory boards and oral presentations sponsored by Allergan; Almirall; Amgen; Eli Lilly and Company; Novartis; and Teva Pharmaceuticals. Prof. Ashina has been the primary investigator for the Amgen 20120178 (Phase 2), 20120295 (Phase 2), 20130255 (OLE), and 20120297 (Phase 3) trials and for the Alder ALD403-CLIN-001 (Phase 3), Amgen PAC1 20150308 (Phase 2a), and electroCore GM-11 trials. Prof. Ashina has no ownership interests and does not own any pharmaceutical company stocks., M. Al-Mahdi Al-Karagholi Conflict with: Travel grants from electroCore, LLC., A. Sinclair Conflict with: Funded by an NIH Clinician Scientist Fellowship (NIHR-CS-011-028) and by the Medical Research Council, UK (MR/K015184/1)., D. Mitsikostas Conflict with: Advisory fees, honoraria, research grants, or travel grants from Allergan; Amgen; Biogen; Cefaly; electroCore, LLC; Eli Lilly and Company; Merz Pharma; Novartis; Roche; Sanofi Genzyme; and Teva Pharmaceuticals., D. Magis Conflict with: Travel grants from electroCore, LLC; is a consultant for Novartis Belgium; and is an associate editor for Cephalalgia., P. Pozo-Rosich Conflict with: Honorary as a consultant and speaker for Allergan; Almirall; Chiesi; Eli Lilly and Company; Novartis; and Teva Pharmaceuticals. Dr. Pozo-Rosich does not own stocks from any pharmaceutical company., M. Lahnez Conflict with: Advisory fees, speaker fees, research grants, and/or research support from ATI Pharma; Allergan; Amgen; Boehringer Ingelheim; electroCore, LLC; Eli Lilly and Company; Lupin Pharmaceuticals; Medtronic; Novartis; Otsuka; Roche; and Teva Pharmaceuticals., C. Gaul Conflict with: Honorary from Allergan; Bayer; Boehringer Ingelheim; Desitin Arzneimittel; electroCore, LLC; Eli Lilly and Company; Grünenthal; Hormosan Pharma; Novartis; Ratiopharm; Reckitt Benckiser Group; and Teva Pharmaceuticals. He has no ownership interests and does not own any pharmaceutical company stocks., N. Silver Conflict with: Honorary from Allergan; electroCore, LLC; Eli Lilly and Company; Novartis; and Teva Pharmaceuticals; and investigator fees paid to the Walton Centre., J. Hoffmann Conflict with: Has consulted for and/or served on advisory boards for Allergan; Autonomic Technologies Inc. (ATI); Chordate Medical AB; Hormosan Pharma; Novartis; and Teva Pharmaceuticals. He received honoraria for speaking from Allergan; Chordate Medical AB; Novartis; and Teva Pharmaceuticals., E. Liebler Conflict with: Employee of electroCore, LLC, and receives stock ownership., M. Ferrari Conflict with: Consultancy fees from Medtronic; and research support from the Netherlands Organisation for Scientific Research (NWO); the European Community; ZonMW; and the Dutch Heart Foundation. Dr. Ferrari is a member of the Editorial Board for Cephalalgia.
**Migraine - preventive therapy**

**MTIS2018-077**

**EFFICACY AND SAFETY OF ERENUMAB IN EPISODIC MIGRAINE PATIENTS WITH 2–4 PRIOR PREVENTIVE TREATMENT FAILURES: RESULTS FROM THE PHASE 3B LIBERTY STUDY**

U. Reuter¹, P. J. Goadsby²,*, M. Lanteri-Minet³, M. D. Ferrari⁴, S. Wen⁵, P. Hours-Zesiger⁶, J. Klatt⁶

¹Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany, ²NIHR-Wellcome Trust Kings Clinical Research Facility, King’s College, London, United Kingdom, ³Department of Pain, CHU-Nice, FHU Inov-Côte Azur University, Nice, France, ⁴Department of Neurology, Leiden University Medical Centre, Leiden, Netherlands, ⁵Novartis Pharmaceutical Corporation, East Hanover, NJ, United States, ⁶Novartis Pharma AG, Basel, Switzerland

**Introduction:** Erenumab is a fully human anti-CGRP receptor antibody being evaluated as preventive treatment for migraine. Current oral preventive therapies are associated with low adherence rates due to lack of efficacy and/or poor tolerability.

**Objectives:** A 12-week, double-blind, Phase 3b LIBERTY study (NCT03096834) was designed to assess efficacy and safety of erenumab in episodic migraine patients with 2–4 prior preventive migraine treatment failures.

**Methods:** Patients (N=246) were randomised (1:1) to erenumab 140 mg or placebo. The primary endpoint was proportion of patients achieving ≥50% reduction from baseline in monthly migraine days (MMDs) during Weeks 9–12. Secondary endpoints included change from baseline in MMDs, monthly acute migraine-specific medication days (MSMDs) at Week 12; and safety/tolerability.

**Results:** At baseline, proportion of patients who failed 2, 3, and 4 prior preventive migraine treatments were 38.6%, 37.8%, and 22.8%, respectively. The mean (SD) MMDs were 9.3 (2.64) and MSMDs were 4.6 (2.89). At Week 12, the proportion of patients achieving ≥50% reduction in MMD was higher in erenumab 140 mg group vs placebo (30.3% vs 13.7%; OR [95%CI]: 2.73 [1.43, 5.19]; p=0.002). There were greater reductions in MMDs and MSMDs with erenumab 140 mg vs placebo (mean difference [95%CI] in MMD: −1.61 [−2.70, −0.52]; p=0.004; mean difference (95%CI) in MSMD: −1.73 [−2.46, −1.01]; p<0.001). Safety and tolerability of erenumab were comparable to placebo. No patients in the erenumab group discontinued due to adverse events.

**Conclusion:** These results confirm efficacy and safety of erenumab in this first dedicated study of a difficult-to-treat population with 2–4 prior preventive migraine treatment failures.

**Disclosure of Interest:** U. Reuter Conflict with: consulting fee, speaking/teaching fee, and/or research grants: Allergan, Amgen, Autonomic Technologies, CoLucid, ElectroCore, Novartis, Pharm Allergan, Eli Lilly, and TEVA, P. Goadsby Conflict with: grants and personal fees from Amgen and Eli Lilly and Company and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Dr Reddy’s Laboratories, Electrocore LLC, eNeura, Novartis, Scion, Teva Pharmaceuticals, and Trigemina Inc., and personal fee from MedicoLegal work, Journal Watch, Up-to-Date, Oxford University Press, Massachusetts Medical Society, and Wolters Kluwer; and a patent Magnetic stimulation for headache assigned to eNeura without fee, M. Lanteri-Minet Conflict with: received honoraria for advisory boards, speaker panels or investigation studies from Allergan, Amgen, Astellas, ATI, BMS, Boehringer, Boston Scientific, CoLucid, Convergence, Glaxo-SmithKline, Grunenthal, Eli Lilly, Medtronic, Menarini, MSD, Novartis, Pfizer, Reckitt Benckiser, Saint-Jude, Sanofi-Aventis, Teva, UCB, Zambon, M. Ferrari Conflict with: grants, consultancy, or trial support from Medtronic, Electrocore, Amgen, Eli Lilly, and Novartis, and independent support from the European Community, NWO, NIH and the Dutch Heart Foundation, S. Wen Conflict with: employee and stocks: Novartis, P. Hours-Zesiger Conflict with: employee and stocks: Novartis, J. Klatt Conflict with: employee and stocks: Novartis
**Migraine - preventive therapy**

**MTIS2018-078**

**EFFECT OF ERENUMAB ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH EPISODIC MIGRAINE WITH 2–4 PRIOR PREVENTIVE TREATMENT FAILURES: RESULTS FROM THE LIBERTY STUDY**

P. J. Goadsby 1,*, U. Reuter 2, M. D. Ferrari 3, M. Lanteri-Minet 4, P. H. Zesiger 5, S. Wen 6, J. Klatt 5

1NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College London, London, United Kingdom,
2Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany, 3Department of Neurology, Leiden University Medical Center, Leiden, Leiden, Netherlands, 4Pain Department, CHU Nice, Nice, France,
5Novartis Pharma AG, Basel, Switzerland, 6Novartis Pharmaceuticals Corporation, New Jersey, United States

**Introduction:** In a phase 3b study (LIBERTY: NCT03096834), patients treated with erenumab, who have failed 2–4 prior preventive treatments, had almost three-times greater likelihood of achieving ≥50% reduction in monthly migraine days versus placebo.

**Objectives:** We report results from additional patient-reported outcome (PRO) scales in the LIBERTY study.

**Methods:** Patients with episodic migraine aged 18–65 years (N=246) were randomised (1:1) to subcutaneous erenumab 140 mg or placebo every 4 weeks for 12 weeks. The PRO scales included Headache Impact Test (HIT-6; change from baseline, % patients with ≥5-point reduction and shift in categorised total score from baseline to final values), Migraine Physical Function Impact Diary (MPFID-global item; change from baseline and % patients with ≥5-point reduction) and Work Productivity and Activity Impairment (WPAI) scores at Week 12. P-values are nominal without multiplicity adjustment.

**Table:**

<table>
<thead>
<tr>
<th>Patient-reported outcomes in patients with episodic migraine who have failed 2–4 prior preventive treatments (Week 12)</th>
<th>Erenumab 140 mg N=119</th>
<th>Placebo N=124</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIT-6</td>
<td>Change from baseline to Week 12</td>
<td>−5.34 ( 0.62)</td>
<td>−2.39 ( 0.52)</td>
</tr>
<tr>
<td></td>
<td>Proportion of patients with at least 5-point reduction from baseline in HIT-6 total score, n (%)</td>
<td>55 (46.2)</td>
<td>33 (26.6)</td>
</tr>
<tr>
<td>MPFID</td>
<td>Change from baseline to Week 12 – Overall impact on everyday activities</td>
<td>−2.94 (0.87)</td>
<td>0.82 (0.83)</td>
</tr>
<tr>
<td></td>
<td>Proportion of patients with at least 5-point reduction from baseline on the physical impairment domain, n (%)</td>
<td>45 (37.8)</td>
<td>24 (19.5)</td>
</tr>
<tr>
<td></td>
<td>Proportion of patients with at least 5-point reduction from baseline on the everyday activities domain, n (%)</td>
<td>49 (41.2)</td>
<td>31 (25.2)</td>
</tr>
<tr>
<td>WPAI</td>
<td>Change from baseline in percent work time missed due to a problem</td>
<td>−2.92 (1.44)</td>
<td>1.19 (2.00)</td>
</tr>
<tr>
<td></td>
<td>Change from baseline in percent impairment while working due to problem</td>
<td>−12.03 (2.62)</td>
<td>−1.94 (2.97)</td>
</tr>
<tr>
<td></td>
<td>Change from baseline in percent activity impairment due to a problem</td>
<td>−6.84 (2.29)</td>
<td>0.89 (2.22)</td>
</tr>
<tr>
<td></td>
<td>Change from baseline in lost productivity score</td>
<td>−13.84 (2.75)</td>
<td>−2.41 (3.23)</td>
</tr>
</tbody>
</table>
Data are presented as mean (standard error) unless specified. P-value is versus placebo. HIT-6, Headache Impact Test; MPFID, Migraine Physical Function Impact Diary; N, number of patients included in the analysis set; n, number of patients who responded; WPAI, Work Productivity and Activity Impairment

Results: At baseline, mean values for all outcome measures were similar between groups. Patients treated with erenumab reported improvement in functional impact versus placebo (HIT-6; P<0.001). Higher proportions of patients reported ≥5-point reduction in HIT-6 scores and a shift in categorised HIT-6 total score in favour of erenumab versus placebo. A similar treatment effect was observed for MPFID in terms of overall impact on everyday activities (P=0.002 versus placebo) and ≥5-point reduction in MPFID scores. In 4/5 domains measured by WPAI, patients treated with erenumab showed greater improvement versus placebo (Table)

Conclusion: Erenumab 140 mg showed favourable treatment effects on PRO scales assessing different functional aspects in patients who have failed 2–4 prior preventive treatments.

References: This study was supported by Novartis Pharma AG, Basel, Switzerland

Disclosure of Interest: P. Goadsby Conflict with: grants and personal fees from Amgen and Eli-Lilly and Company and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Dr Reddy’s Laboratories, Electrocore LLC, eNeura, Novartis, Scion, Teva Pharmaceuticals, and Trigemina Inc., and personal fee from MedicoLegal work, Journal Watch, Up-to-Date, Oxford University Press, Massachusetts Medical Society, and Wolters Kluwer, Conflict with: a patent Magnetic stimulation for headache assigned to eNeura without fee, U. Reuter Conflict with: consulting fee, speaking/teaching fee, and/or research grants: Allergan, Amgen, Autonomic Technologies, CoLucid, ElectroCore, Novartis, Pharm Allergan, M. Ferrari Conflict with: grants, consultancy, or trial support from Medtronic, Electrocore, Amgen, Lilly, and Novartis,, M. Lanteri-Minet Conflict with: 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, Reckitt Benckiser, Saint-Jude, Sanofi-Aventis, Teva, UCB, Zambon, P. H. Zesiger Conflict with: employees and stocks: Novartis, S. Wen Conflict with: employees and stocks: Novartis, J. Klatt Conflict with: employees and stocks: Novartis
Abstracts

Migraine - preventive therapy
MTIS2018-079
REDUCTION IN THE NUMBER OF HEADACHE HOURS IN CHRONIC AND EPISODIC MIGRAINE WITH FREMANEZUMAB
J. M. Cohen, MD, MPH, FAHS*, S. K. Gandhi, MD†, R. Yang, PhD†
†Teva Pharmaceuticals, Frazer, Pennsylvania, United States

Introduction: Fremanezumab, a fully humanized monoclonal antibody that selectively targets calcitonin gene-related peptide (CGRP), has demonstrated efficacy in migraine prevention.

Objectives: To evaluate the efficacy of fremanezumab in patients with chronic and episodic migraine by assessing the change in moderate to severe headache hours.

Methods: These two concurrent Phase 3, multicenter, randomized, double-blind, parallel-group studies included patients with prospectively confirmed chronic (≥15 headache days and ≥8 migraine days per month) or episodic migraine (6–14 headache days and ≥4 migraine days per month). Patients were randomized 1:1:1 to receive subcutaneous injections of either fremanezumab quarterly (675 mg at baseline, and placebo at Weeks 4 and 8), fremanezumab monthly (chronic migraine: 675 mg at baseline and 225 mg at Weeks 4 and 8; episodic migraine: 225 mg at baseline, Weeks 4 and 8), or placebo (at baseline, Weeks 4 and 8) over a 12-week treatment period. The change from baseline (28-day pre-treatment period) in the monthly average number of hours with headache of any severity and of at least moderate severity during the 12-week treatment period was evaluated.

Results: A total of 1121 patients with chronic migraine (quarterly: n=375; monthly: n=375; placebo: n=371) and 865 patients with episodic migraine (quarterly: n=288; monthly: n=287; placebo: n=290) were included in this analysis. In patients with chronic migraine, headache hours of at least moderate severity were reduced from baseline (quarterly [mean ± standard deviation]: 66.4±58.8; monthly: 68.0±53.9; placebo: 68.5±57.0) with both fremanezumab dosing regimens (quarterly: least-squares mean ± standard error: –24.4±2.5 hours, *P*=0.0001; monthly: –26.4±2.4 hours, †P<0.0001) compared with placebo (–14.1±2.5 hours) during the 12-week treatment period. Similar reductions were seen in headache hours of any severity in patients with chronic migraine (quarterly: †*P=0.0002, monthly: ††P<0.0001). In patients with episodic migraine, headache hours of at least moderate severity were reduced from baseline (quarterly [mean ± standard deviation]: 33.3±25.4; monthly: 31.7±23.7; placebo: 31.6±23.2) with both fremanezumab dosing regimens (quarterly: –14.5±2.5 days, †*P=0.0001; monthly: –15.5±1.3 days, ††P<0.0001) compared with placebo (–8.1±1.3 days) during the 12-week treatment period. Similar reductions were seen in headache hours of any severity in patients with episodic migraine (quarterly: ††*P=0.0007, monthly: †††P<0.0001).

Conclusion: Fremanezumab treatment, with both quarterly and monthly dosing, reduced the monthly average number of headache hours of any severity and of at least moderate severity among patients with chronic and episodic migraine.

**Migraine - preventive therapy**

**MTIS2018-080**

**REDUCTION IN THE SEVERITY OF HEADACHE IN PATIENTS WITH CHRONIC AND EPISODIC MIGRAINE WITH FREMANEZUMAB TREATMENT**

M. Ashina, MD¹, J. M. Cohen, MD, MPH, FAHS², S. K. Gandhi, MD², R. Yang, PhD²

¹University of Copenhagen, Copenhagen, Denmark, ²Teva Pharmaceuticals, Frazer, Pennsylvania, United States

**Introduction:** Fremanezumab, a fully humanized monoclonal antibody that selectively targets calcitonin gene-related peptide (CGRP), has demonstrated efficacy in migraine prevention.

**Objectives:** To evaluate changes in headache severity in patients with chronic and episodic migraine after treatment with fremanezumab.

**Methods:** Data from two concurrent Phase 3, multicenter, randomized, double-blind, parallel-group studies included patients with prospectively confirmed chronic (≥15 headache days and ≥8 migraine days per month) or episodic migraine (6–14 headache days and ≥4 migraine days per month). Patients were randomized 1:1:1 to receive subcutaneous injections of either fremanezumab quarterly (675 mg at baseline, and placebo at Weeks 4 and 8), fremanezumab monthly (chronic migraine: 675 mg at baseline and 225 mg at Weeks 4 and 8; episodic migraine: 225 mg at baseline, Weeks 4 and 8), or placebo (at baseline, Weeks 4 and 8) over a 12-week treatment period. The change from baseline (28-day pre-treatment period) in the mean peak severity of headache days during the post-baseline (12-week treatment) period for individual fremanezumab dosing arms were compared with placebo in each trial. The mean peak severity was calculated by averaging the severity of headache days within each period, where 1=low, 2=moderate, and 3=severe. An analysis of covariance model was used to test differences in changes in mean severity across comparison groups.

**Results:** A total of 1121 patients with chronic migraine (fremanezumab quarterly: n=375; fremanezumab monthly: n=375; placebo: n=371) and 865 patients with episodic migraine (fremanezumab quarterly: n=288; fremanezumab monthly: n=287; placebo: n=290) were included in this analysis. In patients with chronic migraine, the baseline percentages of moderate and severe headache days were 67%, 68%, and 69% for fremanezumab quarterly, fremanezumab monthly, and placebo respectively. A decrease in the percentage of moderate and severe headache days from baseline was observed for all three groups (fremanezumab quarterly: 10%; fremanezumab monthly: 11%; placebo: 6%) during the post-baseline treatment period. In patients with episodic migraine, the decreases in moderate and severe headache days were 13%, 10%, and 7% in fremanezumab quarterly, fremanezumab monthly, and placebo, respectively. For both chronic and episodic migraine patients, there was a significant reduction in the mean peak severity of headache days from baseline during the post-baseline treatment period, with both fremanezumab quarterly and monthly compared with placebo (P<0.0001).

**Conclusion:** Fremanezumab quarterly and monthly treatment reduced the severity of headache in patients with chronic and episodic migraine.

**Disclosure of Interest:** M. Ashina, MD Conflict with: Speaker fees from Allergan, Amgen, Novartis and Teva Pharmaceuticals., J. Cohen, MD, MPH, FAHS Conflict with: Employee of Teva Pharmaceuticals., S. Gandhi, MD Conflict with: Employee of Teva Pharmaceuticals., R. Yang, PhD Conflict with: Employee of Teva Pharmaceuticals.
**Migraine - preventive therapy**  
**MTIS2018-081**  

**100% RESPONSE RATE TO GALCANEZUMAB IN PATIENTS WITH EPISODIC MIGRAINE: RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDIES**  
1Nevada Headache Institute, Las Vegas, 2Eli Lilly and Company, and/or one of its subsidiaries, Indianapolis, 3Department of Neurology, Hofstra Northwell School of Medicine at Hofstra University, Hempstead, United States

**Introduction:** Galcanezumab is a humanized monoclonal antibody that selectively binds to calcitonin gene-related peptide (CGRP) and has demonstrated efficacy in reducing migraine headache days (MHD) in patients suffering from episodic and chronic migraine headaches.

**Objectives:** To characterize adult patients with episodic migraine headache who achieved 100% response to galcanezumab treatment.

**Methods:** The proportions of patients with 100% response (100% reduction from baseline in monthly MHD) were calculated for each month from 2 double-blind, 6-month galcanezumab studies in patients with episodic migraine (4 to 14 MHD and ≥2 migraine attacks per month at baseline). Patients were randomized (1:1:2) to monthly subcutaneous galcanezumab 120 mg (after 240 mg initial loading dose) or 240 mg or placebo. 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.

**Table:**

**Results:** The analysis included 1739 patients treated with galcanezumab 120 mg (n=436) or 240 mg (n=428) or placebo (n=875). The mean monthly 100% response rate on an average month in the 6-month double-blind phase was greater for galcanezumab 120 mg (13.5%) and 240 mg (14.3%) groups versus placebo (5.9%) with odds ratios of 2.5 (95% confidence interval [CI] 1.9, 3.2) and 2.6 (95% CI 2.0, 3.4), respectively (p<0.001). The rate of 100% monthly response increased at each month over the 6-month double-blind phase with higher rates for galcanezumab dose groups (9% to 21%) than placebo (2% to 10%) (p<0.001). Evaluation of 100% response by the number of months showed greater proportions of galcanezumab-treated patients in either dose group, compared to placebo, were able to achieve a 100% response (p<0.05) though few patients had ≥4 months of 100% response. The proportions of patients with 100% response were greater in the last 3 months of treatment. Considering the average number days between migraine attacks across the 6-month period (not just during the times of 100% response), the duration of migraine headache free periods in the galcanezumab groups was 29 days for those with at least 1 month of 100% response and 55 days for those with at least 3 months of 100% response– around 6 to 11 times the mean gap of 5 days observed at baseline.

**Conclusion:** More than a third of patients with episodic migraine headache treated with galcanezumab 120 mg or 240 mg achieved 100% response for at least 1 month. More patients had 100% monthly response in the last 3 months of the 6-month double-blind period. For those with 100% response of at least 1 month, the average time between attacks for the entire treatment period was nearly 1 month and approached 2 months for patients with 3 or more months of 100% response.

**Disclosure of Interest:** A. Nagy Conflict with: Research Support: Alder, ATI, Allergan, Lilly, Teva; Advisory Boards: Alder, Amgen, Lilly, Pernix, Supernus, Teva, Upsher-Smith; Consultant: Xenon, Zosano, Impel; Speakers’ Bureau: Amgen, Avanir, Electrocore, Teva, E. Pearlman Conflict with: Employee of Eli Lilly and Company, and/or one of its subsidiaries, D. Ruff Conflict with: Employee of Eli Lilly and Company, and/or one of its subsidiaries, K. Day Conflict with: Employee of Eli Lilly and Company, and/or one of its subsidiaries, S. Aurora Conflict with: Employee of Eli Lilly and Company, and/or one of its subsidiaries, N. Rosen Conflict with: Research Support: Allergan, Axon Optics, Theranica; Advisory Boards: Allergan, Teva, Eli Lilly, Supernus, Promius; Consultant: Curelator; Speakers’ Bureau: Allergan
**Migraine - preventive therapy**

**MTIS2018-082**

**THE COMPARATIVE EFFICACY OF PROPHYLACTIC TREATMENT OF CHRONIC MIGRAINE**

D. Sotnikov*

**Introduction:** Population studies in Ukraine were conducted by us and showed the prevalence of chronic migraine in organized population groups of 0.9%.

**Objectives:** The purpose of this research is to study the comparative efficacy of prophylactic treatment of chronic migraine the combination amitriptyline with propranolol, and anticonvulsants – lamotrigine, gabapentin and pregabalin. The study is also aimed at the search for a differentiated approach and predictors for their use.

**Methods:** The study involved 140 patients suffering from chronic migraine, aged 18 to 60 (mean 37.4±3.9) years. Duration of disease was 18.6±4.2 years. The majority of patients were women – 104 (74.3%) persons. In chronic migraine we differentiated 2 types of cephalgia: the intensity of 5 or more points for visual analogue scale (VAS), which limits the daily activities, was considered an attack, and in other cases, the headache was regarded as “background” (bilateral, moderate). Patients were randomised on four groups. First group (37 patients) used amitriptyline combine with propranolol, second group (35 patients) used gabapentine, third group (39 patients) – pregabaline, fourth group (41 patients) – lamotrigine during 90 days. All patients filled a headache diary. Anxiety and depression were investigated by the tests of Spielberger and Beck. Treatment was started with minimal doses, with subsequent titration every week until the individual maximum and well tolerated.

**Results:** The average daily dose of amitriptyline was 37.0±2.4 mg, propranolol 80.0±4.7 mg, gabapentin 864.0±46.9 mg, pregabalin 167.4±23.6 mg, lamotrigine 111.1±7.2 mg. The combination of amitriptyline with propranolol had the greatest effect on the course of background headaches: the number of days reduced by 56.5%, and intensity – by 27.4%. Among anticonvulsants, the most effective against background cephalgia is pregabalin: the number of days decreased by 46.5%, and intensity by 23.4%. Pregabalin is also preferred among all groups in reducing the number of migraine attacks – by 53.8%. The duration of attacks of headache was reduced approximately equally when taking pregabalin, gabapentin and amitriptyline with propranolol: by 49.1%, 45.4% and 41.4%. Decrease in the level of reactive and personal anxiety was observed in the groups of amitriptyline with propranolol – by 22.8% and 17.9%, and pregabalin – by 20.0% and 16.1%. A significant reduction in the level of depression was observed when using amitriptyline with propranolol by 36.9%, pregabalin by 30.7% and lamotrigine by 29.7%.

**Conclusion:** In patients with the prevalence of background headaches with accompanying psychoemotional disorders, it is necessary to give the combine amitriptyline with propranolol or pregabalin. In case frequent attacks of migraine with severe headaches, pregabalin is most effective. Gabapentin and lamotrigine have shown their effectiveness in the treatment of chronic migraine, but can be used in the ineffectiveness or intolerance the combine amitriptyline with propranolol or pregabalin.
Migraine - preventive therapy
MTIS2018-083

ECONOMIC IMPACT OF MIGRAINE IN THE EU5: A MATCHED ANALYSIS OF THE NHWS 2017 DATA ON WORK PRODUCTIVITY AND HEALTHCARE RESOURCE USE

M. J. Doane 1, P. Vo 2, A. Bilitou 3, J. Fang 4, A. K. Laflamme 2, S. Gupta 5
1Kantar Health, Philadelphia, United States, 2Novartis Pharma AG, Basel, Switzerland, 3Novartis Global Services Centre, Dublin, Ireland, 4Novartis Pharmaceuticals Corporation, New Jersey, 5Kantar Health, New York, United States

Introduction: Migraine is a distinct neurological disease ranking among the top causes of disability globally1. Objectives: This study aimed to describe the incremental burden of migraine on work productivity and healthcare resource utilization (HRU) in those suffering from ≥4 monthly headache days (HDs) in Europe.

Methods: A retrospective, cross-sectional analysis of the 2017 National Health and Wellness Survey (NHWS) data from the EUS (France, Germany, Italy, Spain, and UK) was conducted. Outcomes from respondents who self-reported a doctor diagnosis of migraine, experienced at least one migraine during the prior month and overall ≥4 HDs during the prior month, were stratified by HD frequency (i.e., 4-7, 8-14 and ≥15 HDs) and matched by propensity scores within each subgroup and country using sociodemographic characteristics to respondents without migraine (controls).

Work and activity impairment was assessed via Work Productivity and Activity Impairment Questionnaire – General Health version (WPAI-GH), and HRU via healthcare provider (HCP) visits, emergency room (ER) visits, and hospitalizations during the prior 6 months of survey completion. Mann-Whitney U tests were used for continuous and Chi-square tests were used for categorical variables to determine significant differences between subgroups.

Results: Analyses of the propensity score-matched sample of 1569 respondents with migraine (4-7, 8-14 and ≥15HDs/month) showed that a significantly higher proportion of patients reported at least one visit to a HCP, neurologist, ER or being hospitalized in the prior 6 months compared with matched controls (Table). WPAI outcomes were also significantly impacted across all migraine subgroups compared with controls.
Conclusion: Migraine patients across all migraine frequency subgroups reported significantly higher HRU and work impairment compared with matched non-migraine controls. This study highlights the economic implications of migraine to the healthcare system and society.


Disclosure of Interest: M. Doane Conflict with: Kantar Health employee, P. Vo Conflict with: Novartis employee, A. Bilitou Conflict with: Novartis employee, J. Fang Conflict with: Novartis employee, A. Laflamme Conflict with: Novartis employee, S. Gupta Conflict with: Kantar Health received funding from Novartis to conduct this study
Migraine - preventive therapy

MTIS2018-084

MY MIGRAINE VOICE: A WORLDWIDE SURVEY OF 11,266 MIGRAINE PATIENTS

E. Ruiz de la Torre 1,*, R. Quintana 2, V. Carboni 3, P. Martelletti 4–5, T. J. Schwedt 6, M. Lanteri-Minet 7, H.-C. Diener 8, A. K.-Laflamme 9, A. Vangaa Rasmussen 10, D. Walsh 11, A. Craven 12, S. Evans 13, P. Dumas 14, R. Fink 9, A. Fiorin 9, S. Ribbe 9, P. Vo 9

1European Headache Alliance, Brussels, Belgium, 2GFK, Madrid, Spain, 3GfK Health, Basel, Switzerland, 4Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy, 5EHF, -, -, 6Neurology Arizona, Mayo Clinic, Phoenix, United States, 7Département d’Evaluation et Traitement de la Douleur, Centre Hospitalo-Universitaire de Nice, -, France, 8Department of Neurology and Headache Center, University Duisburg-Essen, -, Germany, 9Novartis Pharma AG, Basel, Switzerland, 10Rigshospitalet Glostrup, Copenhagen, Denmark, 11European Federation of Neurological Associations, Brussels, Belgium, 12Migraine Association Ireland, Dublin, Ireland, 13Migraine Action, Leicester, United Kingdom, 14Migraine Again, -, United States

Introduction: The My Migraine Voice survey was conducted to assess migraine characteristics and describe the current real-world burden and impact of living with migraine from clinical, personal, and economic perspectives amongst those with at least 4 monthly migraine days (MMDs).

Objectives: This analysis reports on survey respondents’ demographics, migraine characteristics, use of migraine therapies, and association with other chronic conditions.

Methods: A worldwide cross-sectional study was conducted using a 30-minute online survey of adults with migraine recruited from 31 countries across Africa, America, Asia and Europe via online panels and patient organizations. To be included, participants had to report >=4 MMDs in the 3 months preceding survey administration (September 2017-February 2018). High-need patients were prioritized by ensuring 90% of patients had reported preventive migraine treatment use (pre-specified).

Results: A total of 11,266 individuals with migraine participated (75% female, mean age=39 years). Of all respondents, 47% were employed full-time, 56% married, 63% had children and 54% had migraine family history. Patients had had migraine for 11.6 years on average (27% for >20 years), 54% received a diagnosis within 6 months of consulting for their symptoms (19% within >=2 years), and 83% reported taking prescription medications for acute treatment (51% also take OTC drugs). Respondents reported 3.3 other chronic conditions on average (top 3: anxiety, insomnia/sleep disorders, and depression).

Conclusion: This large worldwide study constitutes a rich source of data to further describe this economically active population with prior treatment usage and with personal, social and professional commitments, and high healthcare use.

Disclosure of Interest: E. Ruiz de la Torre Conflict with: President of the EHA, R. Quintana Conflict with: Employee of GFK, V. Carboni Conflict with: Employee of GFK, P. Martelletti Conflict with: Consulting fees from various pharmaceutical companies, T. Schwedt Conflict with: Consulting fees from various pharmaceutical companies, M. Lanteri-Minet Conflict with: Consulting fees from various pharmaceutical companies, H.-C. Diener Conflict with: Consulting fees (Advisory board) from Novartis, A. K.-Laflamme Conflict with: Novartis employee, A. Vangaa Rasmussen Conflict with: Consulting fees (advisory board) from Novartis, D. Walsh Conflict with: EFNA Executive Director, A. Craven Conflict with: President of the Migraine Association of Ireland, S. Evans Conflict with: Chief Executive of Migraine Action, P. Dumas Conflict with: CEO of Migraine Again, R. Fink Conflict with: Novartis employee, A. Fiorin Conflict with: Novartis employee, S. Ribbe Conflict with: Novartis employee, P. Vo Conflict with: Novartis employee
**Migraine - preventive therapy**

**MTIS2018-085**

**WORK PRODUCTIVITY AMONGST THOSE WITH MIGRAINE: RESULTS FROM THE MY MIGRAINE VOICE SURVEY**

T. J. Schwedt 1,*, R. Quintana 2, V. Carboni 3, P. Martelletti 4,5, M. Lanteri-Minet 6, H.-C. Diener 7, A. K.-Laflamme 8, E. Ruiz de la Torre 9, A. Craven 10, A. Vangaa Rasmussen 11, D. Walsh 12, S. Evans 13, P. Dumas 14, R. Fink 8, A. Fiorin 8, S. Ribbe 6, P. Vo 8

1Neurology Arizona, Mayo Clinic, Phoenix, United States, 2GfK, Madrid, Spain, 3GfK Health, Basel, Switzerland, 4Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy, 5EHF, -, -,

6Département d’Evaluation et Traitement de la Douleur, Centre Hospitalo-Universitaire de Nice, -, France,

7Department of Neurology and Headache Center, University Duisburg-Essen, -, Germany, 8Novartis Pharma AG, Basel, Switzerland, 9European Headache Alliance, Brussels, Belgium, 10Migraine Association Ireland, Dublin, Ireland, 11Rigshospitalet Glostrup, Copenhagen, Denmark, 12European Federation of Neurological Associations, Brussels, Belgium, 13Migraine Action, Leicester, United Kingdom, 14Migraine Again, -, United States

**Introduction:** Migraine-induced disability results in substantial economic and societal burden globally. However, limited evidence exists for those with migraine who have used preventive medication.

**Objectives:** As part of the worldwide My Migraine Voice survey, this study aimed to describe the impact of migraine on work and activity impairment amongst migraine individuals who suffer from at least 4 monthly migraine days (MMDs) and reported use of preventive medication.

**Methods:** A cross-sectional study was conducted using an online worldwide survey of migraine patients from 31 countries across Africa, America, Asia, and Europe, recruited via online panels and patient organizations. Study participants were adult patients (≥18 years) who reported ≥4 MMDs over the 3 months preceding the time of the survey (September 2017-February 2018), with pre-specified 90% of them having reported having used preventive migraine treatments. The impact of migraine on work productivity and activities during the past seven days (prior to survey completion) was evaluated using the work productivity and activity impairment (WPAI) questionnaire and was compared among treatment naive, no prior treatment failure (TF), 1 TF, and ≥2 TF patient subgroups.

**Image:**

<table>
<thead>
<tr>
<th>Table 1: WPAI outcomes by prior treatment among migraine patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Work time missed due to migraine (%)</td>
</tr>
<tr>
<td>Impairment while working due to migraine (%)</td>
</tr>
<tr>
<td>Overall work impairment due to migraine (%)</td>
</tr>
<tr>
<td>Activity impairment due to migraine (%)</td>
</tr>
</tbody>
</table>

Descriptive analysis was performed among survey respondents who were employed (n=7330) and worked in the past 7 days prior to survey completion (n=6806), TF: treatment failure
Abstracts

Results: A total of 11,266 migraine patients with at least 4MMDs responded to the survey (75% women, mean age: 39 years old). Migraine patients reported overall a reduction of 13% in their working time (absenteeism), 48% in productivity while working (presenteeism), and 52% in both overall work productivity (absenteeism and presenteeism combined) and daily activities due to migraine. Descriptive analysis of results by prior treatment showed that all WPAI outcomes are impacted by migraine especially in those who have failed 2 or more prior prophylactic treatments (Table).

Conclusion: This large worldwide study shows that migraine is associated with work productivity and activity impairment especially in those patients who have experienced two or more treatment failures.

References: This abstract is encore and has been previously submitted to AHS 2018

Disclosure of Interest: T. Schwedt Conflict with: Consulting fees from various pharmaceutical companies, R. Quintana Conflict with: Employee of GFK, V. Carboni Conflict with: Employee of GFK, P. Martelletti Conflict with: Consulting fees from various pharmaceutical companies, M. Lanteri-Minet Conflict with: Consulting fees from various pharmaceutical companies, H.-C. Diener Conflict with: Consulting fees (Advisory board) from Novartis, A. K.-Laflamme Conflict with: Novartis employee, E. Ruiz de la Torre Conflict with: President of the EHA, A. Craven Conflict with: President of the Migraine Association of Ireland, A. Vangaa Rasmussen Conflict with: Consulting fees (advisory board) from Novartis, D. Walsh Conflict with: EFNA Executive Director, S. Evans Conflict with: Chief Executive of Migraine Action, P. Dumas Conflict with: CEO of Migraine Again, R. Fink Conflict with: Novartis employee, A. Fiorin Conflict with: Novartis employee, S. Ribbe Conflict with: Novartis employee, P. Vo Conflict with: Novartis employee
Migraine - preventive therapy

MTIS2018-086

THE BURDEN OF MIGRAINE IN PORTUGAL: RESULTS FROM A PATIENT SURVEY
C. Silva 1, P. Vo 2*, R. Quintana 3, V. Carboni 3, P. A. Laires 1
1HE&OR, Novartis Portugal, Porto Salvo, Portugal, 2Novartis Pharma AG, 3GfK Health, Basel, Switzerland

Introduction: Migraine is estimated to affect about 11 to 15% (1) of the adult population worldwide and ranks among the ten leading causes of disability (2).

Objectives: To characterize the emotional, social and occupational burden of migraine in Portugal.

Methods: A cross-sectional study was conducted using an online survey of migraine patients in 31 countries across Africa, America, Asia and Europe, recruited via online panels and patient organizations. Study participants were adults (≥18 years) who reported having ≥4 monthly migraine days over the 3 months preceding the time of the survey (September 2017-February 2018), with pre-specified 90% among those having reported having used preventive migraine treatment. Results from the Portuguese sample are reported.

Results: A total of 143 migraine patients from Portugal responded to the survey: 80% female, mean age 37 years (SD 12.6; range 18-72), 73% employed and 48% married. 43% were affected by migraine for more than 10 years, 76% reported other chronic conditions and 59% had family history of migraine. Patients reported an average of 10.0 migraine days in the previous month (SD 7.3; range 4-31). Disease is mainly managed by GPs (45%) and neurologists (30%). 44% of patients reported that attacks take one or more days. Almost all participants have migraine-related sleeping difficulties (95%) and prolonged periods in darkness or isolated (90%; average 11.6 hours/month; SD 13.5; range 1-80) during a migraine-attack. About 76% take acute medication of whom 85% pain relievers. Most common preventive treatments were anti-depressants (33%), beta-blockers (28%) and anti-epileptics (26%). About 79% of participants mentioned feeling very/extremely limited in completing daily activities during the migraine attack. Most common negative feelings were lack of understanding of their pain by others (54%), feeling helpless (43%) and depressed (40%). Most patients (63%) claimed that migraine has changed their relationships with relatives/friends/partner and their social life and activities (81%). The majority (80%) feel that migraine has impacted their professional life. Half of employed migraineurs (50%) did miss work due to migraine in the last month (average 3.8 days; SD 3.4; range 1-15).

Conclusion: This study confirms that migraine has a high emotional, social and occupational impact on patients’ life in Portugal.


Disclosure of Interest: C. Silva Conflict with: This study was sponsored by Novartis., P. Vo Conflict with: This study was sponsored by Novartis., R. Quintana Conflict with: This study was conducted by GfK, V. Carboni Conflict with: This study was conducted by GfK, P. Laires Conflict with: This study was sponsored by Novartis
**Migraine - preventive therapy**

**MTIS2018-087**

**SYSTEMATIC COCHRANE REVIEW OF BOTULINUM TOXINS FOR THE PREVENTION OF MIGRAINE IN ADULTS**

C. Herd 1, C. L. Tomlinson 2, C. Rick 2, W. J. Scotton 3, J. Edwards 4, N. Ives 2, A. Sinclair 3,*, C. E. Clarke 1

1Institute of Applied Health Research, 2Birmingham Clinical Trials Unit, 3Institute of Metabolism and Systems Research, University of Birmingham, 4Department of Neurology, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom

**Introduction:** Botulinum toxin type A has been licensed for use in chronic migraine in some countries but systematic reviews of the evidence surrounding its use are sparse.

**Objectives:** To assess the effects of botulinum toxins versus placebo, active treatment or different dose for prevention of episodic or chronic migraine in adults.

**Methods:** Relevant trials were identified through electronic searches of Cochrane Central Register of Controlled Trials, Medline, Embase, and trials registries, handsearching reference lists and citation searches on key publications, and correspondence with manufacturers. Our searches were last carried out in December 2017. We included randomised, double-blind, controlled trials. Screening, data extraction, and risk of bias assessments were carried out independently and in duplicate. Twelve week time-point data following final round of treatment was analysed.

**Results:** We identified 28 trials (N=4192) from 90 articles which were eligible for inclusion. No trial carried out long term follow up. All larger trials (N>100) were commercially sponsored and 75% of trials were at high risk of bias from small size. Otherwise trial quality was mixed. Botulinum toxin was compared with placebo in 23 trials. Four trials (N=1497) of botulinum toxin in chronic migraineurs showed a reduced frequency of -3.1 migraine days/month (95% confidence interval (CI) -4.73 to -1.41) compared with placebo. Addition of one trial (418 participants) in episodic migraine lowered this pooled estimate of effect to -2.39 days/month (95% CI -4.02 to -0.76), still in favour of botulinum toxin. Secondary efficacy measures were inconsistent. Data for number of migraine attacks from six trials including chronic and episodic migraineurs showed no significant between group difference (P=0.30), but severity of migraine (10 cm visual analogue scale), was improved by -3.30 points (95% CI -4.16 to -2.45) more with active treatment. Global assessment and quality of life measures were poorly reported. Botulinum toxin had a relative risk of treatment related adverse events of twice that seen for placebo (2.18, 95% CI 1.73 to 2.75). Insufficient data was available to establish any dose-response relationship for any outcome measure. Three trials of comparisons with oral prophylactic agents independently reported no significant between group differences for a variety of diary data outcomes but meta-analysis was not possible. Compared with oral treatments, botulinum toxin showed a reduced relative risk of treatment-related adverse events of 0.76 (95% CI 0.59 to 0.98).

**Conclusion:** In chronic migraine, botulinum toxin type A reduces frequency of migraine by three days/month, reduces migraine severity by 30% and has a favourable safety profile compared with other preventative drugs. Evidence to support or refute the efficacy of botulinum toxin in episodic migraine was not identified.
**ECONOMIC BURDEN OF MIGRAINE: HEALTHCARE RESOURCE UTILIZATION IN THE MY MIGRAINE VOICE SURVEY**


**Introduction:** Migraine is a distinct neurological disease ranking among the top causes of disability globally. This study aimed to evaluate the real-world healthcare resource utilization due to migraine, particularly among individuals who suffer from at least 4 monthly migraine days (MMDs).

**Objectives:**
- To evaluate the real-world healthcare resource utilization due to migraine, particularly among individuals who suffer from at least 4 monthly migraine days (MMDs).
- The cross-sectional study conducted using an online survey of migraine patients in 31 countries across Africa, America, Asia and Europe, recruited via online panels and patient organizations. Study participants were adults (≥18 years) who reported having ≥4 MMDs over the 3 months preceding the time of the survey (September 2017-February 2018), with pre-specified 90% among those having reported having used preventive migraine treatment.

**Table 1. Resource utilization in previous 12 months in migraine individuals**

<table>
<thead>
<tr>
<th></th>
<th>Overall (N=11266)</th>
<th>No prior prophylactic treatment</th>
<th>No prophylactic TF</th>
<th>1 prophylactic TF</th>
<th>2 or more prophylactic TFs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brain scan</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients (%)</td>
<td>58%</td>
<td>29%</td>
<td>46%</td>
<td>56%</td>
<td>66%</td>
</tr>
<tr>
<td>Average number of scans</td>
<td>2.1</td>
<td>1.7</td>
<td>1.8</td>
<td>1.7</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>ER visits</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients (%)</td>
<td>38%</td>
<td>17%</td>
<td>28%</td>
<td>28%</td>
<td>46%</td>
</tr>
<tr>
<td>Average number of visits</td>
<td>3.3</td>
<td>2.9</td>
<td>2.5</td>
<td>2.7</td>
<td>3.5</td>
</tr>
<tr>
<td><strong>Overnight hospital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>stay in past 12 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients (%)</td>
<td>23%</td>
<td>8%</td>
<td>14%</td>
<td>15%</td>
<td>26%</td>
</tr>
<tr>
<td>Average nights of stay</td>
<td>3.2</td>
<td>2.6</td>
<td>2.6</td>
<td>2.3</td>
<td>3.4</td>
</tr>
</tbody>
</table>

ER: emergency room; TF: treatment failure; Data refer to 12 months prior to survey completion; survey took place between September 2017 and February 2018 in 31 countries.
**Results:** A total of 11,266 migraine patients responded to the survey (75% women, mean age: 39 years old). Migraine patients with at least 4 MMDs reported visiting different healthcare professionals (HCP) in a 6-month period due to their migraine. In the previous 12 months, 38% of patients visited the Emergency room (ER) an average 3.3 times, and 23% stayed in hospital overnight for an average of 3.2 days. Brain scans were performed on 58% of patients on average 2.1 times. These proportions were both higher in Turkey, India, Brazil, Indonesia, Poland, USA, Portugal, Russia, and also for migraine patients who have failed >=2 prophylactic treatments (Table 1).

**Conclusion:** Migraine patients (>= 4MMD) reported a high rate of HCP, ER visits and overnight stays in the hospital due to migraine; results indicate that the burden is higher among those who have failed a prophylactic migraine treatment and this trend increased with the number of prophylactic treatment failures.

**References:** 1Steiner et al. The Journal of Headache and Pain (2018) 19:17

**Disclosure of Interest:** P. Martelletti Conflict with: Consulting fees from various pharmaceutical companies, R. Quintana Conflict with: Employee of GFK, V. Carboni Conflict with: Employee of GFK, T. Schwedt Conflict with: Consulting fees from various pharmaceutical companies, M. Lanteri-Minet Conflict with: Consulting fees from various pharmaceutical companies, H.-C. Diener Conflict with: Consulting fees (Advisory board) from Novartis, A. K.-Laflamme Conflict with: Novartis employee, E. Ruiz de la Torre Conflict with: President of the EHA, A. Craven Conflict with: President of the Migraine Association of Ireland, S. Evans Conflict with: Chief Executive of Migraine Action, D. Walsh Conflict with: EFNA Executive Director, A. Vangaa Rasmussen Conflict with: Consulting fees (advisory board) from Novartis, P. Dumas Conflict with: CEO of Migraine Again, R. Fink Conflict with: Novartis employee, A. Fiorin Conflict with: Novartis employee, S. Ribbe Conflict with: Novartis employee, P. Vo Conflict with: Novartis employee
**HEALTH STATE UTILITIES AND PATIENT PREFERENCES ASSOCIATED WITH ATTRIBUTES OF MIGRAINE PROPHYLACTIC TREATMENT: ROUTE OF ADMINISTRATION AND ADVERSE EVENTS**

L. S. Matza, K. Deger, P. Vo, F. Maniyar, A. Bilitou, P. J. Goadsby

1Patient-Centered Research, 2Evidera, Bethesda, MD, United States, 3Novartis Pharma AG, Basel, Switzerland, 4Basildon and Thurrock University Hospitals and Queen Mary University, London, United Kingdom, 5Novartis Global Services Centre, Dublin, Ireland, 6NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College London, London, United Kingdom

**Introduction:** Cost-utility analyses are often used to examine the value of new treatments. These analyses require utilities representing the strength of patient preference for health states on a scale anchored to 0 (dead) and 1 (full health).

**Objectives:** The purpose of this study was to assess patient preferences (e.g. utilities) associated with migraine treatment process attributes including route of administration (ROA) and adverse events (AEs) using vignette-based methods which are not captured in traditional utility instruments such as the EQ-5D.

**Methods:** In time trade-off interviews, migraine patients in the UK (London, Edinburgh) valued health states, representing migraine with or without aura varying by ROA (daily oral, monthly injection, or 31-39 injections every three months), drafted based on literature, medication labels, and clinician interviews. Each participant also valued eight health states (randomly selected from 15) of AE descriptions added to that of migraine without aura.

**Results:** A total of 200 migraine patients completed interviews (75% female; mean age=46y). The mean utilities of health states varying by ROA suggest that daily oral medication and one monthly injection were preferred over 31-39 injections once every three months (Table 1). Common AEs associated with migraine preventives also had an impact on patient preference with disutilities (i.e., decreases in utility) ranging from -0.001 (pruritus) to -0.132 (brain fog).
Conclusion: Patients showed preference on oral medication and a single monthly injection than 31-39 injections every three months. AEs also had an impact on preference, with AEs of oral medications resulting in the greatest disutility.

Migraine - preventive therapy

MTIS2018-090

EFFECT OF ONABOTULINUMTOXINA ON THE FREQUENCY AND IMPACT OF HEADACHES IN PATIENTS WITH CHRONIC MIGRAINE WITH OR WITHOUT A HISTORY OF ACUTE PAIN MEDICATION OVERUSE: RESULTS OF THE COMPEL STUDY

S. J. Tepper 1,*, M.-C. Wilson 2, J. F. Rothrock 3, A. Orejudos 4, A. Manack Adams 5, A. M. Blumenfeld 6

1Neurology Department, Headache Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH, 2Neurology, Ochsner Health System, Covington, LA, 3Neurology, George Washington School of Medicine, Washington, DC, 4Biostatistics, 5Global Medical Affairs, Allergan plc, Irvine, CA, 6The Neurology Center, Headache Center of Southern California, Carlsbad, CA, United States

Introduction:
Overuse of acute pain medication by people with chronic migraine (CM) can increase the frequency and intensity of headache.

Objectives: This subanalysis of COMPEL Study data evaluates the relative effect of onabotulinumtoxinA on the frequency and impact of headaches in patients with CM based on history of acute pain medication overuse (MO).

Methods: The 108-wk, multicenter, open-label COMPEL Study enrolled adults with CM receiving onabotulinumtoxinA 155 U for 9 treatments. Patients completed a daily diary recording headache days for 28 days before the baseline visit and at intervals following treatments 2, 5, 7, and 9. A 6-item Headache Impact Test Questionnaire (HIT-6) was completed at every administration visit. History of MO was defined as use of acute pain medication ≥2 times/week in any week with diary data on ≥5 days during the 4-week screening period. Efficacy variables included mean change from baseline in overall number of headache days, number of moderate/severe headache days, and HIT-6 total score at weeks 60 (after 5 treatments) and 108 (after 9 treatments). Observed data are reported.

Results: 716 patients were enrolled, 715 of whom had ≥1 efficacy analysis and comprised the intention-to-treat (ITT) population: 456 (63.7%) ITT patients had a history of MO, 259 (36.3%) did not. Throughout the study period onabotulinumtoxinA treatment showed similar efficacy in both groups, including similar reductions in headache frequency and number of moderate to severe headaches. (Table 1) At week 60, 53.3% of patients with a history of MO had a ≥50% reduction in headache days from baseline, as did 55.5% of patients with no history of MO. Additional improvement was seen at week 108: ≥50% reductions were documented in 58.7% of patients with a history of MO and 69.1% of those without. Mean change from baseline (SD) in HIT-6 scores were similar for patients with and without a history of MO at week 60 (−6.8 [6.7] and −6.7 [6.2], respectively) and week 108 (−7.0 [7.19] and −7.2 [7.3], respectively).
Abstracts

Conclusion: These results suggest that onabotulinumtoxinA has similar efficacy in patients with or without a history of medication overuse, and that reductions in headache frequency are sustained over time.

Disclosure of Interest: S. Tepper Conflict with: Stewart J. Tepper, MD is an employee of Dartmouth-Hitchcock Medical Center, and receives a salary from the American Headache Society (AHS); his employer receives research grants from Alder, Allergan, Amgen, ATI, Dr. Reddy's, Scion Neurostim, Teva, Zosano. Dr Tepper has served as a consultant for Acorda, Alder, Allergan, Amgen, ATI, BioVision, Cefaly, Charleston Laboratories, DeepBench, Dr. Reddy's, ElectroCore, Eli Lilly, eNeura, GLG, Guidepoint Global, Impax, NeuroLief, Novartis, Pernix, Pfizer, Scion Neurostim, Slingshot Insights Supernus, Teva, and Zosano. He has received a salary as Editor-in-Chief of Headache Currents from AHS and royalties for books published by Springer., M.-C. Wilson Conflict with: Maria-Carmen Wilson, MD, has received consulting fees from Eli Lilly, Allergan, and Teva., J. Rothrock Conflict with: John F. Rothrock, MD, within the past 12 month 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. His parent institution has received funding from Allergan plc and Dr. Reddy for clinical research he has conducted., A. Orejudos Conflict with: Amelia Orejudos, MSc, is a full-time employee of Allergan plc and owns stock in the company., A. Manack Adams Conflict with: Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company., A. Blumenfeld Conflict with: Andrew M. Blumenfeld, MD, within the past 12 months, has served on advisory boards and/or has consulted for Allergan, Amgen, Adler, Teva, Supernus, Promius, Eaglet and Lilly; and has received funding for speaking from Allergan, Amgen, Pernix, Supernus, Depomed, Avanir, and Promius.
Migraine - preventive therapy

MTIS2018-091

ONSET OF EFFECT OF ONABOTULINUMTOXINA FOR CHRONIC MIGRAINE TREATMENT: ANALYSIS OF PREEMPT DATA

D. W. Dodick 1,*, S. D. Silberstein 2, R. B. Lipton 3, R. E. DeGryse 4, A. Manack Adams 4, H.-C. Diener 5

1 Department of Neurology, Mayo Clinic, Phoenix, AZ, 2 Neurology, Jefferson Headache Center, Philadelphia, PA, 3 Department of Neurology, Department of Epidemiology and Population Health, Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, 4 Global Medical Affairs, Allergan plc, Irvine, CA, United States, 5 Department of Neurology, University of Duisbury-Essen, Essen, Germany

Introduction: The PREEMPT trials demonstrated the efficacy and safety of onabotulinumtoxinA (onabotA) for the prevention of headache in adults with chronic migraine (CM).

Objectives: This analysis assessed the time to onset of treatment effects of onabotA relative to placebo (PBO) on reduction of headache days and migraine/probable migraine days per week from baseline.

Methods: Each PREEMPT trial included a 24-wk, double-blind, PBO-controlled phase followed by a 32-wk open-label phase. Patients were randomized to injections of onabotA (155 U to 195 U) or PBO every 12 wks for 2 cycles; followed by 3 open-label cycles of onabotA (155 U to 195 U). The primary efficacy variable for the pooled analysis was mean change from baseline in frequency of headache days per 28 days (primary endpoint, wk 24). Additional analyses included change in headache days and migraine/probable migraine days per wk vs baseline. Pooled analyses from the double-blind and open-label phases are presented.
Results: 1384 adults were randomized to onabotA (n=688) or PBO (n=696). Baseline values (as assessed during wk 4 of the baseline period) were similar in both groups for mean (SD) headache days/wk (onabotA: 4.8 [1.6] days; PBO: 4.8 [1.6] days, P=0.70) and for migraine/probable migraine days per wk (onabotA: 4.6 [1.7]; PBO: 4.6 [1.7] days, P=0.72). Pooled analyses demonstrated a significant mean decrease from baseline in frequency of headache days per 28 days, favoring onabotA over PBO at the wk 24 primary endpoint (−8.4 vs −6.6; P<0.001) and the end of the open label period (onabotA/onabotA: −11.7 vs PBO/onabotA: −10.8; P=0.02). One wk after the first treatment, onabotA reduced mean (SD) headache days by −0.9 (2.2) vs PBO (−0.7 [2.1]; P=0.046) and migraine/probable migraine days by −1.0 (2.4) vs PBO (0.7 [2.2]; P=0.031); the effect persisted from wk 3 of the first treatment cycle for both measures. OnabotA resulted in continued reduction in headache days (Figure 1A) and migraine/probable migraine days (Figure 1B) over 5 treatment cycles.
**Conclusion:** As early as wk 1 after the first treatment, onabotA treatment significantly reduced headache days/wk and migraine/probable migraine days/wk. This improvement persisted from wk 3 of the first treatment cycle compared with PBO. Treatment with onabotA resulted in a persistent and progressive reduction in headache days over the course of the 56-wk PREEMPT trials, indicating that peak benefit may require multiple treatments.

**Disclosure of Interest:** D. Dodick Conflict with: David W. Dodick, MD, has received compensation from serving on advisory boards and/or consulting within the past 5 years for: Allergan, Amgen, Novartis, Alder, Arteaus, Pfizer, Colucicid, Merck, NuPathe, Eli Lilly and Company, Autonomic Technologies, Ethicon J&J, Zogenix, Supernus, Labrys, Boston Scientific, Medtronic, St Jude, Bristol-Myers Squibb, Lundbeck, Impax, MAP, Electrocore, Tonix, Novartis, Teva, Alcobra, Zosano, ZP Opco, Insy, Ipsen, Acorda, eNeura, Charleston Laboratories, Gore, Biohaven, Biocentric, Magellan, Theranica, Xenon, Dr Reddy’s/Promius Pharma, Vedanta, CC Ford West Group, and Foresight. Dr Dodick owns equity in Epien, GBS/Nocira, Second Opinion, Healint, and Theranica. Dr Dodick has received funding for travel, speaking, editorial activities, or royalty payments from IntraMed, SAGE Publishing, Sun Pharma, Allergan, Oxford University Press, American Academy of Neurology, American Headache Society, West Virginia University Foundation, Canadian Headache Society, Healthlogix, Universal Meeting Management, WebMD, UptoDate, Medscape/WedMD, Oregon Health Science Center, Albert Einstein University, University of Toronto, Starr Clinical, Decision Resources, Synergy, MedNet LLC, Peer View Institute for Medical Education, Medicom, Medlogix, Wolters Kluwer Health, Chameleon Communications, Academy for Continued Healthcare Learning, Haymarket Medical Education, Global Scientific Communications, Miller Medical Communications, MeetingLogiX, and Wiley Blackwell. Dr Dodick, through his employer, has consulting use agreements with NeuroAssessment Systems and Myndshft. He holds board of director positions with King-Devick Technologies, and Epien Inc. He holds the following Patent 17189376.1-1466:vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis (no compensation)., S. Silberstein Conflict with: Dr. Stephen Silberstein acts as a consultant and/or advisory panel member and receives honoraria from Alder Biopharmaceuticals; Allergan, Inc.; Amgen; Avanir Pharmaceuticals, Inc.; eNeura; ElectroCore Medical, LLC; Labrys Biologics; Medscape, LLC; Medtronic, Inc.; Neuraleive; NINDS; Pfizer, Inc.; and Teva Pharmaceuticals. His employer receives research support from Allergan, Inc.; Amgen; Cumberland Pharmaceuticals, Inc.; ElectroCore Medical, Inc.; Labrys Biologics; Eli Lilly and Company; Merz Pharmaceuticals; and Troy Healthcare., R. Lipton Conflict with: Richard B. Lipton, MD has received grant support or honoraria from: Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy’s Laboratories, 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. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS. Dr Lipton serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache., R. DeGryse Conflict with: Ronald E. DeGryse, MS, MA, is a full-time employee of Allergan, Inc. and owns stock in the company., A. Manack Adams Conflict with: Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company., H.-C. Diener Conflict with: Hans-Christoph Diener, MD, has received honoraria for participation in clinical trials, contribution to advisory boards or oral presentations from Addex Pharma, Allergan, Almirall, Autonomic Technology, AstraZeneca, Bayer Vital, Berlin Chemie, Boehhringer Ingelheim, Bristol-Myers Squibb, Coherex, Colucicid, 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.
Abstracts

**Migraine - preventive therapy**

**MTIS2018-092**

**LONG-TERM SAFETY AND TOLERABILITY OF ONABOTULINUMTOXINA TREATMENT IN CHRONIC MIGRAINE PATIENTS TAKING ORAL PREVENTIVE MEDICATIONS: COMPEL ANALYSIS BY TREATMENT CYCLE**


1Palm Beach Headache Center, Premiere Research Institute @Palm Beach Neurology, West Palm Beach, FL, 2Headache Center of Southern California, The Neurology Center, Carlsbad, CA, 3The Phoenix Headache Institute, Scottsdale, AZ, 4Allergan plc, 5Allergan plc / University of California, Irvine, Irvine, CA, United States

**Introduction:** The COMPEL Study was designed to evaluate the long-term efficacy and safety of onabotulinumtoxinA in adults with chronic migraine (CM).

**Objectives:** This sub-analysis of COMPEL study data assessed the safety and tolerability of onabotulinumtoxinA over time in patients receiving concomitant oral preventive medication.

**Methods:** The 108-week, multicenter, open-label COMPEL Study enrolled adults with CM receiving onabotulinumtoxinA 155 U over 9 treatment cycles (108 weeks). Patients could take a single oral preventive medication concomitantly if the dose and regimen were stable for 4 weeks before the first onabotulinumtoxinA treatment and remained unchanged until or after week 24. The primary outcome variable was reduction from baseline in headache day frequency at week 108. Safety and tolerability—overall and by treatment cycle—were assessed. Patients were screened for treatment-emergent adverse events (TEAEs) at each visit through patient self-report, general non-directed questioning and direct questioning. Any adverse event (AE) that started or increased in severity in the period between treatments was attributed to the preceding treatment. The safety population consisted of all patients who received ≥1 dose of onabotulinumtoxinA.

**Results:** 716 patients were enrolled, 715 of whom had ≥1 efficacy analysis; 89 patients (12.4%) received at least one stable oral preventive medication during the study; 89 patients (12.4%) received at least one stable oral preventive medication during the study, including 44 (6.1%) who had oral preventive medications added on or after week 24. TEAEs were more common among patients receiving oral preventive treatment (71.9% vs 59.3%), as were treatment-related AEs (25.8% vs 17.2%). No patient receiving oral preventive treatment presented with a treatment-related serious AE. Patients receiving oral preventive treatment had a higher incidence of treatment-related musculoskeletal stiffness (6.7% vs 1.8%) and injection site pain (4.5% vs 1.6%) and a lower incidence of neck pain (1.1% vs 4.5%). The overall incidence of TEAEs among patients receiving
oral preventive treatment declined over time: from 23.6% after treatment cycle 1 to 14.3% after treatment cycle 9 (Figure 1).

**Conclusion:** In patients receiving concomitant oral preventive medication, onabotulinumtoxinA was generally well tolerated. The overall incidence of TEAEs decreased with repeated administration of onabotulinumtoxinA.

**Disclosure of Interest:** P. Winner Conflict with: Paul Winner has received consulting fees/honoraria from Allergan, Amgen, Supernus, and TEVA; has served on the speaker’s bureau for Allergan, Amgen, Avanir, Supernus, and TEVA; and has received research grants from Allergan, Amgen, NuPathe, AstraZeneca, Avanir, Eli Lilly, Novartis, and TEVA., A. Blumenfeld Conflict with: Andrew M. Blumenfeld, MD, has served on advisory boards and/or has consulted for Allergan, Amgen, Adler, Teva, Supernus, Promius, Eaglet, and Lilly; and has received funding for speaking from Allergan, Amgen, Pernix, Supernus, Depomed, Avanir, and Promius., E. Eross Conflict with: Eric J. Eross, DO, has received grant/research support from Allergan, and has served on speaker bureaus for Allergan, Amgen, Avanir, Depomed, Pernix, Supernus and Teva and has served on advisory boards or as a consultant for Amgen, Promius, and Supernus. Dr. Eross is Owner and President of Glia Sciences, Inc., A. Orejudos Conflict with: Amelia Orejudos, MSc, is a full-time employee of Allergan plc and owns stock in the company., A. Manack Adams Conflict with: Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company., M. Brin Conflict with: Mitchell F. Brin, MD, is an employee of Allergan Inc. and receives stock in the company.
EFFECTS OF ONABOTULINUMTOXINA ON HEADACHE FREQUENCY AND IMPACT IN PATIENTS WITH CHRONIC MIGRAINE WITH OR WITHOUT BASELINE ALLODYNIA: A COMPEL SUBANALYSIS

W. B. Young 1,*, J. F. Rothrock 2, J. I. Lopez 3, A. Manack Adams 4, R. B. Lipton 5, A. M. Blumenfeld 6

1Neurology, Jefferson Hospital for Neuroscience, Philadelphia, PA, 2Neurology, George Washington School of Medicine, Washington, DC, 3Neurology, University of South Alabama College of Medicine, Mobile, AL, 4Global Medical Affairs, Allergan plc, Irvine, CA, 5Department of Neurology, Department of Epidemiology and Population Health, Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, 6Headache Center of Southern California, The Neurology Center, Carlsbad, CA, United States

Introduction: Allodynia is common in the chronic migraine (CM) population and has been linked to reduced response to migraine therapies.

Objectives: This subanalysis of COMPEL Study data assessed the relative effect of onabotulinumtoxinA (onabotA) on the frequency and impact of headaches in patients with CM with a history of allostopy.

Methods: The 108-wk, multicenter, open-label COMPEL Study enrolled adults with CM receiving onabotA 155 U for 9 treatments, every 12 wks. Patients completed a daily diary recording headache days for 28 days before the baseline visit and at intervals after treatments 2, 5, 7, and 9. A 6-item Headache Impact Test Questionnaire (HIT-6) was completed at every administration visit. Patients with baseline allostopy were identified by the Allodynia Screening Checklist (ASC >3) during the 28-day screening period. Primary outcome was reduction in headache frequency per 28-day period at 108 wks (9 treatments). Efficacy variables included mean change from baseline in overall number of headache days, number of moderate/severe headache days, and HIT-6 total score at wks 60 (after 5 treatments) and 108 (after 9 treatments).
Figure 1. Effect of onabotulinumtoxinA on change from baseline in A) headache day frequency, B) moderate/severe headache day frequency, and C) HIT-6 scores in patients with allodynia vs without allodynia at baseline.

**A**

<table>
<thead>
<tr>
<th></th>
<th>Week 24</th>
<th>Week 60</th>
<th>Week 108</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=233)</td>
<td>-8.4</td>
<td>-9.9</td>
<td>-10.8</td>
</tr>
<tr>
<td>(n=310)</td>
<td>-7.7</td>
<td>-10.3</td>
<td>-12.5</td>
</tr>
</tbody>
</table>

P=0.044

**B**

<table>
<thead>
<tr>
<th></th>
<th>Week 24</th>
<th>Week 60</th>
<th>Week 108</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=233)</td>
<td>-7.5</td>
<td>-8.9</td>
<td>-10.5</td>
</tr>
<tr>
<td>(n=310)</td>
<td>-6.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P=0.090

**C**

<table>
<thead>
<tr>
<th></th>
<th>Week 24</th>
<th>Week 60</th>
<th>Week 108</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=243)</td>
<td>-5.7</td>
<td>-7.6</td>
<td>-8.4</td>
</tr>
<tr>
<td>(n=334)</td>
<td>-5.5</td>
<td></td>
<td>-9.4</td>
</tr>
</tbody>
</table>

HIT-6=6-Item Headache Impact test
Results: In patients with (n=289) and without (n=426) baseline allodynia, onabotA reduced 28-day headache frequency relative to baseline (wk 60: allodynia, −9.9±6.7; no allodynia, −10.3±7.3; wk 108: allodynia, −10.8±7.1; no allodynia, −12.5±7.4; Figure 1A). Similarly, onabotA reduced moderate/severe headache days relative to baseline (wk 60: allodynia, −8.7±6.1; no allodynia, −8.9±6.2; wk 108: allodynia, −9.6±6.9; no allodynia, −10.5±7.2; Figure 1B). OnabotA also reduced (improved) mean (SD) HIT-6 total scores (wk 60: allodynia, −7.0±6.9; no allodynia, −7.6±7.3; wk 108: allodynia, −8.4±7.1, no allodynia, −9.4±7.9; Figure 1C). For all but one outcome, there was no significant difference in the effect of onabotA between patients with or without allodynia at baseline; the change in headache days from baseline at wk 108 was significantly greater for patients without allodynia versus those with allodynia at baseline (P=0.044). No new safety concerns were identified.

Conclusion: These results support the efficacy of onabotA in reducing headache burden for up to 108 wks in CM patients with or without allodynia. Despite reports that allodynia contributes to treatment resistance, both groups experienced similar benefit from treatment with onabotA.

Disclosure of Interest: W. Young Conflict with: William B. Young , MD, has served on advisory boards for Alder, Allergan, Cipla, Lilly, and Supernus; has consulted for Allergan and Supernus; and has received research support from AGA, Alder, Allergan, Amgen, Autonomic Technology, Cumberland, Dr. Reddy Laboratories, Eli Lilly, Eneura Inc, Merz, and St. Jude Medical., J. Rothrock Conflict with: 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. His parent institution has received funding from Allergan plc, Amgen and Dr. Reddy for clinical research he has conducted., J. I. Lopez: None Declared, A. Manack Adams Conflict with: Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company., R. Lipton Conflict with: Richard B. Lipton, MD has received grant support or honoraria from: Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy’s Laboratories, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Novartis, Pernix, Pfizer, Supernus, Teva, Trigemnia, 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. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS. Dr Lipton serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache., A. Blumenfeld Conflict with: Andrew M. Blumenfeld, MD, has served on advisory boards and/or has consulted for Allergan, Amgen, Adler, Teva, Supernus, Promius, Eaglet, and Lilly; and has received funding for speaking from Allergan, Amgen, Pernix, Supernus, Depomed, Avanir, and Promius.
Migraine - preventive therapy

MTIS2018-094

EFFECT OF ONABOTULINUMTOXINA PREVENTION ON COMORBIDITIES OF DEPRESSION AND ANXIETY IN CHRONIC MIGRAINE: ANALYSIS IN HEADACHE DAY FREQUENCY RESPONDERS VS HEADACHE DAY FREQUENCY NON-RESPONDERS


1 Headache Center of Southern California, The Neurology Center, Carlsbad, CA, 2 Neurology Department, Dartmouth-Hitchcock Medical Center, Lebanon, NH, 3 Robbins Headache Clinic, Riverwoods, IL, 4 Allergan plc, Irvine, CA, 5 Department of Neurology, Montefiore Headache Center; Albert Einstein College of Medicine, Bronx, NY, 6 Neurology, Jefferson Headache Center, Philadelphia, PA, United States

Introduction: Chronic migraine (CM) is comorbid with anxiety and depression.

Objectives: This analysis of COMPEL Study data assessed the relationship between use of onabotulinumtoxinA and depression and anxiety in people with CM who had that comorbidity and also had a ≥25% reduction in headache day frequency at week 24.

Methods: The 108-week, multicenter, open-label COMPEL Study enrolled adults with CM receiving onabotulinumtoxinA 155 U. Changes in depression (Patient Health Questionnaire [PHQ-9]) and anxiety (Generalized Anxiety Disorder [GAD-7]) sum scores in those with clinically significant depression (PHQ-9 ≥5) and anxiety (GAD-7 ≥10) at baseline were analyzed in those with a ≥25% reduction in headache day frequency at week 24 (i.e., “headache day reduction responders”) vs those who did not (“non-responders”). A ≥1 severity category improvement in the PHQ-9 and/or GAD-7 was considered clinically meaningful.
Results: Patients (N=715) had a mean (range) age of 43 (18–73) years, were primarily women (84.8%; 606/715), and had on average mild or worse depressive symptoms (PHQ-9 ≥5: 74.5%; 529/710) or moderate or worse anxiety 24.6% (GAD-7 ≥10; 175/711). Mean (SD) headache day frequency at week 108 significantly decreased from baseline: 22 (4.8) to 11.3 (7.4) days (P<0.0001). Depressive symptoms significantly (P<0.001) improved in people with mild or worse depression regardless of 25% headache day reduction response (Figure 1A), as did anxiety symptoms in those with moderate or worse anxiety (P<0.001, Figure1B); 79.8% of headache-frequency responders and 53.2% of non-responders experienced a reduction of ≥1 severity category on the PHQ-9 (Figure 1C); 82.2% and 70.4%, respectively, experienced a reduction of ≥1 severity category on the GAD-7 (Figure 1D).

Conclusion: COMPEL study results demonstrate that onabotulinumtoxinA use is associated with a reduction in symptoms of depression and anxiety among people with CM, regardless of whether onabotulinumtoxinA treatment resulted in a ≥25% reduction in headache day frequency, although the change is less robust in the <25% responder group.

GAD-7=7-item Generalized Anxiety Disorder Assessment; PHQ-9=9-item Patient Health Questionnaire.
*Indicates P<0.001 versus baseline.
†Indicates P<0.001 for between group comparison.
Disclosure of Interest: A. Blumenfeld Conflict with: Andrew M. Blumenfeld, MD, within the past 12 months, has served on advisory boards and/or has consulted for Allergan, Amgen, Adler, Teva, Supernus, Promius, Eagle, and Lilly; and has received funding for speaking from Allergan, Amgen, Pernix, Supernus, Depomed, Avanir, and Promius., S. Tepper Conflict with: Stewart J Tepper, MD is an employee of Dartmouth-Hitchcock Medical Center, and receives a salary from the American Headache Society (AHS); his employer receives research grants from Alder, Allergan, Amgen, ATI, Dr. Reddy’s, Scion Neurostim, Teva, Zosano. Dr Tepper has served as a consultant for Acorda, Alder, Allergan, Amgen, ATI, BioVision, Cefaly, Charleston Laboratories, DeepBench, Dr. Reddy’s, ElectroCore, Eli Lilly, eNeura, GLG, Guidepoint Global, Impax, Neurolief, Novartis, Pernix, Pfizer, Scion Neurostim, Slingshot Insights Supernus, Teva, and Zosano. He has received a salary as Editor-in-Chief of Headache Currents from AHS and royalties for books published by Springer., L. Robbins Conflict with: Lawrence D. Robbins, MD, has served as a speaker for Avanir, Pernix, and Merck., A. Orejudos Conflict with: Amelia Orejudos, MSc, is a full-time employee of Allergan plc and owns stock in the company., A. Manack Adams Conflict with: Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company., D. Buse Conflict with: In the past 12 months, Dawn C. Buse, PhD, has received grant support and honoraria from Allergan, Avanir, Amgen, Eli Lilly and Company, and Promius and for work on the editorial board of Current Pain and Headache Reports., S. Silberstein Conflict with: Dr. Stephen Silberstein acts as a consultant and/or advisory panel member and receives honoraria from Alder Biopharmaceuticals; Allergan, Inc.; Amgen; Avanir Pharmaceuticals, Inc.; eNeura; ElectroCore Medical, LLC; Labrys Biologics; Medscape, LLC; Medtronic, Inc.; Neuralieve; NINDS; Pfizer, Inc.; and Teva Pharmaceuticals. His employer receives research support from Allergan, Inc.; Amgen; Cumberland Pharmaceuticals, Inc.; ElectroCore Medical, Inc.; Labrys Biologics; Eli Lilly and Company; Merz Pharmaceuticals; and Troy Healthcare.
Migraine - preventive therapy
MTIS2018-095

EFFECTS OF ONABOTULINUMTOXINA TREATMENT ON HEADACHE FREQUENCY, INTENSITY, AND IMPACT IN PATIENTS WITH AND WITHOUT DAILY HEADACHES AT BASELINE: A COMPEL SUBANALYSIS

J. I. Lopez 1,*, A. M. Blumenfeld 2, W. B. Young 3, A. Manack Adams 4, R. B. Lipton 5, J. F. Rothrock 6

1Neurology, University of South Alabama College of Medicine, Mobile, AL, 2Headache Center of Southern California, The Neurology Center, Carlsbad, CA, 3Neurology, Jefferson Hospital for Neuroscience, Philadelphia, PA, 4Global Medical Affairs, Allergan plc, Irvine, CA, 5Department of Neurology, Department of Epidemiology and Population Health, Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, 6Neurology, George Washington School of Medicine, Washington, DC, United States

Introduction: Chronic migraine (CM) is a disease with varied attack frequency.

Objectives: This subanalysis of COMPEL Study data evaluates the relative effect of onabotulinumtoxinA (onabotA) on the frequency and impact of headaches in patients with CM with and without a history of daily headache.

Methods: The 108-wk, multicenter, open-label COMPEL Study enrolled adults with CM receiving onabotA 155 U for 9 treatments. Patients completed a daily diary recording headache days for 28 days before the baseline visit and at intervals throughout the study period. The 6-item Headache Impact Test Questionnaire (HIT-6) was completed at every administration visit. Patients in this subanalysis completed the daily diary for all 28 days of the baseline period. Daily headache was defined as headache reported for all 28 days of the baseline period. Primary outcome was reduction in headache frequency per 28-day period at 108 wks. Exploratory outcomes included change from baseline in moderate/severe headache days and in HIT-6 total score at wks 60 (after 5 treatments) and 108 (after 9 treatments). Observed data are reported.
Figure 1. Effect of onabotulinumtoxinA on change from baseline in A) headache day frequency, B) moderate/severe headache day frequency and C) HIT-6 scores in patients with versus without daily headache at baseline.
Results: 716 patients were enrolled; 715 had ≥1 efficacy analysis and comprised the intention-to-treat (ITT) population. Of these, 641 had complete diary data for the 28 days of baseline: 138 had daily headache. As in the overall ITT population, treatment with onabotA in patients with or without daily headache at baseline, significantly reduced 28-day headache frequency at wks 60 (−8.3±8.6 and −10.9±6.4, respectively) and 108 (−10.5±9.2 and −12.2±6.7, respectively; Figure 1A). Similarly, onabotA reduced moderate/severe headache days in patients with or without daily headache at baseline, at wks 60 (−9.0±7.9 and −8.9±5.7, respectively) and 108 (−11.5±9.4 and −9.9±6.4, respectively; Figure 1B). OnabotA also reduced (improved) mean (SD) HIT-6 total scores in patients with baseline daily headache and in those without baseline daily headache at wks 60 (−6.6±6.6 and −7.4±7.1, respectively) and 108 (−9.4±7.5 and −8.7±7.4, respectively; Figure 1C). No new safety concerns were identified.

Conclusion: These results support the efficacy of onabotA for reducing headache days, moderate/severe headache days, and the impact of headaches for up to 108 wks in CM patients with daily headache at baseline.

Disclosure of Interest: J. I. Lopez: None Declared, A. Blumenfeld Conflict with: Andrew M. Blumenfeld, MD, has served on advisory boards and/or has consulted for Allergan, Amgen, Adler, Teva, Supernus, Promius, Eaglet, and Lilly; and has received funding for speaking from Allergan, Amgen, Pernix, Supernus, Depomed, Avanir, and Promius, W. Young Conflict with: William B. Young, MD, has served on advisory boards for Alder, Allergan, Cipla, Lilly, and Supernus; has consulted for Allergan and Supernus; and has received research support from AGA, Alder, Allergan, Amgen, Autonomic Technology, Cumberland, Dr. Reddy Laboratories, Eli Lilly, Encura Inc, Merz, and St. Jude Medical., A. Manack Adams Conflict with: Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc and owns stock in the company., R. Lipton Conflict with: Richard B. Lipton, MD has received grant support or honoraria from: Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr. Reddy’s Laboratories, 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. He also receives support from the Migraine Research Foundation and the National Headache Foundation. He has reviewed for the NIA and NINDS. Dr Lipton serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache., J. Rothrock Conflict with: 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. His parent institution has received funding from Allergan plc, Amgen and Dr. Reddy for clinical research he has conducted.
A POST HOC ANALYSIS OF FACTORS ASSOCIATED WITH SIGNIFICANT REDUCTION IN MIGRAINE HEADACHE DAYS FROM THREE PHASE 3 PLACEBO-CONTROLLED TRIALS OF PATIENTS WITH EPISODIC AND CHRONIC MIGRAINE TREATED WITH GALCANEZUMAB

S. K. Aurora 1,*, D. D. Ruff 1, Q. Zhang 1, E. M. Pearlman 1
1Eli Lilly and Company, Indianapolis, United States

Introduction: Migraine is a disabling neurologic disease characterized by severe headache attacks. Calcitonin gene-related peptide (CGRP) has been implicated in migraine pathogenesis. Galcanezumab is a humanized monoclonal antibody that potently and selectively binds to CGRP and has been shown to significantly reduce migraine headache days (MHD).

Objectives: A post hoc analysis was conducted to determine if previously observed galcanezumab response predictors are consistent across three phase 3 episodic and chronic migraine studies.

Methods: This post hoc analysis of 3 randomized, double-blind, placebo-controlled Phase 3 studies examined the effects of galcanezumab in patients 18-65 years of age. Results of two episodic migraine (EM) studies that enrolled patients with a baseline of 4-14 migraine headache days (MHD) per month were pooled. One chronic migraine (CM) study enrolled patients with ≥15 headache days per month, of which 8 had migraine-like features. In all studies, patients were randomized 2:1:1 to placebo, galcanezumab 120 mg, or galcanezumab 240 mg administered subcutaneously once monthly. Three possible predictors of clinical response were evaluated as subgroup analyses of 50% response rate (RR) (≥50% reduction in number of MHD)– prior triptan use, migraine history ≥20 years, and history of failure to preventive treatments. The overall treatment-by-subgroup interaction p-values for the double-blind phase (EM: 6 months; CM: 3 months) are reported with a 2-sided significance level of 0.10.

Results: Baseline characteristics were generally consistent across the 3 studies, with the exception of mean headache days (EM: 10.67 (n=1773) vs. CM: 21.44 (n=1113)) and MHD (9.13 vs. 19.41). Both galcanezumab doses were associated with significantly higher 50% RRs than placebo in most of the examined subgroups for EM and CM. For the 120 mg dose vs. placebo in the EM and CM studies, a greater treatment effect was seen for those with a history of failure vs. without history of failure of ≥1 preventive treatment (treatment-by-subgroup interaction EM: p=0.012; CM: p<0.001), and for those who used a triptan vs. did not use a triptan at baseline (EM: p<0.001; CM: p=0.062). Migraine diagnosis ≥20 years previously was predictive of response to the 120 mg dose for individuals with EM (p=0.056) but not for those with CM (p=0.206).

Conclusion: Analysis of this large data set from three phase 3 trials expands previous findings and suggests that there may be some predictors of clinical response to galcanezumab compared with placebo in EM and CM, primarily driven by placebo response fluctuations, as the magnitude of 50% RR with galcanezumab was similar in all subgroups but was lower and varied with placebo.

**Abstracts**

**Migraine - preventive therapy**

**MTIS2018-097**

**CHANGES IN PATIENT FUNCTIONING AND DISABILITY FROM TWO PHASE 3 DOUBLE-BLIND PLACEBO-CONTROLLED CLINICAL STUDIES OF GALCANEZUMAB**

J. H. Ford 1, D. W. Ayer 1, Q. Zhang 1, J. N. Carter 1*, V. Skljarevski 1, S. K. Aurora 1

1Eli Lilly and Company, Indianapolis, United States

**Introduction:** Galcanezumab is being developed as a preventive for episodic migraine, and patient-reported outcomes related to functioning and disability were studied.

**Objectives:** Data from 2 studies (EVOLVE-1 [E1]: NCT02614183; EVOLVE-2 [E2]: NCT02614196) of galcanezumab and placebo were analyzed to report on migraine-specific measures of functioning and disability.

**Methods:** Patients with episodic migraine were treated (monthly s.c. injections) with either galcanezumab (E1: 120-mg N=210, 240-mg N=208; E2: 120-mg N=226, 240-mg N=220), or placebo (E1 N=425; E2 N=450) during 6 months of double-blind treatment. Migraine-Specific Quality of Life Questionnaire v2.1 (MSQ) was used to measure the impact of migraine on patient functioning (physical and emotional), and the Migraine Disability Assessment (MIDAS) was used to quantify headache-related disability; higher MSQ scores indicate better functioning, while lower MIDAS scores indicate less disability. Both were collected at baseline and during treatment (MSQ=monthly; MIDAS=Month 3 and 6 only). Changes from baseline in MSQ (Month 4-6 average) and MIDAS (Month 6) scores were analyzed using mixed models repeated measures.

**Results:** In E1, mean baseline MSQ Total scores were significantly lower among galcanezumab- (120-mg=56.7; 240-mg=54.6; both \(P<.001\)) than placebo-treated (59.6) patients; similar differences were observed in individual MSQ domains. In E2, mean baseline galcanezumab MSQ Total scores (120-mg=59.6; 240-mg=58.0) were not different compared with placebo (58.0). In E1, mean MIDAS Total score at baseline was not different among galcanezumab- (120-mg=32.9; 240-mg=36.1) and placebo-treated (31.8) patients. In E2, mean MIDAS Total score at baseline was not different among galcanezumab- (120-mg=30.9; 240-mg=32.8) and placebo-treated (34.3) patients. Differences of least squares (LS) mean change from baseline for galcanezumab (120-mg, and 240-mg, respectively) compared with placebo in MSQ Total score were: E1=7.3 and 6.7 (both \(P<.001\)); E2=8.5 and 7.3 (both \(P<.001\)). Differences of LS mean change from baseline for galcanezumab compared with placebo in MIDAS Total score were: E1=-6.3 (\(P<.001\)) and -5.2 (\(P=.002\)); E2=-9.2 and -8.2 (both \(P<.001\)). In E2, each individual item score of MIDAS overall achieved significant improvement (\(P<.05\)) for both galcanezumab doses compared with placebo; significant improvements were also observed for most individual items in E1 for both doses compared with placebo.

**Conclusion:** Patients treated with galcanezumab reported significant and clinically meaningful improvements in daily functioning, as well as decreased disability compared with patients who received placebo.

**Migraine - preventive therapy**

**MTIS2018-098**

**RAPID ONSET OF EFFECT OF GALCANEZUMAB FOR THE PREVENTION OF EPISODIC MIGRAINE: POST-HOC ANALYSES OF TWO PHASE 3 STUDIES**

S. K. Aurora 1, H. C. Detke 1*, Q. Zhang 1, B. A. Millen 1

1Eli Lilly and Company, Indianapolis, United States

**Introduction:** The humanized monoclonal antibody galcanezumab (LY2951742), which binds to calcitonin gene-related peptide (CGRP), has been evaluated for the prevention of episodic migraine.

**Objectives:** The aim of these post-hoc analyses is to describe the onset of effect of galcanezumab for the prevention of episodic migraine based on data from the Phase 3 clinical program.

**Methods:** These analyses included subjects in two randomized, double-blind, placebo-controlled Phase 3 studies (EVOLVE-1 [NCT02614183] and EVOLVE-2 [NCT02614196]) aged 18-65 years with a diagnosis of episodic migraine and a history of migraine headaches for ≥1 year. A total of 1,773 (858 EVOLVE-1, 915 EVOLVE-2) patients were randomized and received either 120 mg or 240 mg galcanezumab (n=879) or placebo (n=894). Study drug was administered subcutaneously once per month for 6 months. The patient population was largely female (83.7% EVOLVE-1, 85.4% EVOLVE-2) and white (80.4% EVOLVE-1, 70.3% EVOLVE-2) with a mean age of approximately 41 years (40.7 years EVOLVE-1, 41.9 years EVOLVE-2). On average, patients had been diagnosed with migraine approximately 20 years prior to study entry (20.1 years EVOLVE-1, 20.6 years EVOLVE-2), most patients experienced severe disability (Migraine Disability Assessment total score: 33.2 EVOLVE-1, 33.0 EVOLVE-2); the approximate mean number of baseline monthly migraine headache days (MHDs) was 9 (9.1 days EVOLVE-1 9.1 days EVOLVE-2). Patients in the 120-mg group received a 240-mg loading dose for the first month. Onset-of-effect analyses therefore evaluated the pooled galcanezumab-treated patients vs placebo as both galcanezumab groups received 240 mg in the first month. The number of weekly MHDs was modeled using a repeated measures ordinal logistic regression, and the odds ratios of having fewer MHDs for the galcanezumab group compared with the placebo group were evaluated for each week in Month 1. Onset of effect was defined as the earliest week in which a statistically significant separation between galcanezumab and placebo was observed and maintained for all remaining weeks in Month 1.

**Image:**

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (EVOLVE-1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 1</td>
<td>2.71</td>
<td>2.00, 3.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 2</td>
<td>3.08</td>
<td>2.27, 4.17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 3</td>
<td>2.11</td>
<td>1.55, 2.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 4</td>
<td>1.56</td>
<td>1.15, 2.11</td>
<td>0.004</td>
</tr>
<tr>
<td>2 (EVOLVE-2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 1</td>
<td>2.88</td>
<td>2.16, 3.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 2</td>
<td>2.76</td>
<td>2.07, 3.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 3</td>
<td>2.41</td>
<td>1.80, 3.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 4</td>
<td>2.67</td>
<td>1.99, 3.58</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Results:** The weekly MHD analyses showed that onset of effect occurred at Week 1 (Table). The odds ratio of having fewer weekly MHDs with galcanezumab vs placebo was statistically significant at Week 1 for each study and remained significant for each of Weeks 2-4.

**Conclusion:** This rapid onset of effect of galcanezumab makes it a promising medication for prevention of migraine.
Migraine - preventive therapy

MTIS2018-099

EPTINEZUMAB FOR PREVENTION OF CHRONIC MIGRAINE (CM): RESULTS OF 2 INFUSIONS IN THE PHASE 3 PROMISE-2 (PREVENTION OF MIGRAINE VIA INTRAVENOUS EPTINEZUMAB SAFETY AND EFFICACY–2) TRIAL

M. Ashina1,*, P. J. Goadsby2, R. B. Lipton3, J. Azimova4, P. Winner5, B. Schaeffler6, D. Biondi6, S. Bhattacharya6, J. Smith7, R. Cady6

1Danish Headache Center, Rigshospitalet Glostrup, University of Copenhagen, Copenhagen, Denmark, 2NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College, London, United Kingdom, 3Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, United States, 4University Headache Clinic, Moscow, Russian Federation, 5Premiere Research Institute, Palm Beach Headache Center, West Palm Beach, 6Alder BioPharmaceuticals, Inc., Bothell, United States, 7Alder BioPharmaceuticals, Ltd., Dublin, Ireland

Introduction: Calcitonin gene-related peptide (CGRP) plays an important role in migraine pathophysiology. Eptinezumab, an anti-CGRP monoclonal antibody with 100% bioavailability following intravenous infusion, selectively and potently inhibits the CGRP ligand.

Objectives: This phase 3 study evaluated the efficacy and safety of 2 quarterly iv infusions of eptinezumab in patients with chronic migraine (CM).

Methods: Following screening and a 28-day baseline run-in with an eDiary to confirm headache and migraine frequency, eligible subjects with CM (ICHD-3 β) were randomized (1:1:1) to eptinezumab 100 mg, 300 mg, or placebo administered by iv infusion on Day 0 and at Week 12. The primary efficacy endpoint was change from baseline in monthly migraine days (MMD) over Weeks 1–12. Key secondary endpoints were ≥75% migraine responder rates (RR; percentages of subjects with ≥75% reduction in MMD) over Weeks 1–4; ≥75% and ≥50% migraine RR over Weeks 1–12; percentages of subjects with a migraine on Day 1 postinfusion. Persistence of efficacy was evaluated up to Week 24 following a second quarterly infusion.

Results: Efficacy analysis included 1072 subjects. Mean baseline MMD in the 100-, 300-mg, and placebo groups were 16.1, 16.1, and 16.2, respectively. Reductions from baseline in MMD over Weeks 1–12 were greater with eptinezumab 300 mg (n=350) vs placebo (n=366) (-8.2 vs -5.6; p=0.0001) and showed further reductions over Weeks 13–24 following a second infusion at Week 12 (-8.8 vs -6.1).

The ≥75% migraine RR for eptinezumab 300 mg vs placebo groups were 36.9% vs 15.6% (p<0.0001) over Weeks 1–4. The ≥75% migraine RR were 33.1% vs 15.0% (p<0.0001) over Weeks 1–12 and increased over Weeks 13–24 (42.3% vs 22.7%) after a second quarterly infusion. The ≥50% migraine RR were 61.4% vs 39.3% (p<0.0001) over Weeks 1–12 and increased to 63.4% vs 44.5% over Weeks 13–24. The percentage of subjects with a migraine on Day 1 postinfusion was reduced from baseline (~58%) to 27.8% for eptinezumab 300 mg vs 42.3% for placebo (p<0.0001). The percentages of subjects with a migraine on any given day through Day 28 were 28.2% vs 39.2% (p<0.0001), respectively. Treatment-emergent adverse event (TEAE) rates (≥2%) were similar between groups.

Conclusion: Eptinezumab (300 mg) significantly reduced MMD over Weeks 1–12 and this reduction was sustained through Week 24, following a second quarterly infusion. ≥75% and ≥50% migraine RR were greater with eptinezumab vs placebo over Weeks 1–12 and were sustained or increased after the second infusion up to Week 24. The percentage of subjects with a migraine was significantly reduced by 52% from baseline (~58%) on Day 1 postinfusion, and this reduction was sustained through Day 28. TEAE rates were similar to placebo and the safety profile for eptinezumab was consistent with previous trials.

Financial Support: Funding and support provided by Alder BioPharmaceuticals, Inc., Bothell, WA, USA.
**HULL PROSPECTIVE ANALYSIS OF ONABOTULINUIMTOXINA (BOTOX) IN THE TREATMENT OF CHRONIC MIGRAINE; A REAL-LIFE DATA IN 796 PATIENTS; UPDATED RESULTS ON OVER SEVEN YEARS OF EXPERIENCE**

F. Ahmed 1, M. Khalil 1*, T. Tanvir 1, A. Buture
1Neurosciences, Hull York Medical School, UK, Hull, United Kingdom

**Introduction:** Chronic Migraine (CM) affects 2% of the general population and is the most disabling form of the headache disorder with substantial impact on quality of life. The efficacy and safety of OnabotulinumtoxinA in adults with CM was confirmed in the Phase III Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) clinical programme leading to licensing authorities to approve its use. We present the data on a large cohort of prospective patients treated in the real life setting.

**Objectives:** 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 796 patients (July 2010 – December 2017) full data were available on 687 patients (126 male, median age 45 years; range 14-79 years, 561 female, median age 45 years; range 17-91 years). A total of 4571 cycles were given. 672 (97.8%) had failed three preventive treatments. 400 (58.2%) patients were overusing analgesics. Patients had CM for a median of 4 years (Range 0.5-67 years). 388 (56.4%) responded based on Hull Criteria and reported improved health related quality of life outcome. 88 (12.8%) reported adverse events mainly stiffness in the neck with 52 (7.5%) reporting mild ptosis.

**Conclusion:** We report on a large cohort of real life patients receiving OnabotulinumtoxinA for chronic migraine. OnabotulinumtoxinA is a safe and effective treatment option in patients with CM

**Disclosure of Interest:** F. Ahmed Conflict with: Consultancy work for Allergan, Novartis, Electrocore, Eneura for which the honorarium is paid to Migraine Trust and British Association for the Study of Headache, M. Khalil Conflict with: Consultancy work for Allergan, T. Tanvir: None Declared, A. Buture: None Declared
Migraine - preventive therapy

MTIS2018-101

DOES MEDICATION OVERUSE MATTER? RESPONSE TO ONABOTULINUMTOXINA IN CHRONIC MIGRAINE (CM) PATIENTS WITH OR WITHOUT MEDICATION OVERUSE; UPDATE FROM REAL-LIFE DATA

F. Ahmed 1, M. Khalil 1*, T. Tanvir 1, A. Buture
1Neurosciences, Hull York Medical School, UK, Hull, United Kingdom

Introduction: 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.

Objectives: 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).

Table:

Results: Of 796 patients, full data for the first cycle was available on 687 patients 400 (58.2%) with analgesic overuse and 287 (41.7%) 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 Interest: F. Ahmed Conflict with: Consultancy work for Allergan, Novartis, Electrocore, Eneura for which the honorarium is paid to Migraine Trust and British Association for the Study of Headache , M. Khalil Conflict with: Consultancy work for Allergan , T. Tanvir: None Declared, A. Buture: None Declared
**Migraine - preventive therapy**

**MTIS2018-102**

**LONG TERM OUTCOME FOR ONABOTULINUMTOXINA THERAPY IN CHRONIC MIGRAINE; A TWO YEAR FOLLOW UP OF 508 PATIENTS FROM THE HULL MIGRAINE CLINIC.**

F. Ahmed ¹, M. Khalil ¹, T. Tanvir ¹, A. Buture* ²

¹Neurosciences, Hull York Medical School, UK, Hull, United Kingdom

**Introduction:** 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 healthcare system and individual clinicians.

**Objectives:** 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).

**Table:**

**Results:** Of a series of 796 patients treated between July 2010 and December 2017 and received 4571 cycles, full data was available on 687 patients. Treatment data for at least two years was available on 508 (July 2010 – January 2016). 294 (57.8%) patients fulfilled either NICE (47.8%) or Hull criteria for responder at cycle 2 and continued treatment. 214 patients (42.2%) stopped treatment at cycle two. Of the 294 patients 117 (39.7%) patients were still on treatment at the end of year two while 177 (60.2%) had stopped treatment for various reasons; 45/177 (25.4%) relapsed after stopping, 20/177 (11.3%) got resistant after initial response and 95/177 (53.6%) or 95 of the original responders (N=294 32.3%) remained episodic.

**Conclusion:** At two years, 40% of initial cohort of responders will still require therapy with OnabotulinumtoxinA.

**Disclosure of Interest:** F. Ahmed Conflict with: Consultancy work for Allergan, Novartis, Electrocore, Eneura for which honorarium is paid to the Migraine Trust and British Association for the Study of Headache, M. Khalil Conflict with: Consultancy work for Allergan, T. Tanvir: None Declared, A. Buture: None Declared
**Migraine - preventive therapy**

**MTIS2018-103**

**FIVE YEAR OUTCOME ON 211 PATIENTS RECEIVING ONABOTULINUMTOXINA FOR CHRONIC MIGRAINE; DATA FROM HULL MIGRAINE CLINIC.**

F. Ahmed 1,*, M. Khalil 1, T. Tanvir1, A. Buture

1Neurosciences, Hull York Medical School, UK, Hull, United Kingdom

**Introduction:** 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.

**Objectives:** 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).

**Table:**

**Results:** Of a series of 796 patients treated between July 2010 and December 2017 and received 4571 cycle, full data was available on 687 patients. Treatment data for five years was available on 211 patients (July 2010 – January 2013). 126 patients (59.7%) fulfilled Hull Criteria for responder; 85 (40.3%) stopped treatment as per negative rule. Of the 126 responders, 15 patients stopped treatment either because of resistance (N=15) or pregnancy (N=5) and 5 were lost to follow up. 28 of remaining 101 patients were still on treatment at 5 years (Cycle 20) of which 15 had stopped treatment earlier but relapsed. 73 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, 27.7% of initial cohort of responders will still require treatment with OnabotulinumtoxinA.

**Disclosure of Interest:** F. Ahmed Conflict with: Consultancy work for Allergan, Novartis, Electrocore, Eneura for which honorarium is paid to the Migraine Trust and British Association for the Study of Headache, M. Khalil Conflict with: Consultancy work for Allergan , T. Tanvir: None Declared, A. Buture: None Declared
**Migraine - preventive therapy**

**MTIS2018-104**

ONABOTULINUMTOXINA FOR CHRONIC MIGRAINE DURING PREGNANCY; EXPERIENCE FROM HULL MIGRAINE CLINIC, UNITED KINGDOM.

F. Ahmed 1,*, M. Khalil 1, T. Tanvir 1, A. Buture 1

1Neurosciences, Hull York Medical School, UK, Hull, United Kingdom

**Introduction:** 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.

**Objectives:** We report pregnancy outcomes on 34 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.

**Table:**

**Results:** Of the 34 patients who reported pregnancy (8-16 weeks), 21 wished to continue with further treatment at three-monthly intervals. 13 patients did not continue further treatment. All but one (miscarriage) of the 21 patients had normal vaginal delivery, live births and no fetal malformations were reported.

**Conclusion:** We report the outcome in 21 pregnant patients with CM exposed to OnabotulinumtoxinA. There is need to collect further data before establishing its safety.

**Disclosure of Interest:** F. Ahmed Conflict with: Consultancy work for Allergan, Novartis, Electrocore, Eneura for which honorarium is paid to the Migraine Trust and British Association for the Study of Headache, M. Khalil Conflict with: Consultancy work for Allergan, T. Tanvir: None Declared, A. Buture: None Declared
ANALYSIS OF PATTERNS OF RESPONSE TO ONABOTULINUMTOXINA IN CHRONIC MIGRAINE IN PREDICTING LONG-TERM OUTCOME.

F. Ahmed¹*, M. Khalil ¹, T. Tanvir ¹, A. Buture ²
¹Neurosciences, Hull York Medical School, UK, Hull, United Kingdom

Introduction: The efficacy of OnabotulinumtoxinA for Chronic Migraine (CM) is established; however, long term outcome data is limited and need for ongoing treatment remains uncertain.

Objectives: 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.

Table:

Results: Of 508 patients followed up for at least two years 294 fulfilled NICE or Hull Criteria for responder and continued treatment beyond cycle 2. Of the 294 responders, 117 patients were still obtaining positive response at year 2 and 95 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 212 responders. We found two distinct patterns of response with 118 (55.6%) patients having a fluctuating ‘wearing off’ pattern with an increase in headache frequency prior to their next treatment; 94 (44.3%) 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 20/118 (16.9%) patients converting to episodic migraine compared to 75/94 (79.8%) with stable non-fluctuating response.

Conclusion: We observed two distinct patterns of response that help to predict long-term outcome for patients receiving OnabotulinumtoxinA for prophylaxis of CM.

Disclosure of Interest: F. Ahmed Conflict with: Consultancy work for Allergan, Novartis, Electrocore, Eneura for which honorarium is paid to the Migraine Trust and British Association for the Study of Headache, M. Khalil Conflict with: Consultancy work for Allergan , T. Tanvir: None Declared, A. Buture: None Declared
Migraine - preventive therapy

MTIS2018-106

EFFICACY OF ERENUMAB IN PATIENTS WITH EPISODIC MIGRAINE WHO HAVE FAILED 2–4 PRIOR PREVENTIVE TREATMENTS: RESULTS FROM PRESPECIFIED SUBGROUP ANALYSES OF THE LIBERTY STUDY

U. Reuter¹, M. D. Ferrari², P. J. Goadsby³, M. Lanteri-Minet⁴, P. Hours-Zesiger⁵, S. Wen⁶, J. Klatt⁵

¹Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany, ²Department of Neurology, Leiden University Medical Center, Leiden, Netherlands, ³NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College, London, United Kingdom, ⁴Pain Department, CHU Nice, France - FHU InovPain, Université Côte d’Azur, Nice, France, ⁵Novartis Pharma AG, Basel, Switzerland, ⁶Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States

Introduction: In the LIBERTY study (NCT03096834), erenumab 140 mg demonstrated efficacy in patients with episodic migraine (EM) who have failed 2–4 prior preventive treatments.

Objectives: We report results from subgroup analyses of the LIBERTY study.

Methods: Patients with EM aged 18–65 years (N=246) were randomised (1:1) to subcutaneous erenumab 140 mg or placebo every 4 weeks for 12 weeks. The treatment effect of erenumab versus placebo in primary and secondary efficacy endpoints at Week 12 was assessed in different subgroups including age (2 treatment failures). In addition, change from baseline in MMD, monthly acute migraine-specific medication days (MSMD), Migraine Physical Function Impact Diary (MPFID) scores and Headache Impact Test (HIT-6) scores were assessed in subgroups of patients with at least 50%/75%/100% response in MMD at Week 12. P-values are nominal without multiplicity adjustment.
### Table: Effect of erenumab versus placebo in primary and secondary efficacy endpoints in different subgroups (Week 12)

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Gender</th>
<th>MMD by stratification factor</th>
<th>Failed preventive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;median</td>
<td>≥median</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>≥50% reduction in MMD</td>
<td>2.80 (1.10, 7.10); 0.027</td>
<td>2.55 (1.05, 6.19); 0.037</td>
<td>6.17 (1.19, 32.04); 0.018</td>
<td>2.23 (1.10, 4.52); 0.024</td>
</tr>
<tr>
<td>≥75% reduction in MMD</td>
<td>2.53 (0.72, 8.86); 0.139</td>
<td>5.92 (0.70, 50.07); 0.067</td>
<td>2.67 (0.47, 15.23); 0.257</td>
<td>3.30 (0.89, 12.15); 0.055</td>
</tr>
<tr>
<td>MMD</td>
<td>−1.55 (−3.20, 0.10); 0.065</td>
<td>−1.60 (−3.03, −0.18); 0.028</td>
<td>−2.41 (−4.84, −0.02); 0.052</td>
<td>−1.39 (−2.61, −0.16); 0.027</td>
</tr>
<tr>
<td>MSMD</td>
<td>−2.28 (−3.51, −1.05); &lt;0.001</td>
<td>−1.15 (−2.22, −0.07); 0.037</td>
<td>−2.55 (−4.17, −0.93); 0.037</td>
<td>−1.57 (−2.52, −0.63); 0.001</td>
</tr>
<tr>
<td>MPFID-PI</td>
<td>−4.38 (−7.78, −0.98); 0.012</td>
<td>−2.47 (−5.30, −0.36); 0.086</td>
<td>−4.41 (−8.41, −0.41); 0.032</td>
<td>−3.13 (−5.72, −0.55); 0.018</td>
</tr>
<tr>
<td>MPFID-EA</td>
<td>−5.32 (−8.83, −1.81); 0.003</td>
<td>−2.50 (−5.19, −0.19); 0.068</td>
<td>−4.98 (−9.11, −0.85); 0.019</td>
<td>−3.52 (−6.02, −1.01); 0.006</td>
</tr>
</tbody>
</table>

Data for ≥50% and ≥75% reduction in MMD are presented as odds ratio (95% CI); Data for MMD, MSMD, MPFID-PI and MPFID-EA are presented as difference in adjusted mean change from baseline (95% CI). P-value: erenumab versus placebo. CI, confidence interval; HIT-6, Headache Impact Test; MMD, monthly migraine days; MPFID-EA, Migraine Physical Function Impact Diary-everyday activities; MPFID-PI, MPFID-physical impairment; MSMD, monthly acute migraine-specific medication days.

*Stratum 1: 4–7 migraine days/month at baseline
**Stratum 2: 8–14 migraine days/month at baseline

Note: Subgroup analyses for the change from baseline in patients with 100% reduction from baseline in MMD at Week 12 could not be calculated since there were zero observations in placebo patients.
**Results:** Overall, treatment with erenumab demonstrated improvement across different endpoints in all subgroups versus placebo (Table). However, interpretation may be limited by sample size. In patients who achieved at least 50%/75%/100% response rate at Week 12, higher treatment effects were seen in variables such as MMD, MSMD, MPFID and HIT-6 versus placebo (details to be presented at the congress).

**Conclusion:** Results from the subgroup analyses were generally supportive of treatment effects of erenumab versus placebo in patients who have failed 2–4 prior preventive treatments.

**Disclosure of Interest:** U. Reuter Conflict with: — consulting fee, speaking/teaching fee, and/or research grants: Allergan, Amgen, Autonomic Technologies, CoLucid, ElectroCore, Novartis, Pharm Allergan, Eli Liily, and TEVA, M. Ferrari Conflict with: grants, consultancy, or trial support from Medtronic, Electrocore, Amgen, Eli Lilly, and Novartis, and independent support from the European Community, NWO, NIH and the Dutch Heart Foundation, P. Goadsby Conflict with: grants and personal fees from Amgen and Eli Lilly and Company and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Dr Reddy’s Laboratories, Electrocore LLC, eNeura, Novartis, Scion, Teva Pharmaceuticals, and Trigemina Inc., and personal fee from MedicoLegal work, Journal Watch, Up-to-Date, Oxford University Press, Massachusetts Medical Society, and Wolters Kluwer; and a patent Magnetic stimulation for headache assigned to eNeura without fee, M. Lanteri-Minet Conflict with: — received honoraria for advisory boards, speaker panels or investigation studies from Allergan, Amgen, Astellas, ATI, BMS, Boehringer, Boston Scientific, CoLucid, Convergence, Glaxo-SmithKline, Grunenthal, Eli Lilly, Medtronic, Menarini, MSD, Novartis, Pfizer, Reckitt Benckiser, Saint-Jude, Sanofi-Aventis, Teva, UCB, Zambon, P. Hours-Zesiger Conflict with: employee and stocks: Novartis, S. Wen Conflict with: employee and stocks: Novartis, J. Klatt Conflict with: employee and stocks: Novartis.
**Migraine - preventive therapy**

**MTIS2018-107**

**EPTINEZUMAB RESULTS FOR THE PREVENTION OF EPISODIC MIGRAINE THROUGH 1 YEAR IN THE PHASE 3 PROMISE-1 (PREVENTION OF MIGRAINE VIA INTRAVENOUS EPTINEZUMAB SAFETY AND EFFICACY–1) TRIAL**

D. Dodick 1,*, M. Janelidze 2, J. Saper 3, D. Kudrow 4, G. Chakhava 5, B. Schaeffler 6, R. Cady 6, J. Hirman 7, J. Smith 8

1Mayo Clinic, Phoenix, United States, 2S. Khechinashvili University Clinic, Tbilisi, Georgia, 3Michigan Headache & Neurological Institute, Ann Arbor, 4California Medical Clinic for Headache, Santa Monica, United States, 5Multiprofile Clinic Consilium Medulla, Georgian Association of Medical Specialties, Tbilisi, Georgia, 6Alder BioPharmaceuticals, Inc., Bothell, 7Pacific Northwest Statistical Consulting, Inc., Woodinville, United States, 8Alder BioPharmaceuticals Ltd, Dublin, Ireland

**Introduction:** Calcitonin gene-related peptide (CGRP) plays an important role in migraine pathophysiology. Eptinezumab, an anti-CGRP monoclonal antibody with 100% bioavailability following intravenous infusion, selectively and potently inhibits the CGRP ligand.

**Objectives:** This study evaluated the efficacy and safety of eptinezumab administered by quarterly infusions for episodic migraine (EM) prevention through 1 year.

**Methods:** Eligible adults with ≤14 headache days/month, of which ≥4 days met ICHD-II, (2nd Edition) migraine criteria, were randomized to eptinezumab 100 mg, 300 mg, or placebo (PBO), administered by iv infusion every 12 weeks (total of 4 doses). The primary efficacy endpoint was change from baseline in monthly migraine days (MMD) over Weeks 1‒12. Key secondary endpoints were ≥75% migraine responder rates (mRR; percentages of subjects with ≥75% reduction in MMD) over Weeks 1–4; ≥75% and ≥50% mRR over Weeks 1–12; percentages of subjects with a migraine on Day 1 postinfusion.

**Results:** Efficacy analysis included 888 subjects. Mean baseline MMD were ~8.5 days/month across groups. Eptinezumab 100 and 300 mg reduced mean MMD from baseline by -3.9 (p=0.0182) and -4.3 (p=0.0001), respectively, vs -3.2 for PBO over Weeks 1–12. The reductions were sustained over subsequent 12-week dosing intervals for eptinezumab 100, 300 mg vs PBO: -4.5, -4.8 vs -3.8 over Weeks 13–24; -4.7, -5.1 vs -4.0 over Weeks 25–36; -4.5, -5.3 vs -4.1 over Weeks 37–48. The ≥75% mRR in eptinezumab 100 and 300 mg vs PBO groups were 30.8% (p=0.011) and 31.5% (p=0.007) vs 20.3% over Weeks 1–4. The ≥75% mRR were 22.2% (NS) and 29.7% (p=0.001) vs 16.2% over Weeks 1–12. The ≥75% mRR over subsequent 12-week dosing intervals were: 33.5%, 40.1% vs 24.8% over Weeks 13–24; 40.3%, 43.2% vs 29.7% over Weeks 25–36; and 39.4%, 54.1% vs 39.6% over Weeks 37–48. The ≥50% mRR were 49.8% (p=0.009; NS after multiplicity control), 56.3% (p=0.0001) vs 37.4% over Weeks 1–12. The ≥50% mRR over subsequent 12-week dosing intervals were: 62.0%, 65.3% vs 51.4% over Weeks 13–24; 63.8%, 69.8% vs 58.1% over Weeks 25–36; 64.7%, 69.8% vs 55.4% over Weeks 37–48.

Percentages of subjects with a migraine on Day 1 postinfusion were reduced from baseline by 52.3% and 54.9% with eptinezumab 100 and 300 mg, respectively, vs 24.5% with PBO. Treatment-emergent adverse event (TEAE) rates were similar to PBO and the safety profile was consistent with previous eptinezumab studies.

**Conclusion:** Eptinezumab reduced MMD over Weeks 1–12; incremental reductions in migraine frequency were achieved with repeat quarterly infusions. The ≥75% mRR and ≥50% mRR were greater with eptinezumab 300 mg vs PBO over Weeks 1–12 and increased over subsequent 12-week dosing intervals. The percentage of subjects with a migraine was significantly reduced on Day 1 postinfusion. TEAE rates were similar to PBO.

NS, not significant

Financial Support: Funding and support provided by Alder BioPharmaceuticals, Inc., Bothell, WA, USA.
**Abstracts**

**Migraine - preventive therapy**

**MTIS2018-108**

**BEYOND THE HEADACHE PHASE OF A MIGRAINE ATTACK: CLOSER LOOK AT THE BURDEN OF MIGRAINE PHASES - RESULTS FROM THE WORLDWIDE MY MIGRAINE VOICE SURVEY**


1Département d’Evaluation et Traitement de la Douleur, Centre Hospitalo-Universitaire de Nice, Nice, France, 2GFK, Madrid, Spain, 3GfK Health, Basel, Switzerland, 4Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy, 5EHF, -/-, 6Neurology Arizona, Mayo Clinic, Phoenix, United States, 7Department of Neurology and Headache Center, University Duisburg-Essen, -, Germany, 8Novartis Pharma AG, Basel, Switzerland, 9European Headache Alliance, Brussels, Belgium, 10Migraine Association Ireland, Dublin, Ireland, 11Migraine Action, Leicester, United Kingdom, 12European Federation of Neurological Associations, Brussels, Belgium, 13Rigshospitalet Glostrup, Copenhagen, Denmark, 14Migraine Again, -, United States

**Introduction:** Limited evidence exists on the quantitative burden associated with premonitory and postdromal phases of the migraine attack.

**Objectives:** This study aimed to evaluate the burden of migraine as described by patients in these specific migraine phases: premonitory, headache, and postdromal.

**Methods:** My Migraine Voice is a cross-sectional study conducted using an online survey of 11,266 migraine patients (31 countries across Africa, America, Asia and Europe) recruited via online panels and patient organizations. Participants were adult migraine patients per ICHD-3 criteria, who reported having had >=4 migraine days/month in the 3 months preceding survey administration, with pre-specified 90% having reported having used preventive migraine treatment.

**Image:**

**Table 1: Description of the migraine phases**

<table>
<thead>
<tr>
<th>Proportion of respondents (%)</th>
<th>Premonitory phase</th>
<th>Headache phase</th>
<th>Postdromal phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of phase</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 4 hours</td>
<td>51%</td>
<td>20%</td>
<td>30%</td>
</tr>
<tr>
<td>4-24 hours</td>
<td>30%</td>
<td>45%</td>
<td>40%</td>
</tr>
<tr>
<td>&gt;24 hours</td>
<td>14%</td>
<td>34%</td>
<td>27%</td>
</tr>
<tr>
<td>Not experiencing this phase</td>
<td>6%</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td><strong>Duration of the phase &gt;24 hours in migraine patients with:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- no failure to migraine preventive treatment</td>
<td>11%</td>
<td>27%</td>
<td>20%</td>
</tr>
<tr>
<td>- 1 failure to migraine preventive treatment</td>
<td>11%</td>
<td>29%</td>
<td>23%</td>
</tr>
<tr>
<td>- ≥2 failures to migraine preventive treatment</td>
<td>17%</td>
<td>38%</td>
<td>30%</td>
</tr>
<tr>
<td>Feeling very to extremely limited during the phase</td>
<td>29%</td>
<td>71%</td>
<td>30%</td>
</tr>
</tbody>
</table>
Results: A total of 11,266 migraine patients responded to the survey and reported that, over the last 3 months, they had on average 9.8 migraine days/month; 37% reported being affected by migraine for >15 years. 44% of respondents’ migraine attack lasted one day or more (19% reported longer than 3 days). Half of patients (49%) reported feeling limited throughout the 3 migraine phases. Almost 1/3 of patients (29%) reported feeling very to extremely limited during the premonitory phase, 71% during the headache phase and 30% in the postdromal phase (Table 1).

Conclusion: This study is the first to quantify the burden experienced by patients during the different phases of migraine. While the attack itself caused the highest degree of impairment, the findings demonstrate that the burden of migraine extends beyond the headache phase and is higher for patients who have failed >=1 preventive treatment.

Disclosure of Interest: M. Lanteri-Minet Conflict with: Consulting fees from various pharmaceutical companies, R. Quintana Conflict with: Employee of GFK, V. Carboni Conflict with: Employee of GFK, P. Martelletti Conflict with: Consulting fees from various pharmaceutical companies, T. Schwedt Conflict with: Consulting fees from various pharmaceutical companies, H.-C. Diener Conflict with: Consulting fees (Advisory board) from Novartis, A. K.-Laflamme Conflict with: Novartis employee, E. Ruiz de la Torre Conflict with: President of the EHA, A. Craven Conflict with: President of the Migraine Association of Ireland, S. Evans Conflict with: Chief Executive of Migraine Action, D. Walsh Conflict with: EFNA Executive Director, A. Vangaa Rasmussen Conflict with: Consulting fees (advisory board) from Novartis, P. Dumas Conflict with: CEO of Migraine Again, R. Fink Conflict with: Novartis employee, A. Fiorin Conflict with: Novartis employee, S. Ribbe Conflict with: Novartis employee, P. Vo Conflict with: Novartis employee
Migraine - preventive therapy
MTIS2018-109

ONABOTULINUMTOXINA IN CHRONIC MIGRAINE; PREDICTING RESPONSE TO TREATMENT BASED ON HEADACHE DAYS AT BASELINE
M. Khalil*, T. Tanvir 1, A. Buture 1, F. Ahmed 1
1Hull York Medical School, Hull, United Kingdom

Introduction: Chronic migraine (CM) is a very disabling condition with substantial impact on quality of life1; in the UK, the use of OnabotulinumtoxinA on the National Health Service (NHS) for CM is approved provided that patient failed three preventive treatments2,3 Predicting response to treatment, although unknown, may help decide which patients are suitable for treatment where issues of cost-efficiency contribute towards decision in recommending treatment

Objectives: To establish whether the number of headache days at the baseline predict response to treatment with Botox in patients with CM

Methods: Adult CM patients received OnabotulinumtoxinA as per the PREEMPT study protocol at the Hull Migraine Clinic were followed up prospectively Data were extracted for headache, migraine, and headache-free days, 1 month before and after treatment at cycle 1 between July 2010 and December 2017 Patients were categorised into three groups based on the number of headache days pre-treatment. Classifications were made into low frequency (15-20 days), moderate frequency (21-25 days) and high frequency (26-30 days); Chi-Square test was used to compare the three groups’ responses

Table:

Results: Full data were available on 689 patients, 17.6% had low frequency headaches; 20.6% had moderate frequency headaches and 61.8% had high frequency headaches Results suggest that low or moderate frequency headache patients tend to have more chances of response than those with high frequency headaches, the improvement in migraine days was similar in the low and moderate frequency groups, the achievement of headache-free days are more likely in the moderate headache frequency

Conclusion: Our results indicate a better response in those with 21-25 days of headache (moderate frequency) than those with 16-20 or 26-30 days. Applying Hull criteria patients with moderate headache frequency have a better response in terms of fulfilling at least one of the three criteria. The group also show better response in all the three criteria although the results did not reach statistical significance.

If only headache days were to be taken in to account, the response is better in both low and moderate frequency. This is important given NICE only considers response with reduction in headache days.


Disclosure of Interest: M. Khalil Conflict with: Received honararium from Allergan for delivering talks at Migraine Masterclass, T. Tanvir: None Declared, A. Buture: None Declared, F. Ahmed Conflict with: Received honararia from Allergan which were forwarded to the British Association for the Study of Headache
Migraine - preventive therapy

MTIS2018-110

EFFICACY OF ERENUMAB IN PATIENTS WITH CHRONIC MIGRAINE ACHIEVING ≥50% RESPONSE: SUBGROUP ANALYSIS OF A DOUBLE-BLIND, RANDOMISED STUDY


1Prague Headache Center, DADO MEDICAL s.r.o., Prague, Czech Republic, 2Novartis Pharma AG, Basel, Switzerland, 3Amgen Inc., Thousand Oaks, CA, 4Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States

Introduction: Erenumab is a fully human anti-CGRP receptor antibody approved as a preventive treatment for migraine by the US FDA. A 12-week, randomised, double-blind, placebo-controlled study demonstrated efficacy of erenumab (70 mg and 140 mg) in patients with chronic migraine (CM). At Week 12, a greater proportion of patients treated with erenumab achieved ≥50% reduction in MMDs vs placebo (140 mg: 41.2%; 70 mg: 39.9%; placebo: 23.5%).

Objectives: Since in clinical practice, patients achieving/not achieving sufficient response to treatment are likely to continue/discontinue treatment, we sought to contextualise the actual treatment benefit among patients achieving (or not) response at the ≥50% threshold.

Methods: Patients (N=667; aged 18-65 years, inclusive) with CM (≥15 headache days/month; ≥8 migraine days/month) were randomised (2:2:3) to receive subcutaneous, once-monthly erenumab 70 mg, 140 mg or placebo. In this subgroup analysis, responders/non-responders were defined by the threshold of ≥50% reduction in MMD, and outcomes were change from baseline to Week 12 in: MMDs, migraine-specific medication treatment days (MSMD), the Headache Impact Test (HIT-6™) scores, Migraine Disability Assessment (MIDAS) scores, and Migraine-Specific Questionnaire (MSQ) scores.

Table: Effect of erenumab in patients achieving ≥50% response in MMDs vs non-responders and overall population

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>≥50% Responders (N=75)</th>
<th>Non-responders (N=113)</th>
<th>Overall population (N=188)</th>
<th>≥50% Responders (N=77)</th>
<th>Non-responders (N=110)</th>
<th>Overall population (N=187)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMD</td>
<td>−12.2 (2.9)</td>
<td>−2.6 (4.3)</td>
<td>−6.6 (6.1)</td>
<td>−12.5 (4.6)</td>
<td>−2.2 (4.4)</td>
<td>−6.5 (6.8)</td>
</tr>
<tr>
<td>MSMD</td>
<td>−5.2 (5.2)</td>
<td>−1.8 (4.1)</td>
<td>−3.3 (4.9)</td>
<td>−6.9 (5.6)</td>
<td>−2.4 (3.9)</td>
<td>−4.3 (5.2)</td>
</tr>
<tr>
<td>HIT-6</td>
<td>−10.0 (7.6)</td>
<td>−2.8 (5.1)</td>
<td>−5.7 (7.2)</td>
<td>−10.7 (8.0)</td>
<td>−1.7 (5.1)</td>
<td>−5.5 (7.9)</td>
</tr>
<tr>
<td>MIDAS total score</td>
<td>−29.1 (45.4)</td>
<td>−12.6 (41.5)</td>
<td>−19.5 (43.8)</td>
<td>−35.0 (45.2)</td>
<td>−5.8 (38.4)</td>
<td>−18.1 (43.7)</td>
</tr>
<tr>
<td>MSQ-RFP</td>
<td>23.0 (19.4)</td>
<td>6.0 (19.8)</td>
<td>13.0 (21.3)</td>
<td>25.7 (23.2)</td>
<td>4.8 (16.2)</td>
<td>13.7 (22.1)</td>
</tr>
<tr>
<td>MSQ-RFR</td>
<td>29.7 (18.6)</td>
<td>9.4 (19.8)</td>
<td>17.7 (21.7)</td>
<td>32.7 (23.7)</td>
<td>8.2 (18.5)</td>
<td>18.7 (24.1)</td>
</tr>
<tr>
<td>MSQ-EF</td>
<td>30.5 (25.4)</td>
<td>11.1 (26.7)</td>
<td>19.1 (27.8)</td>
<td>33.3 (27.2)</td>
<td>6.3 (19.9)</td>
<td>17.8 (26.8)</td>
</tr>
</tbody>
</table>

Data are expressed as mean (SD).

HIT-6, Headache Impact Test (higher score indicates worse outcome); MIDAS, Migraine Disability Assessment (higher score indicates worse outcomes); MMD, monthly migraine days; MSQ, Migraine-Specific Quality-of-Life Questionnaire (higher scores indicate better outcomes); MSQ-RFR, Migraine-Specific Quality-of-Life Questionnaire role function-restrictive; MSQ-RFP, Migraine-Specific Quality-of-Life Questionnaire role function-preventive; MSQ-EF, Migraine-Specific Quality-of-Life Questionnaire emotional functioning; SD, standard deviation.
Results: Mean (SD) baseline MMDs in the overall study population were 18.0 (4.6). The baseline MMDs in responders and non-responders were comparable. Greater reductions were observed in MMDs in responders (140 mg: −12.5; 70 mg: −12.2) vs non-responders (140 mg: −2.2; 70 mg: −2.6) at both erenumab doses. Similarly, both doses of erenumab showed greater improvements in terms of MSMDs, HIT-6, total MIDAS and MSQ scores in responders than the non-responders (Table). Across all outcome measures, change from baseline was 50-100% greater in responders than the overall population and 2-6 times (70 mg: 2-4 folds; 140 mg: 3-6 folds) greater in responders vs non-responders.

Conclusion: Among the 39.9%/41.2% of patients with CM treated with erenumab 70 mg/140 mg in this study who achieved ≥50% reduction MMD, there were substantial reductions in the frequency of migraines, the use of migraine-specific medication, and disability as assessed by the HIT-6, MIDAS and MSQ scores compared with non-responders and with the overall patient population. These findings may help to provide context for setting realistic patient expectations for response to treatment with erenumab.

**Migraine - preventive therapy**

**MTIS2018-111**

**PATIENT-REPORTED EXPERIENCES WITH SELF-INJECTIONS USING PREFILLED SYRINGE AND AUTOINJECTOR DEVICES IN AN OPEN-LABEL, LONG-TERM STUDY OF GALCANEZUMAB IN PATIENTS WITH MIGRAINE**

V. L. Stauffer¹,*, R. Sides¹, M. Lanteri-Minet², W. Kielbasa¹, Y. Jin¹, K. J. Selzler¹, S. J. Tepper³

¹Eli Lilly and Company, Indianapolis, United States, ²Centre Hospitalier Universitaire de Nice, Nice, France, ³Geisel School of Medicine at Dartmouth, Hanover, United States

**Introduction:** Galcanezumab is a humanized monoclonal antibody that selectively binds to the calcitonin gene-related peptide and is being studied for migraine prevention as a once monthly subcutaneous injection that can be self-administered.

**Objectives:** To compare the usability and patient-rated experiences of an autoinjector with a prefilled syringe in patients with migraine, who self-administered galcanezumab, and to compare pharmacokinetic parameters between these devices.

**Methods:** Patient-rated experiences with an investigational autoinjector and a prefilled syringe were compared in an open-label, 12-month study of once-monthly injections of galcanezumab 120 mg or 240 mg (NCT02614287). Patient-rated ease of usability was assessed with the Subcutaneous Administration Assessment Questionnaire (SQAAQ) and compared between devices. Positive responses to 12 statements of the SQAAQ were rated as “agree or strongly agree”. Tolerability was assessed by the frequency of injection site-related adverse events (AEs) by device and injection location. In a separate study, galcanezumab pharmacokinetics in healthy subjects were compared between the devices (NCT02836613).

**Results:** In the open-label study with migraine, 179 patients used both the prefilled syringe and autoinjector at least once. The majority of patients (91% to 97%) had positive responses as measured by the SQAAQ items regarding use of the autoinjector. There were 23 injection site-related AEs with the first self-administered injection with the prefilled syringe (N=7) or the autoinjector (N=16; p=.061), with the most common AE for either device being injection site pain. The majority of the patients, reported injection site-related AEs that were considered mild-to-moderate severity with each device type (prefilled syringe=96.5%; autoinjector =97.4%). The pharmacokinetic study determined that the 90% confidence interval for the ratio (autoinjector/prefilled syringe) of geometric least square means for the area under the galcanezumab concentration and maximum concentration was between 0.8 and 1.25, indicating the galcanezumab concentrations were comparable with both devices.

**Conclusion:** The ease of usability with either device was comparable and there were no significant differences in tolerability between the prefilled syringe and autoinjector after the first self-administration. Galcanezumab pharmacokinetics were also comparable between devices.
Disclosure of Interest: V. Stauffer Conflict with: Full-time employees and minor shareholders of Eli Lilly and Company, R. Sides Conflict with: Full-time employees and minor shareholders of Eli Lilly and Company, M. Lanteri-Minet Conflict with: In the last five years has received honoraria for advisory boards, and has been in speaker panels or investigation studies from Allergan, Amgen, Astellas, ATI, BMS, Boehringer, Boston Scientific, CoLucid, Convergence, Glaxo-SmithKline, Grunenthal, Eli Lilly, Medtronic, Menarini, MSD, Novartis, Pfizer, Reckitt Benckiser, Saint-Jude, Sanofi-Aventis, Teva, UCB, and Zambon., W. Kielbas Conflict with: Full-time employees and minor shareholders of Eli Lilly and Company, Y. Jin Conflict with: Full-time employees and minor shareholders of Eli Lilly and Company, K. Selzler Conflict with: Full-time employees and minor shareholders of Eli Lilly and Company, S. Tepper Conflict with: In the last year has research grants paid to Dartmouth without personal compensation from Alder, Allergan, Amgen, ATI, Dr. Reddy’s, ElectroCore, eNeura, Scion Neurostim, Teva, and Zosano., Conflict with: Received honoraria for consultation from Acorda, Alder, Allergan, Amgen, ATI, Cefaly, Charleston Laboratories, DeepBench, Dr. Reddy’s, ElectroCore, Eli Lilly, eNeura, GLG, Guidepoint Global, Impax, Neurolief, Pfizer, Scion Neurostim, Slingshot Insights, Supernus, Teva, and Zosano. And has stock options in ATI, receives royalties for textbooks from Springer, and receives salary from Dartmouth-Hitchcock Medical Center and the American Headache Society.
**Migraine - preventive therapy**

**MTIS2018-112**

**PREDICTORS OF TOLERABILITY OF ONABOTULINUMTOXIN A INJECTION IN CHRONIC MIGRAINE: REAL-LIFE DATA AND POTENTIAL IMPLICATIONS**

D. García-Azorín, B. Martínez, M. Ruiz-Piñero, Á. Sierra Mencía, Á. L. Guerrero Peral

1Headache unit, Hospital Clinico Universitario Valladolid, Valladolid, 2Hospital de Elche, Elche, Spain

**Introduction:** OnabotulinumtoxinA (OnabotA) has proven efficacy and safety in adults with Chronic Migraine (CM) as it has been shown both in clinical trials and real world setting. OnabotA administration is not always well tolerated but factors influencing tolerability have not been systematically assessed.

**Objectives:** We aimed to evaluate in a population of patients with Chronic Migraine, which variables modulate tolerability of first two OnabotA procedures and to consider its potential impact on efficacy.

**Methods:** We conducted an observational and descriptive study including patients diagnosed as CM according to International Classification of Headache Disorders (ICHD) III edition, beta version. OnabotA was initiated in patients who had not responded to at least topiramate and another oral preventative. During the inclusion period (April 2017 – April 2018), we prospectively assessed clinical and demographic data. Tolerability was evaluated with a Likert type scale from 0 to 10 where 0 is the worst imaginable tolerability and 10 a perfect tolerability. This scale was administered to patient, relative, nurse and clinician. Headache just before the injection was assessed with an analogical scale (0: No pain, 10: the worst imaginable pain. We considered response after the first two OnabotA procedures.

**Results:** We included 49 patients, (6 male, 43 female). Mean age at inclusion was 43.8 years. At the time of infiltration a headache was present in 68.7% of the procedures. Pain intensity just before the injection correlated with tolerability (r=-0.45; p=0.04). Mean tolerability in the first two sessions was evaluated as: patient (7.1 – 7.3), relative (8.5 – 7.7), nurse (7.7 – 7.8) and neurologist (8.2 – 8.4). Tolerability of first session correlated with that observed with second procedure (r=0.7; p=0.02) and with age (r=0.53; p=0.03). Tolerability was worse among women than in men (6.8 vs 9.3, p=0.05). We also found a correlation between tolerability and OnabotA efficacy when evaluating number of migraine days (r=-0.51; p=0.02) and triptan intake days (r=-0.5, p=0.02).

**Conclusion:** CM patients in our series rated tolerability worse than their relatives and health providers. Tolerability to OnabotA injection might be influenced by age at inclusion, sex and the presence of headache at the moment of infiltration. We have also observed that a good tolerability could be a predictor of OnabotA response.

**Disclosure of Interest:** None Declared
Abstracts

Migraine - preventive therapy
MTIS2018-113

CHANGES IN SPECTRAL ANALYSES OF SPONTANEOUS ELECTROENCEPHALOGRAPHIC ACTIVITY AFTER TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS): RESULTS IN A SERIES OF 6 PATIENTS WITH REFRACTORY CHRONIC MIGRAINE

D. Garcia-Azorín*, J. Gómez Pilar 1, M. I. Pedraza Hueso 2, Á. Sierra Mencia 3, Á. L. Guerrero Peral 3, R. Hornero 1

1Biomedical Engineering Group, University of Valladolid, 2Neurology department, 3Headache unit, Hospital Clinico Universitario Valladolid, Valladolid, Spain

Introduction: Despite recent advances in migraine therapy, some patients with migraine are refractory to guideline-based therapy. Both American Headache Society and European Headache Federation have proposed consensual definitions of Refractory Chronic Migraine (RCM) in order to appropriately use innovative therapeutic techniques. Growing evidences support the security and efficacy of tDCS in chronic pain conditions in small pilot studies. However, further studies in this line are needed in order to confirm these preliminary findings.

Objectives: We aimed to assess security and efficacy of tDCS in RCM patients and to explore changes in spectral features from spontaneous electroencephalographic (EEG) activity before and after treatment.

Methods: We included 6 female patients fulfilling European Headache Federation Criteria of ECM. Age at inclusion was 41.7 ± 7.6 years. They received 10 sessions during 10 consecutive working days of 2 mA, and 20 minutes anodal stimulation of the primary motor cortex contralateral to dominant side of pain attacks. The equipment used was the StarStim® model (Neuroelectrics). Two EEG recordings in resting state conditions were acquired using Brain Vision® (BrainProducts GmbH; Munich; Germany) from 28 electrodes placed according to the revised 10-10 International System referenced over the Cz electrode. The former recording was acquired 2-5 days pre-stimulation and the latter 2-5 days post-stimulation. Spontaneous brain activity was continuously recorded during 10 minutes, while subjects were asked to remain awake and with their eyes closed. Electrode impedance was always kept under 5 kΩ. All patients were free of migrainous pain on the day of the recording. A filter between 1.5 to 70 Hz was applied to eliminate artefacts and base drift. Once we estimated the Power Spectral Density, the following spectral parameters were obtained: Relative Power, Medium Frequency, and Spectral Entropy. We have previously found a significant decrease in relative power in beta2, gamma and theta frequency bands in migraine patients compared to controls. The protocol was approved by local ethics committee.

Results: No side effects were observed. Five patients achieved a partial response consisting in reduction in pain intensity, reduction in the consumption of symptomatic drugs and a better response to symptomatic therapy. We had previously found a significant decrease in relative power in beta2, gamma and theta frequency bands in migraine patients compared to controls. Considering EEG features before and after stimulation, a modification of the measured values was observed, especially an increase of Relative Power in beta2 and theta frequency bands.

Conclusion: tDCS was a safe and partially effective therapy in a small series of patients with RCM. The observed changes in spectral features from resting state EEG before and after stimulation approach them towards non-Migrainous population.
**Migraine - preventive therapy**

**MTIS2018-114**

**THE IMPACT OF FREMANEZUMAB ON MIGRAINE-SPECIFIC HEALTH-RELATED QUALITY OF LIFE IN CHRONIC MIGRAINE PATIENTS WITH CONCOMITANT PREVENTIVE MEDICATION USE**

R. B. Lipton, MD, T. Fitzgerald, MA, PhD, J. M. Cohen, MD, MPH, FAHS, S. K. Gandhi, MD

1Albert Einstein College of Medicine, 2Montefiore Medical Center, Bronx, New York, 3Teva Pharmaceuticals, Frazer, Pennsylvania, United States

**Introduction:** Chronic migraines (CM) are characterized by frequent attacks, which adversely affect health-related quality of life (HRQoL). Fremanezumab, a fully humanized monoclonal antibody that selectively targets calcitonin gene-related peptide, has been investigated for the preventive treatment of CM.

**Objectives:** This study evaluated the effect of fremanezumab on HRQoL using the Migraine-Specific Quality of Life (MSQoL) questionnaire in patients with CM who received concomitant preventive migraine medication.

**Methods:** In this phase 3, multicenter, randomized, double-blind, parallel-group study, patients with CM (≥15 headache days and ≥8 migraine days per month) were randomized 1:1:1 to receive subcutaneous injections of either fremanezumab quarterly (675 mg at baseline, and placebo at Weeks 4 and 8), fremanezumab monthly (675 mg at baseline and 225 mg at Weeks 4 and 8), or placebo at each time point during a 12-week treatment period. A subset of patients was allowed use of one preventive migraine medication if the dosing was stable ≥2 months before the pre-treatment period. The MSQoL questionnaire (version 2.1) assessed the role function-restrictive (RR), role function-preventive (RP), and emotional function (EF) domains (range 0–100; higher scores indicate better HRQoL). MSQoL domains were analyzed using an analysis of covariance model (with treatment, gender, region, and baseline preventive medication use as fixed effects and baseline score and years since onset of migraines as covariates).

**Results:** A total of 239/1121 patients with CM (fremanezumab quarterly: n=77; fremanezumab monthly: n=85; placebo: n=77) received concomitant preventive migraine treatment and were included in this analysis. Fremanezumab treatment led to significantly greater improvements from baseline in MSQoL RR domain scores (quarterly least-squares mean ± standard error: 22.6±2.8, P=0.0259; monthly: 24.0±2.6, P=0.0048) compared with placebo (15.9±2.7) during the 12-week treatment period. Monthly fremanezumab treatment led to significantly greater improvements from baseline in MSQoL RP domain scores (quarterly: 17.6±2.4, P=0.1467; monthly: 19.1±2.2, P=0.0337) compared with placebo (13.7±2.4) during the 12-week treatment period. Fremanezumab treatment did not have a significant effect on MSQoL EF domain scores.

**Conclusion:** Fremanezumab improves some MSQoL domain scores in patients with CM who are using a concomitant preventive medication.

**Disclosure of Interest:** R. Lipton, MD Conflict with: Consultant to Teva Pharmaceuticals., T. Fitzgerald, MA, PhD Conflict with: Employee of Teva Pharmaceuticals., J. Cohen, MD, MPH, FAHS Conflict with: Employee of Teva Pharmaceuticals., S. Gandhi, MD Conflict with: Employee of Teva Pharmaceuticals.
**Migraine - preventive therapy**

**MTIS2018-115**

**THE IMPACT OF FREMANEZUMAB ON MIGRAINE-SPECIFIC HEALTH-RELATED QUALITY OF LIFE IN CHRONIC MIGRAINE PATIENTS WHO PREVIOUSLY USED TOPIRAMATE**

R. B. Lipton, MD, T. Fitzgerald, MA, PhD, J. M. Cohen, MD, MPH, FAHS, S. K. Gandhi, MD

1Albert Einstein College of Medicine, 2Montefiore Medical Center, Bronx, New York, 3Teva Pharmaceuticals, Frazer, Pennsylvania, United States

**Introduction:** Chronic migraine (CM) is characterized by frequent attacks, which adversely affect health-related quality of life (HRQoL). Fremanezumab, a fully humanized monoclonal antibody that selectively targets calcitonin gene-related peptide, has been investigated for the preventive treatment of CM.

**Objectives:** This study evaluated the effect of fremanezumab on HRQoL using the Migraine-Specific Quality of Life (MSQoL) questionnaire in patients with CM who previously used topiramate.

**Methods:** In this phase 3, multicenter, randomized, double-blind, parallel-group study, patients with CM (≥15 headache days and ≥8 migraine days per month) were randomized 1:1:1 to receive subcutaneous injections of either fremanezumab quarterly (675 mg at baseline, and placebo at Weeks 4 and 8), fremanezumab monthly (675 mg at baseline and 225 mg at Weeks 4 and 8), or placebo at each time point over a 12-week treatment period. The MSQoL questionnaire (version 2.1) assessed the role function-restrictive (RR), role function-preventive (RP), and emotional function (EF) domains (range 0–100; higher scores indicate better HRQoL). MSQoL domains were analyzed using an analysis of covariance model (with treatment, gender, region, and baseline preventive medication use as fixed effects and baseline score and years since onset of migraines as covariates).

**Results:** A total of 338/1121 patients with CM (fremanezumab quarterly: n=106; fremanezumab monthly: n=115; placebo: n=117) previously used topiramate and were included in this analysis. Fremanezumab treatment led to significantly greater improvements from baseline in MSQoL RR domain scores (quarterly [least-squares mean ± standard error]: 18.5±2.4, P=0.0026; monthly: 18.5±2.3, P=0.0022) compared with placebo (10.9±2.5) during the 12-week treatment period. Quarterly fremanezumab treatment led to significantly greater improvements from baseline in MSQoL RP domain scores (quarterly: 15.6±2.1, P=0.0248; monthly: 13.5±2.0, P=0.1834) compared with placebo (10.6±2.2) during the 12-week treatment period. Fremanezumab treatment did not have a significant effect on MSQoL EF domain scores.

**Conclusion:** Fremanezumab treatment improves certain MSQoL domain scores in patients with CM, regardless of previous use of topiramate.

**Disclosure of Interest:** R. Lipton, MD Conflict with: Consultant to Teva Pharmaceuticals., T. Fitzgerald, MA, PhD Conflict with: Employee of Teva Pharmaceuticals., J. Cohen, MD, MPH, FAHS Conflict with: Employee of Teva Pharmaceuticals., S. Gandhi, MD Conflict with: Employee of Teva Pharmaceuticals.
Abstracts

*Migraine - preventive therapy*

**MTIS2018-116**

**EFFECT OF GALCANEZUMAB ON POSSIBLE MENSTRUAL-RELATED MIGRAINE: EXPLORATORY ANALYSES RESULTS FROM EVOLVE-1, EVOLVE-2 AND REGAIN**

M. F. S. Fernandes¹, H. C. Detke ¹, Q. Zhang ¹, J. M. Pavlovic², S. Aurora ¹

¹Eli Lilly and Company, Indianapolis, ²Albert Einstein College of Medicine, Montefiore Headache Center, Bronx, United States

**Introduction:** Migraine is a common neurologic disease that affects more than 36 million people in the United States, being more prevalent in females of reproductive age. Attacks of migraine in more than 50% of women correlate with menstrual cycle hormonal fluctuations, and are typically more severe and difficult to manage with conventional therapies. Menstrual migraine attacks are defined as attacks occurring during the 5-day perimenstrual interval (-2 to +3, where first day of bleeding is defined as +1).

**Objectives:** These exploratory post-hoc analyses focus on the effect of galcanezumab, a Calcitonin gene-related peptide (CGRP) monoclonal antibody studied for the prevention of chronic and episodic migraine, on the incidence and severity of menstrual migraine attacks.

**Methods:** Post-hoc analyses were performed using data from 3 double-blind, placebo (PBO)-controlled, Phase 3 studies in patients aged 18-65 years with episodic (EVOLVE-1 & EVOLVE-2) or chronic migraine (REGAIN). A total of 2,886 patients (858 EVOLVE-1, 915 EVOLVE-2, 1,113 REGAIN) randomly received 120mg (with 240mg loading dose at first month) or 240mg galcanezumab (GMB) or placebo (PBO), which was administered subcutaneously once/month for 6 months in EVOLVE-1&2 and for 3 months in REGAIN. Menstruation was assessed on a daily basis via self-reported diary, as well as headache characteristics, duration, and severity.

A menstrual-related migraine headache day (MRMHD) is defined as a headache with migraine characteristics (definition adapted from the standard IHS ICHD-3 beta definition) within the 5-day perimenstrual period (-2 to +3). Exploratory analyses included intent-to-treat (ITT) patients who had >0 MRMHD during a one-month baseline period and who were females with menstrual periods. Using a negative binomial repeated measures model, the number of MRMHDs per 30-day period was estimated each month and overall across 6 months for pooled EVOLVE-1 & EVOLVE-2 data, and across 3 months for REGAIN.

**Image:**

---

204
Results: For ITT patients with >0 MRMHD, baseline mean number of MRMHDs were 2.4, 2.4 and 2.6 for 120mg GMB, 240mg GMB, and PBO, respectively, for pooled EVOLVE-1 & EVOLVE-2 studies (n=650). Corresponding values were 4.0, 4.5, and 4.4 days, respectively, for REGAIN (n=407). Statistically significantly lower incidence of MRMHDs per 30-day period was observed for both GMB doses compared with PBO overall across 6 months for pooled EVOLVE-1 & EVOLVE-2 and across 3 months for REGAIN (Table 1).

Conclusion: Galcanezumab, given monthly, was effective in reducing migraine headache days during the perimenstrual period.

CHRONIC MIGRAINE IN THE ELDERLY: EXPERIENCE WITH ONABOTULINUMTOXINA IN 25 PATIENTS
J. Camiña 1*, F. J. Molina 2
1Neurology, Quirónsalud - Clínica Rotger, 2Neurology, Hospital Universitari Son Espases, Palma, Spain

Introduction: The overall prevalence of headache decreases in the elderly, although craniofacial pain remains a substantial issue for those over 60 years old. Chronic migraine is not a rare condition in this population in which it frequently becomes a more debilitating condition, because of common comorbidities and the physiological changes linked to aging, resulting in reduction of drug tolerance and increase of side effects.

Objectives: To analyze the demographic, clinical and therapeutical characteristics of 25 elderly patients treated in two outpatient headache units. In addition, to highlight the even more importance of individualized treatment for these patients, with unsatisfied needs because of their usual vulnerability.

Methods: We have retrospectively searched for patients with a diagnosis of chronic migraine in our headache units’ databases. We have checked all the prescriptions of onabotulinumtoxinA in this subgroup. The demographic and clinical characteristics of the patients are collected from the clinical history through the Powerchart® and CR Informes® applications.

Results: Twentyfive (25) patients over 60 years old with chronic migraine and current treatment with onabotulinumtoxinA were found. Of those 84% were women, 24% also met criteria for Medication Overuse Headache and 56% had tried at least 3 oral prophylactic treatments prior to the use of onabotulinumtoxinA, with inadequate response due to inefficacy or tolerability failure.

Conclusion: OnabotulinumtoxinA is a safe and effective prophylactic treatment for elderly people with chronic migraine, and its profile of efficacy, safety and tolerability make it especially suitable in this population, in whom comorbidities, side effects and drug-drug interactions may be serious.
Migraine - preventive therapy

MTIS2018-118

PHLEBOTOMY AS A TREATMENT OF PATIENT’S MIGRAINE WITH POLYCYTHEMIA

J. Beato-Coelho 1, B. Silva 1, P. Correia 1, I. Luzeiro*

1Neurology, Centro Hospitalar Universitário de Coimbra, Coimbra, Portugal

Introduction: Phlebotomy as a therapy for headache is described in clinical cases of clusters associated with polycythemia. The mechanism thought to be behind the development of headache in patients with hyperviscosity may be related with microcirculatory changes that occur. The applicability of phlebotomy in cases of migraine without aura is not described.

Objectives: Not applicable

Methods: Not applicable

Results: Not applicable

Conclusion: Clinical report

Male patient with 56 years followed in Hematology because a polycythemia. For complaints of headache was oriented to specialty consultation. In this case, a bifrontal-type, moderate-to-severe type of pulsatile headache was observed interfering with the patient’s life activities and involving rest. It was associated with phonophobia, photophobia and kinesiophobia. Sporadically he also referred nausea. Headache assumed a pattern typically associated with aggravation of polycythemia, indicating a clear worsening of the pattern of headache. After phlebotomy, it improved significantly and although migraine attacks recurred, they no longer implied a cessation of activity. It was decided to start prophylactic therapy with topiramate 25mg 2id.

Conclusion

56-year-old man with ICDH-3 criteria for migraine without aura with diagnosis of polycythemia. It was established a clear association between elevation of haemoglobin and migraine attacks. The literature reports that hyperviscosity in patients with genetic susceptibility translates into different patterns of headache. There are no descriptions of cases with migraine characteristics and the response that this patient presents to phlebotomy.
Migraine - preventive therapy

MTIS2018-173

ONABOTULINUM TOXIN A IN REFRACTORY CHRONIC MIGRAINE WITH MEDICATION OVERUSE
A. Benchiheub 1,*, L. McCorkell 1, C. Rankin 1, A. Tyagi 1
1Neurology, Queen Elizabeth Univ. Hospital, Glasgow, United Kingdom

Introduction: Onabotulinum toxin A is standard treatment for chronic migraine once medication overuse is addressed. This treatment in Scotland is currently only used for refractory migraine where at least 6 oral preventive treatments have been tried.

Objectives: To compare the response rates to onabotulinum toxin A treatment in patients with refractory migraine with or without medication overuse.

Methods: We conducted a retrospective analysis on all patients who were commenced on Onabotulinum toxin A treatment over a 3 month time period between Aug 17 and Nov 17. Data was collected directly from the patients medical records, clinic letters and Headache diaries, as well as from the Onabotulinum toxin A database.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Total No of Patients</th>
<th>No of Patients who had a Positive response (Continuing)</th>
<th>No of Patients who met Positive stopping Criteria</th>
<th>No of Patients who met Negative Stopping Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication overuse</td>
<td>17</td>
<td>8</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Non Medication Overuse</td>
<td>14</td>
<td>9</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

Results: 31 patients were commenced on Onabotulinum toxin A treatment over 3 months. 17 of these patients were overusing their abortive treatments prior to their first Onabotulinum toxin A cycle. Of these patients; 4 met the positive stopping criteria after 2 cycles, 8 have had a positive response and are continuing treatment, and 5 were discontinued after their 2nd cycle as they met the negative stopping criteria. Of the remaining 14 patients who were not overusing abortive treatments prior to first Onabotulinum toxin A cycle; there were no patients who met the positive stopping criteria after 2 cycles, 9 patients had a positive response and are continuing treatment, 5 patients discontinued after their 2nd cycle as they met the negative stopping criteria.

Conclusion: There was no difference in response to Onabotulinum toxin A between Medication overuse patients and non medication overuse patients; suggesting that medication overuse does not affect the success rate of Onabotulinum toxin A treatment even in patients with refractory Chronic Migraine.
Abstracts

Migraine - preventive therapy

MTIS2018-174

Efficacy, safety, and tolerability of orally administered atogepant for the prevention of episodic migraine: results from a phase 2b/3 study


1NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College, London, United Kingdom, 2Mayo Clinic, Phoenix, 3Allergan plc, Madison, United States

Introduction: Atogepant is a novel, oral CGRP receptor antagonist in development for the prevention of migraine. Objectives: This study evaluated the efficacy, safety, and tolerability of atogepant versus placebo for the prevention of episodic migraine.

Methods: Multicenter, randomized, double-blind, placebo-controlled, parallel-group study (NCT02848326). Adult patients with a history of migraine, with or without aura, were included. Patients with 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 for the prevention of episodic migraine. Primary efficacy endpoint was change from baseline in mean monthly migraine days across the 12-week treatment period. Safety and tolerability were evaluated.

Results: Of patients randomized (n=834), 825 were in the safety population, and 795 were included in the primary efficacy population. Mean age was 40.1 years; majority white (76.1%), female (86.5%), and had not taken preventive treatment for migraine in the past (n=593, 71.9%). At baseline, patients reported an average 7.67 (SD=2.49) migraine days. Mean change in migraine days across the 12-week treatment period (adjusted p-values for comparisons versus placebo): placebo (-2.85), atogepant 10 mg QD (-4.00, p=0.0236), 30 mg QD (-3.76, p=0.0390), 60 mg QD (-3.55, p=0.0390), 30 mg BID (-4.23, p=0.0034), 60 mg BID (-4.14, p=0.0031). A total of 480 patients (58.2%) reported treatment-emergent adverse events (AEs); 170 (20.6%) were considered treatment-related. The most common treatment-emergent AEs were nausea, fatigue, constipation, upper respiratory tract infection, nasopharyngitis, urinary tract infection, and blood creatine phosphokinase increase (reported in >5% of patients in at least one treatment group). Seven patients (0.8%) reported serious AEs; none were considered related to treatment. Following daily dosing, 11 cases of ALT/AST elevations >3x the upper limit of normal were reported; the number of cases were balanced across treatment groups (placebo [n=3], 10mg QD [n=2], 30mg QD [n=1], 60mg QD [n=3], 30mg BID [n=1], 60mg BID [n=1]).

Conclusion: All 5 atogepant treatment arms showed statistically significant differences from placebo in reductions from baseline in mean migraine days across the 12-week treatment period. Reductions in mean migraine days and treatment differences versus placebo were clinically relevant. Atogepant was well-tolerated with no treatment-related serious adverse events.
**Migraine - preventive therapy**

**MTIS2018-175**

**DAITH PIERCING, VAGUS NERVE STIMULATION AND MIGRAINE PREVENTION**

C. Blatchley 1,*, A. Wilkins 2

1London Migraine Clinic, LONDON, 2University of Essex, Colchester, United Kingdom

**Introduction:** Daith ear piercing has been associated with anecdotal reports of reduced migraines for over 20 years, corroborated by three recent retrospective online surveys researched by the authors (over 3000 respondents, of which 500 had migraines >10yrs and piercing >12 months). Recent anecdotal reports from piercers suggest immediate headache reduction and improved visual comfort directly after piercing. Daith piercings pass through a ridge of cartilage innervated by the vagus nerve, unlike other ear piercings which do not and are not associated anecdotally with migraine reduction.

**Objectives:** To follow patients undergoing Daith piercing for migraines, and ascertain immediate changes in visual discomfort induced by high-contrast gratings and assess any subsequent changes in headache frequency

**Methods:** 40 consecutive patients (39 women) completed a headache questionnaire before undergoing a Daith piercing as treatment for longstanding headache. Visual discomfort was assessed before and immediately after piercing. Patients looked at a succession of 10 gratings of increasing contrast and reported any discomfort measured on a 6-point ordinal scale. The responses were compared to a control group of 40 healthy women (The gratings were horizontal, circular in outline, subtending 10 degrees; they had a square-wave luminance profile, a spatial frequency of three cycle per degree and increased linearly in log contrast from 2.7% to 94%)

Patients were followed up 1-3 months after piercing. This follow-up will continue.

**Table:** Table 1 Mean (SD) headaches per month

<table>
<thead>
<tr>
<th>Reported improvement at follow-up</th>
<th>Before piercing</th>
<th>At 1-3 month follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;None&quot;</td>
<td>20.2 (13.6)</td>
<td>21.1 (12.4)</td>
</tr>
<tr>
<td>&quot;Little&quot;</td>
<td>13.6 (12.9)</td>
<td>6.4 (7.5)</td>
</tr>
<tr>
<td>&quot;Great&quot;</td>
<td>15.3 (9.8)</td>
<td>2.0 (2.8)</td>
</tr>
</tbody>
</table>

**Results:**

**Control group:** the gratings induced no visual discomfort in any volunteer

**Patient group:** follow-up data were available for 34(74%) of the 40 patients. Of these, 8 reported no effect on migraines and 26 reported improvement (13 “a little” and 13 “great”). Prior to piercing, 0 of the 8 non-responders reported severe visual discomfort, compared to 15 of the 26 responders (p<.005 by Fishers exact test). Immediately after piercing, only 4 of the 26 reported severe discomfort (p<.003 by Fishers exact test). There was no significant difference in visual discomfort between those later reporting “little” and “great” improvement in their migraines

We then analysed the change in headache days before and 1-3 months after piercing. See Table 1

Other migraine symptoms were also reduced in responders but not in non-responders
**Conclusion:** The data suggest Daith piercing can reduce:

1. migraine frequency
2. visual discomfort from grating patterns (which is known to reflect cortical excitability in migraine\[^{1,2}\])

The retrospective surveys also suggest a specific non-responder group, and a long term action >12 months in some responders.

Electrical stimulation of the vagus nerve reduces cortical excitability in epilepsy\[^{3}\]. Transcutaneous electrical stimulation of the auricular branch is used in the treatment of migraines\[^{4}\].

The response to Daith piercing is consistent with vagus nerve stimulation and an associated reduction in cortical excitability.

Extended follow-up and a randomised controlled trial are indicated.

**References:**
Migraine - preventive therapy

MTIS2018-176

STUDY CGAL: A PLACEBO-CONTROLLED STUDY OF GALCANEZUMAB IN PATIENTS WITH EPISODIC CLUSTER HEADACHE: RESULTS FROM THE 8-WEEK DOUBLE-BLIND TREATMENT PHASE

J. M. Martinez 1, P. J. Goadsby 2,3, D. W. Dodick 4, J. N. Bardos 1, T. M. Myers Oakes 1, B. A. Millen 1, C. Zhou 1, S. A. Dowsett 1, S. Aurora 1,*, J. Y. Yang 1, R. R. Conley 1,5

1Eli Lilly and Company, Indianapolis, 2University of California, San Francisco, United States, 3NIHR-Wellcome Trust King’s Clinical Research Facility, King’s College London, London, United Kingdom, 4Mayo Clinic, Phoenix, 5University of Maryland School of Medicine, Baltimore, United States

Introduction: Cluster headache is one of the most disabling pain disorders but, to date, preventive treatments have not been developed specifically.

Objectives: We assessed the efficacy and safety of galcanezumab, a humanized monoclonal antibody that selectively binds to calcitonin gene-related peptide (CGRP), in individuals with episodic cluster headache.

Methods: This study comprised a screening period; a prospective baseline period; an 8-week, double-blind, placebo-controlled treatment period; and a washout period. We present findings from the double-blind treatment period. Participants were randomized 1:1 to galcanezumab 300 mg (N=49) or placebo (N=57) subcutaneously (SC) once monthly. The primary endpoint was overall mean change from baseline in weekly cluster headache attack frequency across Weeks 1-3. The key (gated) secondary endpoint was the proportion of participants achieving a reduction from baseline of ≥50% in weekly cluster headache attack frequency at Week 3.

Results: The mean change in weekly cluster headache attack frequency across Weeks 1-3 was -8.7 for galcanezumab versus -5.2 for placebo (treatment groups difference in mean change, -3.5 [95% CI -6.7, -0.2]; p=0.036). The percentage of participants achieving ≥50% reduction in weekly cluster headache attack frequency at Week 3 was 76% for galcanezumab versus 57% for placebo (p=0.04). Four participants (8%) in the galcanezumab group discontinued during the double-blind period versus 12 (21%) in placebo. In the placebo group, 8 (14%) discontinued due to lack of efficacy versus 1 (2%) with galcanezumab (p=0.036). There were no clinically meaningful differences between treatment groups on tolerability or safety parameters except for a greater incidence of injection site pain with galcanezumab versus placebo (8.2% vs 0%, p=0.043).

Conclusion: In individuals with episodic cluster headache, galcanezumab reduced the weekly cluster headache attack frequency across Weeks 1-3 and resulted in a greater percentage achieving a ≥50% reduction in the weekly cluster headache attack frequency at Week 3. The safety profile of galcanezumab in this population was similar to that seen previously in patients with episodic or chronic migraine.
Abstracts

**Migraine - preventive therapy**

**MTIS2018-177**

**PREVENTIVE TREATMENTS (ACUPUNCTURE, NUTRACEUTICALS OR DRUG) FOR PEDIATRIC MIGRAINE: A PROSPECTIVE STUDY**

I. Toldo*, A. C. Milocchi 1, E. Piretti 2, M. P. Rossaro 3, M. Nosadini 3, S. Sartori 1, P. A. Battistella 1

1Department of Woman’s and Child’s Health, University of Padua, Padua, 2Child Neurology and Psychiatric Unit of Cavalese, Azienda Provinciale per i Servizi Sanitari di Trento, Trento, Italy

**Introduction:** The use of preventive treatments for paediatric migraine may be limited by partial efficacy, adverse effects, contraindications for comorbidities, off-label use in children, lack of definite guidelines and scarcity of controlled studies. Studies on acupuncture as preventive treatment of pediatric migraine are rare (1,2).

**Objectives:** The aim of the study is to describe the effect of three interventions (acupuncture, nutraceuticals or drug) for migraine prevention in children and adolescents.

**Methods:** Observational and prospective clinical study conducted at the Juvenile Headache Centre of Padua between October 2016 and June 2018, with the following inclusion criteria: children age 6-17 years; diagnosis of migraine according to the International Classification of Headaches Disorders (ICHD-3, 2018); migraine without or with aura with more than 4 attacks per month or chronic migraine lasting for at least 6 months; preventive treatments for 3 months with acupuncture (A) (1/week for 2 months then 2/month, total 10 times) or nutraceuticals (N) (magnesium with multivitamins) or pizotifen (P) (the only drug licensed in Italy for migraine prophylaxis in children). The following outcomes were evaluated at the baseline (T0) before treatment, and 1 month after the end of treatment (T1): headache diary (number of attacks per month, number of symptomatic drugs per month); PedMidas questionnaires (total score); patient satisfaction (0-10). The outcomes have been evaluated

**Table:**

<table>
<thead>
<tr>
<th></th>
<th>ACUPUNCTURE (N=18)</th>
<th>NUTRACEUTICAL (N=16)</th>
<th>PIZOTIFEN (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of migraine attacks /30 days, median [IQR]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>10 (4 ; 19)</td>
<td>5 (3 ; 23)</td>
<td>3 (1 ; 6)</td>
</tr>
<tr>
<td>T1</td>
<td>3 (1 ; 8)</td>
<td>2 (1 ; 4)</td>
<td>2 (1 ; 3)</td>
</tr>
<tr>
<td>T0-T1</td>
<td>4 (1.25 ; 9)</td>
<td>3 (0 ; 6)</td>
<td>0 (0 ; 0)</td>
</tr>
<tr>
<td><strong>Number of symptomatic drugs /30 days, median [IQR]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>4 (2 ; 5)</td>
<td>3 (1 ; 6)</td>
<td>3 (0 ; 4)</td>
</tr>
<tr>
<td>T1</td>
<td>2 (0 ; 3)</td>
<td>1 (0 ; 2)</td>
<td>1 (0 ; 4)</td>
</tr>
<tr>
<td>T0-T1</td>
<td>2 (0 ; 3)</td>
<td>1,5 (-0.5 ; 4.2)</td>
<td>-0,5 (-1 ; 0)</td>
</tr>
<tr>
<td><strong>PedMIDAS, median [IQR]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>47 (17 ; 85)</td>
<td>16 (11 ; 30)</td>
<td>19 (10 ; 34)</td>
</tr>
<tr>
<td>T1</td>
<td>15 (5 ; 64)</td>
<td>9 (6 ; 20)</td>
<td>7 (1 ; 24)</td>
</tr>
<tr>
<td>T0-T1</td>
<td>13 (7 ; 34)</td>
<td>7 (-0.25 ; 15.4)</td>
<td>12.7 (8.7 ; 24)</td>
</tr>
</tbody>
</table>

**Legend:** T0=baseline; T1=1 month after the end of a 3-months treatment; T1-T0= difference between T0 and T1. IQR= interquartile range.

**Results:** 56 cases were enrolled in the study (18 A, 16 N, 22 P). The most interesting results of the study have been summarized in Table 1. The median score of patient satisfaction (0= insufficient; 10= very satisfied) was higher for A (9; IQR: 8-9.5), than N (7; IQR 3.5-8) and P (7; IQR 6-9).

**Conclusion:** It is not possible to statistically compare the three groups (A, N, P) because the characteristics at baseline differ. However, the effect (on all the variables) of A and N appears clinically significant and superior to that of P. Patients treated with A were very satisfied. Acupuncture may be a valid preventive treatment for migraine in children and adolescents, and warrants further studies.
ONE-YEAR TREATMENT WITH GALCANEZUMAB IN PATIENTS WITH CHRONIC MIGRAINE: RESULTS FROM THE OPEN-LABEL PHASE OF THE REGAIN STUDY

H. C. Detke*, L. Q. Li¹, S. Wang¹, S. K. Aurora¹
¹Eli Lilly and Company, Indianapolis, United States

Introduction: Chronic migraine is a neurological condition with a high disease burden and unmet clinical need. Objectives: To assess long-term efficacy and safety of galcanezumab (GMB), a humanized monoclonal antibody that selectively binds to calcitonin gene-related peptide, in adult patients with chronic migraine.

Methods: This was a phase 3, double-blind (DB), randomized, placebo-controlled, 3-month study with a 9-month open-label extension (OLE). Eligible patients aged 18 to 65 years with chronic migraine, defined as ≥15 headache days per month, of which ≥8 met criteria for migraine, were randomized 2:1:1 to subcutaneous injections of placebo (N=558), GMB 120 mg with a 240 mg loading dose (N=278), or GMB 240 mg (N=277), given once monthly for 3 months. Patients who entered the OLE received a 240 mg loading dose of GMB, followed by a maintenance dose of 120 mg/month at the next month, with flexible dosing thereafter (120 or 240 mg/month). Efficacy measures included number of monthly migraine headache days (MHD), ≥50% reduction in monthly MHD, and Role Function-Restrictive (RF-R) domain score of the Migraine-Specific Quality of Life Questionnaire (MSQ). Change from baseline in continuous and categorical measures over 12 months was analyzed using mixed model repeated measures analysis and generalized linear mixed models (GLIMMIX), respectively. OLE results are reported by prior DB treatment assignment.

Results: Of 1037 patients who completed DB treatment, 1022 subsequently entered the OLE, with 825 completing. Patients previously treated with placebo showed a rapid mean reduction in monthly MHDs after the first open-label dose and maintained this improvement over time, whereas the previous 120 mg and 240 mg GMB groups generally maintained or improved upon gains from the DB treatment phase (month 12: placebo, -8.41; GMB 120 mg, -8.89; GMB 240 mg, -7.99 from a baseline of 19.4 MHDs). The mean percentage of patients with ≥50% reduction from baseline ranged from 44.5% to 45.6% at month 6 and 53.3% to 56.9% at month 12. Mean improvement from baseline on the MSQ RF-R ranged from 26.5 to 30.2 points at month 6 and 29.0 to 32.9 points at month 12 on the 100-point scale. The most common (≥5%) treatment-emergent adverse events were nasopharyngitis (9.6%), upper respiratory tract infection (6.2%), and injection-site reaction (5.9%). A total of 4.5% of patients discontinued due to an adverse event, and 4 patients (0.4%) discontinued due to an injection site–related adverse event. There were no clinically meaningful changes in any of the safety measures.

Conclusion: Final OLE results support the observation that GMB appears effective, safe, and well tolerated for the preventive treatment of chronic migraine. Galcanezumab had a favorable safety profile after 1 year of treatment at doses of 120 or 240 mg/month. No new safety findings were identified.

Migraine - preventive therapy

MTIS2018-179

SINGLE-PULSE TRANSCRANIAL MAGNETIC STIMULATION (STMS) FOR THE TREATMENT OF MIGRAINE: A PROSPECTIVE REAL WORLD EXPERIENCE

G. Lambru 1 2, B. Hill 1 *, J. Lloyd 2, A. Al-Kaisy 3, A. P. Andreou 1 2

1The Headache Centre, Guy’s and St Thomas’ Hospital, 2Wolfson CARD, King’s College London, 3Pain Management and Neuromodulation, Guy’s and St Thomas’ Hospital, London, United Kingdom

Introduction: Single pulse transcranial magnetic stimulation (sTMS) is a non-invasive neuromodulation technique which has been approved in 2014 by the National Institute for Health and Care Excellence (NICE) for the acute and preventive treatment of migraine. However, its effectiveness in a real world NHS service has not been explored yet. The Headache Centre, Guy’s and St Thomas’ NHS Trust is currently the only NHS service commissioned to offer sTMS to migraine patients. Here we present our interim results.

Objectives: This is an open-label prospective clinical audit. It aims to evaluate the effectiveness of sTMS (eNeura) as a non-pharmacological modality for the treatment of migraine with and without aura in a real world setting.

Methods: The audit is ongoing. We present here the outcome of the first 44 consecutive treated patients with chronic or high frequency episodic migraine. Audit inclusion criteria were a documented diagnosis of chronic migraine documented in a headache diary and patients willingness in filling a headache diary and HIT-6 score, which were used to collect clinical outcomes. Change in headache days, migraine days and HIT-6 at 3 months of treatment compared to baseline were analysed. Adverse events and treatment compliance were also collected.

Results: Forty-two migraine patients (11 with aura, 31 without aura) treated with sTMS were analysed. Twenty patients (47.6%) received sTMS after failing BotoxÒ therapy, hence were considered refractory to medical treatments. At baseline, patients displayed an average of 14.7 headache days (HD)/month, 11.1 migraine days (MD)/month and HIT-6 score of 63.3. Following 3-month trial, 28 patients (64%) obtained a clinically meaningful benefit (-2.7 MD/month and -5.4 points on HIT-6 score) hence continued the treatment. Seventeen patients (36%) did not benefit from the therapy and discontinued the treatment. Of those, the majority were Botox non-responders. At 6 months 1 out of 28 responders stopped the treatment due to lack of effect durability. Amongst responders, five patients continued sTMS treatment for 12 months, 10 for nine months and 12 for six 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) and scalp tenderness (n = 2).

Conclusion: sTMS may constitute an effective and well tolerated preventive treatment option for difficult-to-treat high frequency/chronic migraine patients in a real world setting. Since sTMS is less costly than BotoxÒ on the NHS, it could be included as one of the three preventive treatment to offer to chronic migraine patients prior to Botox.

Disclosure of Interest: G. Lambru Conflict with: honoraria for travelling and educational material from Allergan, ATI, Novartis, Nevro., B. Hill: None Declared, J. Lloyd: None Declared, A. Al-Kaisy: None Declared, A. Andreou Conflict with: Eneura
Migraine - preventive therapy

**MTIS2018-180**

**ONABOTULINUMTOXINA: AN EFFECTIVE TOOL IN THE THERAPEUTIC ARSENAL FOR CHRONIC MIGRAINE WITH MEDICATION OVERUSE**

E. Caronna 1*, V. J. Gallardo 2, N. Hernández-Beltrán 3, M. Torres-Ferrus 4 5, P. Pozo-Rosich 1 6

1Neurology, Hospital Universitari Vall d’Hebron, 2Headache and Neurological Pain Research Group, 3Vall d’Hebron Research Institute (VHIR), Barcelona, Spain, 4Neurology, Neuroclinica and Promedan, Medellín, Colombia, 5Neurology, Hospital Universitari Vall d’Hebron, 6Headache and Neurological Pain Research Group, Vall d’Hebron Research Institute (VHIR), Barcelona, Spain

**Introduction:** Up to 50% of patients with chronic migraine (CM) associate acute pain medication overuse (MO). In daily practice, patients seemed to improve after treatment with onabotulinumtoxinA, but there are no established therapeutic protocols.

**Objectives:** To evaluate the early response of onabotulinumtoxinA as a treatment tool in patients with CM and MO.

**Methods:** This is a retrospective study in patients with CM and MO who received two cycles of onabotulinumtoxinA infiltrations following PREEMPT protocol. We evaluated the efficacy of onabotulinumtoxinA in MO resolution, defined as less than 10 days/month of acute medication intake (triptans, opioids and combinations) or 15 days/month (non-steroidal anti-inflammatory drugs - and simple analgesics). In addition, we analyzed changes in headache frequency, pain intensity, and headache-related disability (MIDAS scale). A multivariate analysis was carried out to identify factors independently related to MO resolution.

**Results:** We included 139 consecutive patients with CM and MO. After 2 cycles of onabotulinumtoxinA, 73.4% had >50% reduction in acute medication intake and 57.6% achieved MO resolution. A 7.9% of patients did not use any acute medication after treatment. Even though both MO-ongoing group and MO-resolution group improve headache frequency, the reduction was significantly higher for the group which discontinued the use of acute medication after onabotulinumtoxinA treatment (p<0.001). In this group, 73.0% reduced headache frequency >50% and daily headache changed from 71.2% to 23.2% (p<0.001). Both groups showed an improvement in pain intensity and in MIDAS score (p<0.05). In the multivariate analysis we observed that MO resolution had an inverse association with medication intake at baseline (OR:0.294, p<0.05) and a direct association with frequency (OR:20.455, p<0.001) and MIDAS score (OR: 6.465, p<0.05) improvements.

**Conclusion:** OnabotulinumtoxinA has an early beneficial effect on the discontinuation of acute medication in patients with CM and MO. Therefore, onabotulinumtoxinA might be considered a therapeutic tool in CM with MO.
**Migraine - preventive therapy**

**MTIS2018-181**

**ANTI-CGRP MONOCLONAL ANTIBODIES FOR THE TREATMENT OF EPISODIC MIGRAINE: AN OVERVIEW OF AVAILABLE RESULTS AND COMPARISON WITH THE CURRENTLY USED PROPHYLACTICS**

F. Vandervorst* and Laura Van Deun, Jacques De Keyser, Koen Paemeleire, Jan Versijpt

**Introduction:** Recently, the first anti-CGRP monoclonal antibody, *erenumab*, was approved by both the FDA and EMA for the preventive treatment of migraine in adults, probably announcing the use of this novel treatment in clinical daily practice in the near future.

**Objectives:** The objective of the present study was to present an early overview on currently available, combined efficacy results of all four anti-CGRP monoclonal antibodies in the treatment of episodic migraine. Secondly, these results and the amount of evidence gathered until now from randomized controlled trials (RCTs), is compared to the results of the currently used prophylactics for episodic migraine.

**Methods:** Results from published RCTs in non-refractory episodic migraine patients (published in full article, abstract or press release) available up to the 1st of August 2018, were included. The mean reduction of monthly migraine days (MMD) versus placebo was used as the endpoint of choice. This same endpoint was calculated for 6 other currently used prophylactics in episodic migraine, all with level A or B evidence for use in clinical practice.

**Results:** Results from five phase 2 and four phase 3 RCTs with anti-CGRP monoclonal antibodies were available where, in total, 2519 patients were treated. The latter number is already the highest number of patients studied in RCTs with a prophylactic agent in episodic migraine although the number of RCTs with topiramate was equal (1293 subjects treated) and for beta-blockers even higher (26 with 1425 subjects treated, combined for propranolol and metoprolol). The other number of subjects studied in RCTs were 436 for valproate (6 RCTs), 132 for candesartan (2 RCTs), 436 for valproate (6 RCTs), 41 for venlafaxine (1 RCT) and 383 for amitriptyline (5 RCTs). The overall mean reduction of MMD versus placebo for the anti-CGRP monoclonal antibodies was -1.58 days. This endpoint could only be calculated in a fraction of the RCTs of the other migraine prophylactics and yielded -0.86 for candesartan (2 RCTs), -0.75 for topiramate (2 RCTs), -1.75 for valproate (3 RCTs), -0.92 for beta-blockers (4 RCTs), -3.02 for venlafaxine (1 RCT) and -1.10 for amitriptyline (1 RCT).

**Conclusion:** Efficacy results of anti-CGRP monoclonal antibodies are at least comparable to those of the currently used prophylactics in episodic migraine. The level of evidence however seems already as high or even higher given the number of RCTs conducted, all with large groups of patients. Although long term safety data and efficacy results in treatment-refractory migraine patients are still partly lacking, from a purely clinical point of view, the treatment of episodic migraine with anti-CGRP monoclonal antibodies is emerging as a first line treatment.
**Other primary headache**

**MTIS2018-119**

**IMPACT OF YOGA BASED INTERVENTION ON CHRONIC DAILY HEADACHE: RANDOMIZED SINGLE BLIND CONTROLLED TRIAL**

Neha Sharma*, Plachril John ¹, Chandra M. Sharma²

¹Rajasthan University, ²SMS Medical College and Hospital, Jaipur, India

**Introduction:** Yoga has been shown to reduce pain, disability in headache patients. There has been no randomized controlled trial of yoga therapy in treatment of chronic daily headache.

**Objectives:** Our objective in this randomized, single-blind, controlled trial was to determine whether yoga-based intervention can reduce pain and disability in patients among chronic daily headaches.

**Methods:** Eligible adults with CDH were randomized to receive either yoga therapy (n = 42) or Usual care (n = 40). The main outcome measures were headache related quality of life using headache impact test, headache intensity using Headache Index and analgesic consumption measured using the Medication Quantification Scale. Both the groups had medical management provided by neurologists, but yoga therapy was given in addition to Yoga group.

**Results:** Usual care group receiving medical management did not show improvement in any of the outcome measures. Pain intensity reduced but did not reach to significance level compared to yoga group. Yoga significantly reduced headache intensity (P = 0.009), and analgesic consumption (p=0.002). There were significant within- or between-group improvement in quality of life.

**Conclusion:** Supplementing medical management, Yoga produces meaningful clinical reduction in disability, pain intensity and analgesic use. This study supports yoga for clinical management of CDH.
**Other primary headache**  
**MTIS2018-120**  

**BODY MASS INDEX AND ITS RELATIONSHIP WITH DISABILITY, IMPACT ON DAILY LIFE, SEVERITY AND FREQUENCY OF HEADACHES IN TENSION TYPE HEADACHE PATIENTS**  
Faraidoon Haghdoost* 1, Alireza Zandifar1, Mohammad Saadatnia2  
1Physiology Research Center and Medical Student Research Center, 2Neurosciences Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, Islamic Republic Of

**Introduction:** Tension-type headache (TTH) is the most common form of primary headache. Recent studies have highlighted that obesity is significantly associated with headache and disability in adults.  
**Objectives:** The aims of the current study were to evaluate the relation of Body Mass Index (BMI) with disability, impact on daily life, severity and frequency of headaches in TTH patients.  
**Methods:** In this cross-sectional study we enrolled TTH patients based on ICHD-3 beta criteria from four clinics in Isfahan, Iran and divided into episodic TTH (ETTH) and chronic TTH (CTTH) groups. MIDAS (Migraine Disability Assessment), a valid and reliable short questionnaire for assessment of headache related disability, and HIT-6 questionnaire, a valid and reliable questionnaire for evaluating a wide spectrum of headache burden, were fulfilled by the patients. Each patient was asked to determine the number of headaches days per month (HDPM) and also headache severity by numeric rating scale (NRS). NRS is defined as a scale for severity of pain from zero to 10 that is described by the patient (zero stands for lack of pain and 10 describes the worst pain ever experienced by the patient). Height and weight in order to calculate the BMI were measured. BMI was calculated as the weight in kilograms divided by the height in meters squared. Pearson correlation coefficient was used for evaluating the correlations.  
**Results:** A total of 56 TTH (32 ETTH and 24 CTTH) with the mean age (±SD) of 32.34±10.37 and 29.82±10.91 years respectively, were included. Mean BMI were 25.42±5.48 for ETTH and 23.62±4.74 for CTTH patients. BMI was significantly correlated with MIDAS score in ETTH (r=0.507, P=0.019) but not in CTTH (r=0.280, P=0.378). BMI was significantly associated with NRS in ETTH (r=0.445, P=0.030) but no association was found for CTTH patients (r=0.433, P=0.140). In ETTH and CTTH no associations were obtained between BMI and HIT-6 score (r=0.111, P=0.614 and r=-0.060, P=0.845 respectively) and also on HDPM (r=0.262, P=0.227 and r=-0.300, P=0.320 respectively).  
**Conclusion:** Results of this study showed that higher BMI is associated with higher severity and more disability in ETTH patients but not in CTTH patients. No associations were found between BMI and headache impact on daily living and also headache frequency in both episodic and chronic TTH patients.
**Other primary headache**

**MTIS2018-121**

**CLINICAL AND DEMOGRAPHICAL CHARACTERISTICS IN A SERIES OF 107 PATIENTS WITH CLUSTER HEADACHE**

David Garcia-Azorin*1, Elvira Martinez Fernandez1, Enrique Martinez Pias2, Javier Trigo López2, Álvaro Sierra Mencía3, Ángel Luis Guerrero Peral1

1Headache unit, 2Neurology, Hospital Clinico Universitario Valladolid, Valladolid, Spain

**Introduction:** Cluster Headache (CH) is the most frequent trigeminal autonomic headache. Its clinical picture is well established but there are variants regarding pain location and temporal pattern; besides, accompanying symptoms are not always considered in previous series. Despite the great disability it produces, CH is not always easy to recognize.

**Objectives:** We aimed to analyze the clinical and demographic characteristics of a series of patients with CH.

**Methods:** Observational, retrospective study, reviewing the histories of patients diagnosed with CH according to the International Classification of Headache Disorders (ICHD) criteria. Cases had been recorded in a prospective registry of a headache unit in a tertiary hospital (January 2008 - June 2018). Clinical and demographic data were collected.

**Results:** We included 107 cases corresponding to 1.8% of the 5707 patients of the aforementioned registry. The majority of patients were male (96, 89.7%), young (age at onset of CH of 33.4 ± 12.3 years) and with episodic CH (91, 85%). Latency between onset and diagnosis of CH was 7.8 ± 8.3 years and 5.2 ± 5.8 pain cycles. Pain attacks were predominantly right-sided in 59 cases (55.1%) and in 48 (44.9%) left sided; in 13 (12.1%), a side shift between individual attacks or cycles was described. The location of pain attacks corresponded to the first branch of the trigeminal nerve in most of the patients, although in some cases it was located, at least at the beginning of the attacks, in occipital scalp (6, 5.6%), temporal scalp (2, 1.9%), or territory of maxillary (8, 7.5%) or mandibular nerves (1, 0.9%). A point to highlight in our series is that in 53 cases (49.5%) there was a latency time of 4.8 ± 4.5 minutes between the onset of pain and its maximum intensity. The quality of the pain was usually lancinating or stabbing, although 21 patients (19.6%) referred to it as throbbing, something considered unusual in the literature.

The intensity of pain attacks was 9.2 ± 0.9 on an analogical scale and exceptionally less than 8. Regarding the accompanying symptoms, in 93 cases (86.9%), autonomic symptoms appeared (especially lacrimation, conjunctival injection and nasal rhinorrhea), in 23 (21.5%) vegetative symptoms (only in one case bradycardia) and in 58 (54.2%) restlessness. In 75 (70.1%) of the patients a circadian rhythm in pain attacks was described, and in 24 (22.4%) a circannual rhythm between pain cycles.

**Conclusion:** Cluster headache is a primary headache in which, despite being clinically well characterized and extremely disabling for most patients, the time latency between onset and diagnosis seems too long. The clinical and demographic characteristics of our series are comparable to those previously published, although it shows the frequency of pain localization outside the first trigeminal branch, an occasional pattern of increased pain intensity during attacks, and that “migrainous-associated” symptoms or throbbing quality of pain attacks are not uncommon.
Abstracts

Other primary headache

MTIS2018-122

CLINICAL CHARACTERISTICS OF HERPES ZOSTER THAT MIMICKING PRIMARY STABBING HEADACHE

Byungkun Kim* 1, Seung-Han Lee2

1 neurology, eulji hospital, seoul, 2 neurology, Chonnam National University Medical School, Gwangju, Korea, Republic Of

Introduction: Primary stabbing headache (PSH) is the third most common cause of a visit to headache clinics in Korea after migraine and tension type headache. Herpes zoster has been reported as common causes of secondary stabbing headache. However, clinical characteristics of herpes zoster that mimicking PSH has not been studied yet.

Objectives: To vestigate clinical characteristics of herpes zoster that mimicking PSH

Methods: From May 2015 to June 2018, fifteen patients with herpes zoster, which clinically compatible with PSH, were recruited consecutively. These patients derived from a total 200 consecutive first-visit headache patients with recurrent brief stabs on head at Eulji Headache Clinic during the same period.

Results: Herpes zoster patients consisted of 10 females and 5 males (age range, 45 to 85 years, mean age: 67 years). Mean age of herpes zoster group was older than PSH group (p<0.01). 40% of herpes zoster group have history of prior PSH without vesicular eruption. Total symptom duration of stabbing pain from the onset was ranged from 4 to 19 days (mean: 7 days, no difference with PSH group). Except one case, pain precede the vesicular eruption by 1-6 days. Three patients have extra-cephalic herpetic lesions (C2-4, C4,5 and T2,3 each)

Conclusion: Although recurrent brief stabs on head is benign self-remitted headache disorder, 7.5% of patients were proven to have herpes zoster, which are clinically indistinguishable from PSH. The dermatomal distribution can be extra-cephalic. Our results suggest that some proportion of PSH could be a zoster sine herpete.
EXAMINING THE IMPACT OF SPHENOPALATINE GANGLION STIMULATION ON LONGITUDINAL PATTERNS OF ACUTE PAIN RELIEF ACROSS MULTIPLE CLUSTER HEADACHE ATTACKS: RESULTS FROM THE PATHWAY CH-2 TRIAL
Stewart J. Tepper* 1, James S. McGinley 1
1ATI, Los Angeles, United States

Introduction: Cluster headache (CH) is a highly disabling chronic neurological condition and the pain is recognized as among the most severe known to humans.1,2,3 Current treatment options have significant efficacy and side effect limitations and recent clinical trial failures in chronic cluster headache have further underscored the need for effective treatments to treat this disabling condition.4,56,7,8,9 The sphenopalatine ganglion (SPG) has long been a clinical target to treat headache disorders.10 SPG stimulation with the SPG Microstimulator System was shown to be effective for the treatment of CH in a previous study.

Objectives: The goals of the current study were two-fold. First, we identified common patterns of pain relief through the first hour post-treatment across multiple ipsilateral cluster headache (CH) attacks. Second, we tested whether treating attacks with sphenopalatine ganglion (SPG) stimulation produced more favorable patterns of change in pain relief over time compared to a sham comparison group.

Methods: Data for the current study came from the Pathway CH-2 Trial, a multi-centre, interventional, randomised, placebo-controlled, parallel group, double-blind study focused on evaluating the safety and efficacy of an SPG neurostimulation system for the treatment of chronic CH. The current study focused on evaluating acute data where subjects reported on multiple attacks during the experimental period of the trial. Our primary outcome was pain relief at 15 minutes and 60 minutes post-treatment. Multilevel latent class analysis (MLCA) was used to identify unique patterns of change in pain relief and test for treatment group differences in these patterns of change over time.

Table:

<table>
<thead>
<tr>
<th>Model-implied probabilities of class membership by treatment group</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPG Sham Comparison</td>
</tr>
<tr>
<td>Early Sustained Relief (ESR) 79.5% 29.6% χ²(1) = 10.51, p=.001</td>
</tr>
<tr>
<td>Late Onset Relief (LOR) 5.7% 10.7% χ²(1) = 0.73, p=.39</td>
</tr>
<tr>
<td>No Relief (NR) 14.9% 59.6% χ²(1) = 6.90, p=.009</td>
</tr>
</tbody>
</table>

Results: The analysis sample consisted of 76 participants reporting a total of 992 attacks (across individuals, median number of attacks reported was 10). Results from the pain relief MLCA showed that attacks were best represented by 3 different patterns of relief: 1. Early Sustained Relief (ESR: High probability of relief at 15 min and 60 min), 2) Late Onset Relief (LOR: low probability of relief at 15 min and high probability of relief at 60 min, and 3) No Relief (NR: low probability of relief at both 15 min and 60 min). Individuals varied in their propensity to experience each of these attack subtypes (p<0.05). Contrasting the three attack subtypes showed that, using both LOR and NR attacks as references, an average individual treating with SPG stimulation group had greater odds of ESR attacks compared to sham (ORESR/LOR = 10.75; ORESR/NR = 5.08; p <0.05). Findings showed that the probability of an individual in the SPG group having an ESR attack was 80% compared to 30% for sham (p<0.01) and their probability of NR attacks was significantly reduced (SPG: 15% vs. Sham: 60%, p<0.01).
Conclusion: Previous research has demonstrated that SPG stimulation works to relieve pain rapidly during CH attacks, but this study uniquely assessed how treatment impacts clinically meaningful attack subtypes that arise in practice. MLCA supported a three-class solution and showed that the SPG group had an increased likelihood of experiencing ESR attacks compared to sham. Future research should replicate these analyses in other representative samples and extend this work to other important CH outcomes.
Abstracts

Paediatric headache
MTIS2018-123

EFFICACY OF NON-PHARMACOLOGICAL METHODS OF TENSION-TYPE HEADACHE MANAGEMENT IN ADOLESCENTS
K. Stepanchenko*

Introduction: Psychotropic drugs cannot be widely used in pediatric patients with tension type headache (TTH) due to side effects. Non-drug therapy in this situation is the option of choice.

Objectives: To assess the efficacy of non-pharmacological therapy (heart rate variability biofeedback-based training (HRV-BBT) and exercise) in the model of differentiated therapeutic intervention in adolescents with TTH.

Methods: 137 adolescents (ages 13-18) were examined. We formed four groups of adolescents with episodic (ETTH) and chronic TTH (CTTH) who received only drug therapy and only non-drug therapy and 5th group - adolescents with CTTH who received combination of drug and non-drug therapy.

The intensity of pain was assessed by visual analogue scale; the level of reactive and personal anxiety - by the self-esteem scale Spielberger-Hanin; the level of school anxiety-by Phillips method; the level of depression – by the scale of V.A. Zhmurova; the quality of life—by PedMIDAS. Vegetative indicators were estimated by spectral analysis of HRV; brain activity – by EEG using visual, spectral and nonlinear multidimensional (calculated Kolmogorov-Sinai entropy) analyzes.

Adolescents received conventional pharmacotherapy for 1 month. Adolescents received non -drug therapy in the form of HRV-BBT (10-12 sessions) and a complex of isometric exercises (IE) (to eliminate painful musculoskeletal syndrome).

Results: The groups of non-drug therapy in comparison with only pharmacotherapy groups had statistically more pronounced decrease in the intensity of headache, a decrease in reactive anxiety and depression level, the improvement of the quality of life, an increase in total spectral power (TP), an increase in %HF and a decrease in %LF and %VLF spectral power of HRV, a reduction of dysrhythmia and disorganization EEG patterns, a significant increase in spectral power of alpha rhythm, a decrease in slow-wave EEG activity, positive shifts in the level of chaotic neurodynamic (an increase in Kolmogorov-Sinai entropy, which means an increase in number of active concurrent functional processes in the brain, the ability to form ordered adaptive dissipative structures, increase neuropsychological processes of the brain and the ability to adapt), (p<0,05).

In catamnesis (6 months) persistent retention effect with a decrease in pain intensity, as well as the complete absence of episodes of headache and associated symptoms were observed. Considering some indicators non-drug therapy in ETTH group and complimentary therapy in CTTH group favorably differs from using only drug therapy on its own.

Conclusion: Pathogenetic non-drug therapy in the form of HRV-BBT and IE improves functional state of the body of adolescents with TTH and has high efficiency in the treatment of TTH with a stable catamnestic effect. The efficacy of non-drug therapy (HRV-BBT and IE) in adolescents with episodic form of TTH is the same as pharmacotherapy. The most rational appointment for patients with chronic TTH should be complementary treatment (pharmacotherapy + HRV-BBT + IE).
Paediatric headache

MTIS2018-124

EVALUATION OF AN INTERACTIVE HEADACHE SERVICE FAMILY EVENT: THE USE OF PATIENT CENTRED OUTCOME MEASURES

H. Bullock 1, J. Mortimer 2*, H. Williams 2, O. Hall 1, S. Farrell 1, P. Prabhakar 2

1Psychological Services, 2Neurology Department, Great Ormond Street Hospital, London, United Kingdom

Introduction: Children and families attending a specialist headache clinic were invited to attend an interactive headache service family event. The aims of the day from the perspective of the team were to offer the opportunity to meet other children and families, to engage in discussion about living with a headache condition and to attend education and information sessions delivered by a Consultant Neurologist, Clinical Nurse Specialists, a Clinical Psychologist and a young adult recently transitioned to adult services.

Objectives: Patient centred outcome measures were used in order to ensure the day met the objectives of the families attending and to determine the outcomes achieved through attendance of the day.

Methods: Two interactive headache service days took place one year apart. On the first day the session was split into a session for younger children and a session for adolescents. In response to feedback, the second day a year later was altered to include one, longer session for all families. However, the overall content remained largely similar.

On both occasions, all attendees were asked to complete a goal based outcome form, identify up to three goals for attending the event and to rate their progress towards their goals before the event started from 0-10 (10=goal reached). At the end of the event, everyone was asked to re-rate their goals.

In 2017, the forms were returned by 9 parents and 9 children/young people. In 2018, they were returned by 6 parents and 5 children/young people. The goals were categorised according to themes, with average ratings pre and post event and change in goal ratings calculated.

Results: For 2017 and 2018 combined, there was an average increased in goal rating of 4.32 across 31 goals for parents and 3.45 across 31 goals for children/young people.

Seven themes were identified, in order of frequency these were; meeting others/shared experiences, education/general functioning, coping strategies, information on treatment/research/next steps, understanding of condition, ways to support child (parents only) and reduced migraines.

Conclusion: Parents and children/young people attending an interactive headache day reported progress on a patient centred outcome measure towards their goals through attending the day. Their goals for attending largely corresponded with the aims of the team in offering the event. Events such as this can form a beneficial part of the provision offered to children and young people with headache conditions accessing a specialist service.

Disclosure of Interest: H. Bullock: None Declared, J. Mortimer: None Declared, H. Williams: None Declared, O. Hall: None Declared, S. Farrell: None Declared, P. Prabhakar Conflict with: Over the last five years PP has advised, lectured in meetings sponsored by, received honorarium in association with the following commercial organisations - Amgen, Bristol Myers Squibb (BMS), Merck Sharpe and Dohme (MSD), Janssen India, Allergan and Novartis.
Paediatric headache

MTIS2018-183

AN AUDIT IN TO THE NEUROIMAGING EXPERIENCE OF PATIENTS REFERRED TO THE HEADACHE SERVICE – HOW CLOSE ARE WE ALIGNED WITH THE NICE GUIDELINE (CG150) FOR IMAGING IN CHILDREN WITH PRIMARY HEADACHES?

S. Talib, S. Ramji, H. Nightingale, P. Prabhakar, K. Mankad

1Neurology, Great Ormond Street Hospital, London, United Kingdom

Introduction: The Children’s Headache at Great Ormond Street Hospital (GOSH) sees many children with irretactable primary headaches. Often these children have a form of brain imaging done prior to their appointment. NICE recommends against imaging in individuals with primary headaches that lack signs of secondary headaches as it often results in incidental findings that have no correlation with their clinical symptoms inciting anxiety in patients rather than reassurance.

Objectives: This audit investigates how closely aligned the Headache Clinic is with the NICE guidelines CG150, specifically looking at whether these patients had prior imaging, and whether these showed abnormal or incidental findings. The audit aims to identify any correlation between a specific headache diagnosis and incidental findings on brain imaging, and whether brain imaging altered the diagnosis.

Methods: Our audit looks at 280 patients over the age of 12 years seen at the GOSH Headache Clinic from September 2012, over a period of 5 years. Data was sourced from the electronic clinical patient database, reviewing clinic letters to see if they aligned with the guidelines on specific recommendations. All diagnoses were cross-referenced with the International Classification of Headache Disorders. Brain imaging at GOSH was scrutinised to look for any abnormalities and the classify the findings.

Results: 246 patients had a form of brain imaging, 29 patients had a brain scan at GOSH, and 232 had a scan at their local hospital. Overall 88% of patients had brain imaging and 83% had a scan prior to their appointment. Of these scans, 52 had abnormal findings, equating to 21% of scanned patients with an incidental finding. None of these however altered the patients’ diagnoses in clinic.

Correlations between abnormal findings and patient diagnosis were minimal, as the majority of the diagnoses were common headache disorders. However of the patients diagnosed with migraine with aura, 34% had an abnormal finding, of which 25% were due to white matter changes. Patients with CSF pressure changes all had an abnormal finding of an arachnoid cyst, however this was limited to only 2 patients. 26% of patients with a secondary headache had an abnormal finding on imaging, however this did not change diagnosis.

Conclusion: Whilst NICE recommends against brain imaging in the setting of a primary headache, sometimes imaging is necessary to exclude diseases, particularly at a specialist paediatric centre. Patients in this sample may have had complex underling diseases, which could explain deviation from guidelines. The abnormalities found on imaging did not alter patient diagnoses as these were incidental findings. However the patients with altered CSF pressure all had arachnoid cysts, and patients diagnosed with migraine with aura were more likely to have an abnormal brain scan. Whilst migraine with aura is a primary headache, it may be worthwhile further investigating if there is a link between migraine with aura, and risk of abnormalities on imaging.
Psychological and behaviour factors

**MTIS2018-125**

**PSYCHIATRIC CO-MORBIDITIES IN PATIENTS WITH MIGRAINE**  
M. S. Alnafisah¹, T. A. Almuayqil¹, Y. Abuoras²  
¹Neurology, King Saud University, Riyadh, Saudi Arabia, ²Neurology, Aleppo University, Aleppo, Syrian Arab Republic

**Introduction:** Migraine is common, with an estimated lifetime prevalence of 7-17%. Population-based studies have reported an association between various psychiatric conditions and migraine. This is a population-based study exploring the association between migraine and psychiatric disorders in a large cohort and assessing various health-related outcomes.

**Objectives:**
- To determine the prevalence of psychiatric disorders in patients with migraine
- To describe the patterns of association of these comorbidities with a variety of health-related outcome.

**Methods:**
This case-control study was carried out in Aleppo, Syria and Riyadh, Saudi Arabia. Participants had to be 16 years of age or older to be included. Cases were those who met migraine criteria, while healthy participants served as controls. The outcomes of interest were the presence of depression (measured by the Patient Health Questionnaire PHQ-9), bipolar disorder, anxiety and phobias (measured by the M.I.N.I.). Cases and controls were enrolled from neurology or primary care clinics, patient companions, willing healthcare workers and other volunteers.

**Table:**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non Migrainuers (n=518)</th>
<th>Migrainuers (n=102)</th>
<th>P value ($X^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 15-25</td>
<td>243 (46.9%)</td>
<td>39 (38.2%)</td>
<td>0.52</td>
</tr>
<tr>
<td>- 26-40</td>
<td>234 (45.2%)</td>
<td>52 (51%)</td>
<td></td>
</tr>
<tr>
<td>- &gt;40</td>
<td>41 (7.9%)</td>
<td>11 (10.8%)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Male</td>
<td>149 (28.8%)</td>
<td>21 (20.6%)</td>
<td>0.09</td>
</tr>
<tr>
<td>- Female</td>
<td>367 (70.8%)</td>
<td>81 (79.4%)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Single</td>
<td>294 (56.8%)</td>
<td>44 (43.1%)</td>
<td>0.01</td>
</tr>
<tr>
<td>- Married</td>
<td>223 (43%)</td>
<td>58 (56.9%)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ≤ High school</td>
<td>132 (25.5%)</td>
<td>23 (22.5%)</td>
<td>0.52</td>
</tr>
<tr>
<td>- &gt; High school</td>
<td>385 (74.3%)</td>
<td>79 (77.5%)</td>
<td></td>
</tr>
<tr>
<td>Depression (PHQ-9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- None to mild</td>
<td>373 (72%)</td>
<td>58 (56.9%)</td>
<td>0.002</td>
</tr>
<tr>
<td>- Moderate to severe</td>
<td>144 (27.8%)</td>
<td>44 (43.1%)</td>
<td></td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- None</td>
<td>476 (91.9%)</td>
<td>96 (94.1%)</td>
<td>0.58</td>
</tr>
<tr>
<td>- Present</td>
<td>38 (7.3%)</td>
<td>6 (5.9%)</td>
<td></td>
</tr>
</tbody>
</table>
Results: 1.

A total of 620 subjects were recruited. 102 migraine patients and 518 healthy controls were included. The prevalence of physician-diagnosed migraine was 15.2% for females and 6.1% for males among total sample. Migraine was significantly associated with depressive and panic disorders, occurring more than twice as often than those without migraine. The higher prevalence of psychiatric disorders in migraineurs was significantly related to sociodemographic variables. The Syrian population had a higher rate of depressive disorder compared to Saudis. Health-related outcomes were worse in those with both migraines and psychiatric disorders than those with either condition alone.

Conclusion: Environmental stressors are associated with an increase of depressive comorbidity in migraineurs. The strong association of migraine with psychiatric comorbidities necessitates observing for these conditions in order to adequately manage patients and guide public health policies.

References:
Abstracts

**Psychological and behaviour factors**

**MTIS2018-126**

QUALITY OF LIFE CARE AMONG MIGRAINE HEADACHE AND RELATED NEUROLOGICAL DISORDERS IN LOW INCOME COUNTRIES.

M. D. Joshi*

**Introduction:** Stigma is a social devaluation of a person because of personal attribute leading to an experience of sense of shame, disgrace and social isolation. Developing countries are facing more stigma, discrimination due to poverty, illiteracy, migration, gender inequalities and lack of government policy

**Objectives:** To find out the social and behaviour constraints among migraine patients

**Methods:** The nature of stigma in migraine headache and related neurological disorders and its relationship to attribution was studied in one hundred and fifty-nine urban and rural patients during 2 years. The response of the primary care givers to fourteen questions on stigma and fourteen on what they thought attributed to the illness was elicited. Based on the mean stigma score, the entire sample was divided into two groups- those with high and low stigma. Consent were taken.

**Results:** Marriage, fear of rejection by neighbor, and the need to hide the fact from others were some of the more stigmatizing aspects. Many care givers reported feelings of depression and sorrow. Discriminant function analysis showed that female sex of the patient and a younger age of both patient and caregiver were related to higher stigma. Among attribution items, having no explanation to offer, and attributions to faulty biological functioning, character of life style, substance abuse and intimate interpersonal relationship discriminated between the two groups.

**Conclusion:** The relevance of stigma in the cultural context is increasing due to illiteracy, poverty, high health economic burden, superstition and lack of awareness in developing countries like Nepal and India.
DO PERSONALITY TRAITS INFLUENCE ONABOTULINUMTOXIN A RESPONSE IN PATIENTS WITH CHRONIC MIGRAINE?

A. Gonzalez Martinez 1,*, E. Rodriguez 2, H. de la Red 2, D. Garcia Azorin 3, M. Gallego de la Sacristana 1, A. L. Guerrero 3, A. B. Gago Veiga 1

1Neurology, Hospital Universitario de La Princesa, Madrid, 2Psychiatry, 3Neurology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain

Introduction: Patients with migraine have a higher degree of neuroticism (neurotic triad: hypochondria, depression and hysteria) and higher scores on anxious or obsessive personality traits; moreover patients with a neurotic premorbid personality do not usually respond to standard preventive or symptomatic treatment satisfactorily. However, the influence of abnormal personality traits in Onabotulinumtoxin A (OnabotA) response in patients with Chronic Migraine (CM) has not been studied so far.

Objectives: The aim of this study is to analyse the potential predictive value of personality traits for OnabotA response in patients with CM.

Methods: We included patients with CM who had received at least two treatment cycles of OnabotA attended in two headache units between January and May 2018. OnabotA response was defined as a reduction of at least 50% in the number of monthly migraine days. Personality traits were evaluated using the Salamanca screening test, a validated inventory assessing 11 personality traits by using a total of 22 questions, two for each trait with four answers for each question. To screen for the traits, for each answer a maximum of three points can be given. Thus, a scale from 0 to 6 indicates the degree of matching that specific personality trait. Normal population score up to 2 points for each trait; scores over 2 points for each trait were considered positive. Traits assessed by the Salamanca test are grouped in 3 clusters (Group A, B & C). Cluster A includes paranoid, schizoid and schizotypal traits; Cluster B comprises antisocial, narcissistic, histrionic, and emotional instability disorders subtypes limit and impulsive, while Cluster C includes dependent, anancastic and anxious traits.

Results: We included 112 patients (89.3% females, mean age 43.1 ± 11 years). 96 (85.7%) achieved response to Onabot A. Dependent (p:0.005) and emotional instability disorder subtype limit (p:0.02) were significantly more present among non-responders (TABLE)

Conclusion: Our results show that there might be an association between certain personality traits and Onabotulinumtoxin A response in CM patients.
Psychological and behaviour factors

MTIS2018-128

LIFE TRAUMATIC EXPERIENCES AND STRESSFUL EVENTS AS PREDICTORS OF DETOXIFICATION-THERAPY OUTCOME AT 6 MONTHS IN CHRONIC MIGRAINE WITH MEDICATION OVERUSE

S. Bottiroli 1,*, G. Sances 1, D. I. Roberto 1, V. Bitetto 1, E. Guaschino 1, M. Allena 1, S. Pazzi 1, G. Nappi 1, C. Tassorelli 1
1Headache Science Center, IRCCS Mondino Foundation, Pavia, IRCCS Mondino Foundation, Pavia, Italy

Introduction: Withdrawal from overused drug is the treatment of choice for subjects suffering from chronic migraine and medication overuse headache (CM+MOH). This approach frequently reverses the headache pattern from chronic to episodic. Many factors are likely involved in CM+MOH prognosis and outcome.

Objectives: In this study we evaluated the association between early life traumatic experiences and recent stressful events with the outcome following detoxification therapy in a 6-month follow-up in 164 subjects with CM+MOH.

Methods: This study was conducted at the Mondino Foundation in Pavia, Italy. All consecutive patients with CM+MOH undergoing inpatient detoxification program were enrolled and followed-up in a prospective study. Diagnosis was operationally defined according to ICHD-III. The protocol consisted in an inpatients detoxification treatment and a 6-month follow-up. Data on early life traumatic experiences – distinguished in terms of physical and emotional traumas – and recent stressful events were collected by means of self-report questionnaires. Data were analyzed with univariate and multivariate logistic regressions.

Results: Of the 164 patients who completed the 6-month follow-up, 111 (54%) stopped overuse and their headache reverted to an episodic pattern, whereas 53 (32%) had a negative outcome given that they either stopped overuse without experiencing any benefit on headache frequency or they failed to stop overuse. At the univariate analysis the following variables resulted associated to the negative outcome: having experienced emotional traumas (OR 3.409; p = 0.002), having experienced both traumas and stressful events (OR 12.429; p < 0.001), presence of mood disorders (OR 2.373; p = 0.014), higher MIDAS scores (OR 1.015; p < 0.001), higher number of days with medication intake (OR 2.373; p = 0.014) and higher number of days with headache (OR 1.193; p = 0.002). At the multivariate analyses, having experienced both childhood traumas and recent stressful events (OR 14.229; p = 0.002) together with higher MIDAS scores (OR 1.026; p = 0.004), and presence of mood disorders (OR 8.527; p = 0.009) were prognostic for the negative outcome.

Conclusion: Our data suggest the synergistic impact of childhood traumas and recent stressful events, together with other psychological variables, in determining a negative outcome in subjects with CM+MOH. These findings have important practical implications on how to treat these patients.
PERSONALITY TRAITS IN CHRONIC MIGRAINE WITH ASSOCIATED ARTERIAL HYPERTENSION PATIENTS
G. Oxana*, C. Galina 1, M. Ion
1National Institute of Neurology and Neurosurgery, INN, Chisinau, Moldova, Republic of

Introduction: According to previous studies the chronic migraine patients presented “conversive” profile and patients with high blood pressure – “emotionally overwhelmed” profile.

Objectives: The aim of the study was to asses the personality traits in chronic migraine patients with associated high blood pressure and compare them with chronic migraine patients without high blood pressure, patients with high blood pressure alone and healthy subjects.

Methods: The study sample consist of 127 persons divided in four groups: Gr. 1 chronic migraine with high blood pressure (N=44), Gr. II with chronic migraine without high blood pressure (N=32), Gr. III with high blood pressure without migraine (N= 28) and Gr. IV – healthy subject (N= 23). All persons underwent a neurologic examination, ambulatory blood pressure monitoring for 24 hours (ABPM). For migraine diagnosis was used International Headache Classification (IHC-3 beta) criteria, by a headache specialist. The Minnesota Multiphasic Personality Inventory – 2 (MMPI) was used to explore personality traits. The data was analyzed with SPSS package for Windows.

Results: Patients with chronic migraine with or without high blood pressure compared to healthy subjects presented elevated scores on scales: hypochondriasis, depression, hysteria, psychopathic deviate, psychasthenia and hypomania. The Gr. I with chronic migraine and high blood pressure presented pathologic scores on scales: hypochondriasis, hysteria and depression, where depression is higher than others which correspond with “neurotic triad” and “depressive” profile. In the Gr. II with chronic migraine without high blood pressure presented the pathologic scores on the “neurotic triad” and depression lower than others which correspond to “conversive” profile. The Gr. III with high blood pressure without migraine presented pathologic scores on “neurotic triad” and psychopathic deviate, psychasthenia and hypomania which correspond to “emotionally overwhelmed” profile. Healthy subjects presented normal scores in all scales which correspond to “coper” profile.

Conclusion: The study shows that chronic migraine patients with or without high blood pressure presented pathologic values on 6 MMPI-2 scales compared to healthy subjects. In chronic migraine with associated arterial hypertension patients presented the “depressive” profile.
Psychological and behaviour factors

COGNITIVE FLUCTUATIONS ALONG THE MIGRAINE CYCLE : PRODROMAL EFFECTS
I. P. Martins*, M. A. Quadros 1, C. Maruta 1, R. Gouveia 2
1Lisbon Faculty of Medicine , 2Hospital de Sta Maria, Lisbon, Portugal

Introduction: Migraine attacks are often preceded by subtle systemicl and cognitive symptoms that correspond to a specific pattern of brain dysfunction.

Objectives: In this study we aimed to evaluate cognitive performance during the prodromal phase of migraine and to determine if a brief cognitive assessment could predict incoming attacks

Methods: Consecutive patients with episodic migraine, with or without aura, fulfilling the diagnostic criteria of ICHD-3, observed in the Headache outpatient clinic of a University Hospital performed a brief cognitive battery (processing speed, shifting and inhibitory control) on the day of the consultation, after informed consent. Patients were contacted by telephone 48 hours later to check subsequent migraine attacks. Cognitive performance, adjusted for age and literacy, was used to predict the occurrence of an attack in the following two days. Attack frequency, menstruation, prophylactics and age were entered as covariates.

Results: Preliminary results, obtained with the first 32 patients (all female, age average 36.6±8.8 years) showed that, in general, patients had a better performance before migraine attacks on measures of set shifting and inhibitory control, but the difference did not reach significance. Menstruation and higher age were significantly associated with the incoming attack.

Conclusion: Migraine prodromal phase is known to be associated with an excessive processing on neurophysiological measures, this would fit the findings of a better processing ability in these preliminary results.
Secondary headaches
MTIS2018-131
THERAPEUTIC LUMBAR PUNCTURE FOR HEADACHE IN IDIOPATHIC INTRACRANIAL HYPERTENSION: MINIMAL GAIN, IS IT WORTH THE PAIN?


1Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, 2Metabolic Neurology, Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, 3Department of Neurology, 4NIHR/Wellcome Trust Clinical Research Facility, University Hospitals Birmingham NHS Foundation Trust, 5Birmingham Clinical Trials Unit, College of Medical and Dental Sciences, University of Birmingham, 6Birmingham Neuro-Ophthalmology Unit, Ophthalmology Department, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

Introduction: Headache is disabling and prevalent in Idiopathic intracranial hypertension (IIH). Therapeutic lumbar punctures (LP) maybe considered to manage headache. There is a lack of prospective data describing the improvement and exacerbations in IIH headaches in the week post-LP.

Objectives: This study aimed to evaluate the temporal change in headache severity in the week following a standardised LP, in patients with active IIH. Furthermore, we aimed to stratify the response to LP by baseline headache severity and evaluate the extent of improvement and the likelihood of an exacerbation. Importantly we also sought to define the influence of LP opening pressure on post-LP headache.

Methods: Active IIH patients were prospectively recruited to a cohort study, LP pressure and papilloedema grade were noted. Headache severity was recorded using a numeric rating scale (NRS) 0-10, pre-LP and following LP at 1, 4 and 6 hours and daily for 7 days.

Results: 52 patients were recruited (mean LP opening pressure 32 (28-37 cmCSF). At any point in the week post-LP, headache severity improved in 71% (but small reduction of -1.1 ± 2.6 NRS) and exacerbated in 64%, with 30% experiencing a severe exacerbation ≥4 NRS. Therapeutic LP’s are typically considered in IIH patients with severe headaches (NRS ≥7). In this cohort the likelihood of improvement was 92% (modest reduction of headache pain by-3.0 ± 2.8 NRS, p=0.012, day 7), while 33% deteriorated. IIH patients with mild (NRS 1-3) or no headache (on the day of LP, prior to LP) had a high risk of post-LP headache exacerbation (81% and 67% respectively). Importantly, there was no relationship between LP opening pressure and headache response after LP.

Conclusion: Following LP, the majority of IIH patients experience some improvement, but the benefit is small and post-LP headache exacerbation is common and in some prolonged and severe. LP pressure does not influence the post-LP headache.
THE EXPANDING BURDEN OF IDIOPATHIC INTRACRANIAL HYPERTENSION: INCIDENCE, DEPRIVATION, AND COSTS

S. P. Mollan 1,*, M. Aguiar 2, F. Evison 3, E. Frew 2, A. J. Sinclair 4

1Neuro-Ophthalmology, University Hospitals Birmingham NHS FT, Birmingham, 2Health Economics Unit, University of Birmingham, Birmingham, 3Department of Informatics, University Hospitals Birmingham NHS FT, 4Metabolic Neurology, University of Birmingham, Birmingham, United Kingdom

Introduction: Idiopathic Intracranial Hypertension is considered rare, yet its clear association with obesity is predicted to inflate the incidence in line with the global obesity epidemic.

Objectives: To determine the incidence and financial impact of IIH related hospital care.

Methods: Hospital Episode Statistics (HES) national data sets were extracted between 1st January 2002 and 31st December 2016. All those within England with a diagnosis of Idiopathic Intracranial Hypertension were included. Those with secondary causes of raised intracranial pressure such as tumours, hydrocephalus and cerebral venous sinus thrombosis were excluded.

Results: 23,182 new IIH cases were diagnosed. 52% resided in the most socially deprived areas (quintiles 1 and 2). Incidence rose between 2002 to 2016 from 2.3 to 4.7 per 100,000 in the general population. Peak incidence occurred in females aged 25 (15.2 per 100,000). 91.6% were treated medically, 7.6% had a cerebrospinal fluid diversion procedure, 0.7% underwent bariatric surgery and 0.1% had optic nerve sheath fenestration. Elective caesarean sections rates were significantly higher in IIH (16%) compared to the general population (9%), p<0.005. Admission rates rose by 442% between 2002 and 2014, with 38% having repeated admissions in the year following diagnosis. Costs rose from £9.2 to £50 million per annum over the study period with potential predicted costs of £462 million per annum by 2030.

Conclusion: There is a rising incidence of IIH (by greater than 100% over the study). Notably, incidence is highest in areas of social deprivation and mirrors obesity trends. Re-admissions rates are high and growing yearly. There is an escalating financial burden of managing IIH.
**Secondary headaches**

**MTIS2018-133**

CONSENSUS GUIDELINE IN ADULT IDIOPATHIC INTRACRANIAL HYPERTENSION

S. P. Mollan\(^1\)*, C. Hornby\(^2\), A. J. Sinclair\(^3\) on behalf of Idiopathic Intracranial Hypertension Specialist Interest Group

\(^1\)Neuro-Ophthalmology, University Hospitals Birmingham NHS FT, \(^2\)Medical School, \(^3\)Metabolic Neurology, University of Birmingham, Birmingham, United Kingdom

**Introduction:** Idiopathic intracranial Hypertension (IIH) is commonly associated with obesity, younger age and females. Patients present acutely to many different specialities, and often through the course of their disease will have multiple acute visits. The investigation and management of IIH is complex involving many specialities.

**Objectives:** The aim was create key pathways based on the recommendations of a multidisciplinary, patient involving and multi-professional specialist interest group on the investigation and management of Idiopathic Intracranial Hypertension (IIH).

**Methods:** Following systematic literature review, Population, Intervention, Comparison, Outcome (PICO) questions were constructed. Through a large Delphi group, expertise was captured from a wide-reaching group of clinicians reflecting practice from across the United Kingdom and internationally; whose statements have been critically reviewed international key opinion leaders, patients and by Association of British Neurologists, British Association for the Study of Headache, the Society of British Neurological Surgeons and the Royal College of Ophthalmologists.

**Results:** The lumbar puncture (LP) opening pressure was one key area of debate. Within the wider Delphi group it was clear that a “grey zone” existed between 25\text{cmCSF} and 30\text{cmCSF}, as to what each expert considered a pathologically raised LP opening pressure. Evaluation of the headache phenotype is essential, so that targeted treatment can be used and helps identification of medication overuse headache. Acute exacerbation of headache often leads to repeat LP and neuroimaging. The collective expert opinion reflected unless red flag signs were present, re-investigation is not warranted. Principles of management need to address both the rapidity of the disease that may lead to visual loss in some and require surgical intervention; and the morbidity of the headache that can develop in the majority, that substantially affects the quality of life.

**Conclusion:** This is the first consensus guidance for optimal management of IIH.
Secondary headaches

MTIS2018-134

RECURRENT THUNDERCLAP HEADACHES AND REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME SECONDARY TO PHEOCHROMOCYTOMA- A CRITICAL PRIMARY THUNDERCLAP HEADACHE MIMIC NOT TO BE MISSED.

I. Garza1, C. E. Robertson1, N. R. Kissoon1
1Neurology, Mayo Clinic, Rochester, MN, United States

Introduction: Pheochromocytoma as a cause of thunderclap headaches (TCHs) is rare and reversible cerebral vasoconstriction syndrome (RCVS) is even more rare in this context. Because RCVS can have negative initial neurovascular imaging, associated headaches can be mistakenly diagnosed as a primary headache disorder.

Objectives: We report a case of recurrent TCHs with negative initial neurovascular imaging. Investigations later found RCVS and a pheochromocytoma. Surgical resection of the tumor rendered her asymptomatic.

Methods: Case report.

Results: A 31-year-old woman reported bimonthly TCHs throughout 7 months, one year prior to her visit. Head magnetic resonance imaging (MRI), craniocervical magnetic resonance angiography (MRA), and head magnetic resonance venogram (MRV) were negative and TCHs resolved with pregnancy. Following labor/delivery with associated preeclampsia, she experienced intermittent, mild, featureless headaches but also TCH every 1-2 days. Head computed tomography (CT), craniocervical computed tomography angiogram (CTA), head computed tomography venogram (CTV), and neurologic exam were normal. Blood pressures were 140s/80s (on labetalol for recent preeclampsia). Although primary thunderclap headache (PTCH) was considered, 24-hour urine catecholamines/metanephrines were obtained. Her TCHs became more frequent and repeat MRA head/neck (23 days after delivery) showed multiple focal segments of cerebral arterial vasoconstriction affecting both anterior and posterior circulations. Her catecholamines/metanephrines proved to be markedly elevated and an abdominal CT showed a 3.6 x 3.5 x 3.8 cm left suprarenal complex solid and cystic mass most likely arising from the left adrenal gland. She developed more TCHs, resistant hypertension, episodic chest pain and tachycardia. Surgical resection of the mass resolved all symptoms and subsequent head/neck MRA were normal. Tumor pathology was consistent with a pheochromocytoma.

Conclusion: Pheochromocytoma can present with TCHs and RCVS. Screening for pheochromocytoma should be considered in all subjects with TCHs when a cause is unclear.
MEDICATION OVERUSE HEADACHE AND THE INTERVENTION OF THE CLINICAL NURSE SPECIALIST IN HEADACHE AT THE ROYAL VICTORIA INFIRMARY, NEWCASTLE UPON TYNE

S. Hurst 1,*

1Newcastle Upon Tyne Foundation Trust, Newcastle, United Kingdom

**Introduction:** Medication overuse headache (MOH) is a common and highly disabling headache disorder. MOH is classified in the International Classification of Headache Disorders as ‘headache occurring on half or more days per month as a consequence of regular overuse of acute headache medication on 10-15 or more days per month for more than three months’. Patients who suffer from migraine are particularly susceptible to MOH.

**Objectives:** 30% of patients who present with an underlying headache complaint may have MOH. The clinical nurse specialist identified this group of patients who could benefit from additional support whilst undergoing medication overuse withdrawal. A recent study indicated that the support by a headache nurse can improve adherence to detoxification when patients are asked to withdraw from acute painkillers. To assess the effectiveness of the intervention by the clinical nurse specialist a review was undertaken.

**Methods:** Data was collected via a postal questionnaire and a database. Patients were entered onto a database where information was collated during the withdrawal period. Patients were requested to stop taking all analgesia and triptans for a period of two months to allow for a ‘washout’ period. Various coping strategies were discussed with the patient during the nurse consultation. A telephone support call was offered after one month. A follow-up appointment was conducted after the washout period, usually two months, to discuss further management. A headache diary was completed to assess whether any change in headache frequency had occurred.

**Results:** 32 patients completed the questionnaire and had a consultation with the nurse following their clinical diagnosis. The patients were asked which strategies they found helpful during their period of withdrawal - 37% relaxation techniques 32% lifestyle changes 13% breathing techniques 10% support group 8% cognitive control techniques. 97% were offered a support call. Of these patients 69% found the call helpful. When asked about their headache following their period of withdrawal 50% agreed that their headache had improved 25% reported that they were not waking with headache 19% reported reduced severity and 6% reported that their headache was shorter. The analgesia that patients had been overusing included paracetamol 58%, triptans 42%, Ibuprofen 25%, Codeine 22% and naproxen 5%.

**Conclusion:** 50% of patients who were asked to stop all of their analgesia for two months saw an improvement in their headache. Patients utilised coping strategies to deal with headache rather than taking analgesia. Paracetamol was identified as the most common painkiller that was being overused. The support from the clinical nurse specialist has been identified as being a beneficial intervention in the process of withdrawal from analgesia.
Secondary headaches

MTIS2018-136

PITUITARY TUMOUR AND CLUSTER HEADACHE: A CASE REPORT AND REVIEW OF LITERATURE ON IMAGING RECOMMENDATIONS IN TRIGEMINAL-AUTONOMIC CEPHALALGIA.

S. Dorsey 1,*, S. M. Nadir 1, A. Buture 1, F. Ahmed 1
1Neurosciences, Hull York Medical School, Hull, United Kingdom

Introduction: The relationship between pituitary tumour and any form of headache is a major area for research and currently there is lack of understanding whether there is direct or indirect correlation between the two. The commonest phenotype headache associated with pituitary macroadenoma is chronic migraine although different forms of trigeminal-autonomic cephalalgia (TAC) have been reported including cluster headache (CH), SUNCT and SUNA and paroxysmal hemicrania. It may be that due to the rarity of TAC, they are over represented in pituitary disease. The indication for imaging remains debatable particularly in CH, the most common form of TAC.

Objectives: A case report of Pituitary macroadenoma presenting with cluster headache that prompted imaging only following visual symptoms.

Methods: We present a case of a 26 year old gentleman who had treatment resistant chronic cluster headache since December 2015. Multiple treatments trials failed including verapamil, indomethacin, lithium, Topirimate, Beta blockers, Greater occipital nerve block and the CGRP antibody trial. He had been referred for a sphenopalatine stimulator (SPGs) in May 2017. While waiting for SPGs he developed visual symptoms and developed visual loss of 6/24 right and 6/9 in left eye with severe reduction in colour vision. His MRI showed pituitary macroadenoma with prolactin levels of 90,000. His vision improved with cabergoline treatment with reduction of pituitary mass and prolactin levels (170).

Results: CH remains the most common form of TAC. The exact prevalence of pituitary macro-adenoma in CH remains unknown. One series reported 30% of symptomatic CH having pituitary adenoma (1). Another series of 84 reported cases of pituitary tumours of which only 4% presented with CH (2). This raises a very pertinent question as to whether all cases of CH be imaged with MRI. It is proposed that patients that are treatment resistant or atypical in presentation should be scanned although this is not a universal practice.

Conclusion: The poster reviews the literature and discusses for and against routine imaging.

**Abstracts**

**Secondary headaches**

**MTIS2018-137**

**BURNING MOUTH SYNDROME: A CASUISTIC REVIEW OF HEADACHE CONSULTATION**

R. Machado 1, A. Mestre 1, I. Luzeiro 1,*

1Neurology, CENTRO HOSPITALAR E UNIVERSITARIO DE COIMBRA, Coimbra, Portugal

**Introduction:** Burning Mouth Syndrome (BMS) is a chronic oral pain characterized by a burning sensation or other persistent dysesthesias in the oral cavity without evidence of mucosal alterations.

**Objectives:** The aim of this study was to compare the experience of the Headache Consultation of the Neurology Department of Centro Hospitalar e Universitário de Coimbra (CHUC) with the current scientific evidence.

**Methods:** The informatic database of the Headache Consultation of CHUC was consulted and 8 patients with the codification “ardor bucal” or “burning mouth” were identified between January 2014 and December 2017 which fulfilled the diagnostic criteria of The International Classification of Headache Disorders (ICHD-3 beta) for BMS. A retrospective analysis was performed taking into account demographic data, syndromic characterization, comorbidities and response to treatment.

**Results:** Patients mean age was 55 ± 11 years with a female predominance (n=6) and the mean duration of symptoms was 12.2 ± 11.7 months. The majority of patients described the pain as a burning sensation (n=5), all reported bilateral symptoms and 4 patients generically localized the pain to the oral mucosa. The most frequent accompanying symptom was dysgeusia (n=3). The continuous diurnal pattern of symptoms was the most frequent (n=5). Diabetes Mellitus, hypothyroidism and anemia were possible secondary causes identified in this sample. 4 patients had the diagnosis of depression and 2 patients of generalized anxiety disorder. The most frequent chronic medication was the antidepressant (n=5) and the anxiolytic (n=5). As first-line treatment, gabapentin (n=5) was effective in only one patient, carbamazepine (n=1) was effective and pregabalin (n=1) and amitriptyline (n=1) were ineffective. Second-line therapeutic strategies included topical clonazepam or topical lidocaine.

**Conclusion:** BMS is a rare entity in the Headache Consultation of CHUC. Overall, these cases are in line with the prevailing literature. There is a probable association between BMS and psychogenic factors. BMS represents a therapeutic challenge since there is no effective treatment clearly established. The main limitation of this study is the reduced sample size.

**References:**


Secondary headaches

MTIS2018-138

HEADACHE IN THE ACUTE MEDICAL UNIT: IS IT MANAGED EFFECTIVELY?

C. Parker 1,*, H. Johnston 2, S. Main 2, O. Seglah 2, J. Selvarajah 3

1Acute Medicine, Queen Elizabeth University Hospital, 2School of Medicine, University of Glasgow, 3Institute of Neurological Sciences, Queen Elizabeth University Hospital, Glasgow, United Kingdom

Introduction: Defining best practice in the management of acute headache remains a source of controversy. Clinical approaches to assessment and investigation can vary between centres and physicians (1, 2).

Objectives: In order to improve efficiency and quality of care, we explored routine practice in the assessment and treatment of headache in the acute medical service of our large, urban teaching hospital.

Methods: We conducted a retrospective analysis of clinical data in all patients with a primary complaint of non-traumatic headache admitted to our acute medical service in Glasgow, UK, in 2012. Hospital re-attendances were recorded over 3 years follow-up. We excluded any patient that did not require admission to a medical bed. From a total population of 345 patients, 108 patients were randomly selected for this study and data were collated from clinical records. These data were reviewed by a neurologist with an interest in headache.

Results: The mean age was 44 years (range 15 – 91 years). Median duration of admission was 3 days. In 44% (n=47), documented clinical features were inadequate for classification of headache. Past history of headache was unexplored in 57% (n=62) and in 31% (n=34) the bedside examination was considered incomplete. Brain imaging, mainly with CT, was performed in 82% (n=89). Only 3 patients with acute headache underwent initial imaging within 6 hours of symptom onset. Brain imaging identified a secondary cause in only 5 patients. Lumbar puncture was performed in 54% (n=58) and identified a secondary cause in only 6 patients. In 39% (n=42), no diagnosis was made on discharge from hospital. Final diagnosis was a primary headache syndrome in 31% (n=33), but discharge prescriptions included appropriate therapies in only 4 of these patients. Final diagnosis was a secondary headache in 31% (n=33), but in approximately half of these cases the diagnosis was not considered secure. Only one subarachnoid haemorrhage was identified. On follow-up, 33% (n=36) patients attended outpatient headache services and 6% (n=7) were readmitted with headache.

Conclusion: In patients admitted with headache to our acute medical unit, bedside assessment must be refined, investigations are overused, diagnosis is often incomplete and treatment strategies can be inappropriate. Addressing these issues may improve clinical efficiency in diagnosis and treatment, reduce bed occupancy and reduce the rate of recurrent headache. We have developed various service interventions to achieve these goals, including an algorithm for investigation of acute headache and an admission clerking proforma. These will be available for review at the conference.

References:
SECONDARY HEADACHES
MTIS2018-139

FIRST BITE SYNDROME – A CLINICAL CASE SEEN AT THE HEADACHE CONSULTATION
A. Silva¹, H. Gens, I. Luzeiro*¹
¹Neurology, Coimbra University and Hospital Centre, Coimbra, Portugal

Introduction: First Bite Syndrome (FBS) is an uncommon pathology. Refers to a facial pain due to spasms in the parotid region, which appears at the first chewing of each meal or simply by contact with food, decreasing in intensity over time. It is characterized by the development of intense pain, lasting seconds, paroxysmal, like an electric shock, at the beginning of the meal. The pathogenesis of SPD is uncertain, however, the classical hypothesis argues that the mechanism is based on sympathetic innervation of the parotid gland, with an increase in parasympathetic nervous system activity. The hyperactivation of the parasympathetic will overstimulate the contraction of the myoepithelial cells in the parotid gland, causing pain and increased salivary secretion. Most often, it arises as a consequence of superior cervical surgery.

Objectives: To characterize the First Bite syndrome clinical aspects, physiopathology and treatment.

Methods: We based on a clinical case of a 56-year-old female patient, that attended the consultation in January 2018, for a daily facial pain. She complains about intense pain at the beginning of chewing or with the ingestion of very acidic foods, lasting for seconds, like an electric shock, associated with sialorrhea. Notion of relief with manual compression of the face. She had a history of internal carotid artery aneurysm surgery in November 2014, with sequential dysphagia and left eye ptosis.

Results: She had already done Carbamazepine for 2 months, with no result. She started Gabapentin in July 2015, with some improvement, but she is symptomatic again. As the pharmacological treatment was not effective and the patient was very symptomatic, botulinum toxin and bupivacaine nerve block were applied in March 2018.

Conclusion: It is important to recognize this rare syndrome, to alert patients to that possibility in the preoperative period of cervical surgery. Patients who have been submitted to external carotid artery bypass or who have Horner Syndrome in the postoperative period, appear to be more likely to develop FBS.
Secondary headaches

**MTIS2018-140**

**POST-TRAUMATIC HEADACHE – A SAMPLE CHARACTERIZATION**

A. Silva ¹, H. Gens, I. Luzeiro*

¹Neurology, Coimbra University and Hospital Centre, Coimbra, Portugal

**Introduction:** Traumatic Brain Injury (TBI) is a problem frequently found in the general population. It can trigger a new headache (with a close temporal relationship to the trauma) or lead to a worsening of a pre-existing headache. Post-traumatic headache (PTH) is one of the most common secondary headache subtypes.

**Objectives:** To identify and analyze the parameters that characterize posttraumatic headache in patients attending the CHUC Headache Consultation.

**Methods:** Historical cohort study comprising 48 consecutive patients over a 38-month period with complaints of headache after having undergone TBI. Data was obtained through the registry of the consultation that appears in the patient's clinical record.

**Results:** The study of the socio-demographic characteristics of PTH and its socioeconomic context showed that PTH occurred at a mean age of 56.25 years and was more frequent in women (72.9%) and in individuals with no history of previous headache (77.1%). It is more frequent in married people (68.8%), with a low level of education, 4th grade (56.3%) and in the retired (20.8%). 87.5% of patients suffered minor TBI. The most common headache was tension type (45.8%), with no associated symptoms (47.9%), medium intensity (50%) and occurred on average 4.1 days after the TBI, with 60.4% of patients maintaining their pain complaints in the last evaluation. The most used therapy in the crisis was paracetamol (39.6%), while in the prophylaxis was amitriptyline (31.3%). 41.7% of the patients presented psychiatric comorbidities, 29.2% suffering from depression.

**Conclusion:** After a head trauma, several patterns of pain may arise, even simulating a primary headache. Regardless of the intensity of TBI, headache has been perpetuated over time in more than half of cases. Therapy, as a whole, was adequate.
**Secondary headaches**

**MTIS2018-141**

NOVEL NOTCH3 CYSTEIN-ALTERING MUTATION IN A PATIENT WITH CADASIL PRESENTING AS MIGRAINE WITH AURA

A. Fabjan*, A. Maver, B. Peterlin

**Introduction:** CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) is a progressive hereditary cerebral small vessel disease. It is an important cause of multiple subcortical strokes in younger patients with no traditional risk factors, which leads to early cognitive decline and often presents with severe migraine with aura (1).

**Objectives:** We describe a non-familial case of novel mutation in NOTCH3 gene.

**Methods:** A 36 year-old female secretary complained of 3 to 4 yearly attacks of migraine with prominent left-sided visual and sensory aura, with onset 8 years ago. The patient reported no difficulties in daily activities outside migraine attacks, showed no signs of cognitive decline or other neurological problems. She was otherwise healthy and non-smoker. The patient had two spontaneous abortions followed by two non-complicated deliveries of two healthy children. Migraines started after the second delivery. She reported recent improvement with no migraine attacks in the past year. Family history was unremarkable. MR brain imaging performed 6 years ago revealed multiple confluent symmetrical T2 and FLAIR hyper-intense subcortical and periventricular white matter lesions. Laboratory studies of blood and cerebrospinal fluid excluded thrombophilia, autoimmune/rheumathologic or infectious origin of lesions. There were no cardiac or precerebral vessel abnormalities. Repeated MR imaging 1 year ago showed no disease progression. Next-generation molecular genetic analysis was performed on patient’s DNA with advanced post-processing tools to determine pathogenicity of variants.

**Results:** We discovered a novel pathogenic variant in NOTCH3 gene which substitutes cysteine for phenylalanine at position 311. This variant is absent from control population of 123,000 subjects of the gnomAD project. Theoretical predictive tools of pathogenicity consistently predicted its likely damaging effect (SIFT, Polyphen2, Mutation Taster). According to American College of Medical Genetics and Genomics guidelines for the interpretation of sequence variants, the variant was classified as a likely pathogenic and regarded as a probable cause of patient’s clinical presentation.

**Conclusion:** CADASIL is an important differential diagnosis in secondary migraine. Our patient had an earlier disease onset than typically described, with migraines being the only presenting feature (2). Early disease onset might predict a more progressive disease course due to cysteine-altering NOTCH3 protein mutation. However, no sign of radiological or clinical progression of the disease was noted in our patient in the course of the last 6 years. This suggests an important role of potentially modifiable risk factors for disease progression worth considering in practice, albeit not yet recognized. The case also highlights impaired cerebral small vessel function in the pathogenesis of migraine with aura.

**References:**
Secondary headaches
MTIS2018-184

PRIORITY SETTING PARTNERSHIP DISCOVERS THE TOP 10 RESEARCH QUESTIONS FOR IDIOPATHIC INTRACRANIAL HYPERTENSION

S. P. Mollan 1,*, K. Hemmings 2, C. P. Herd 3, A. Denton 2, S. Williamson 2, A. J. Sinclair 4

1Neuro-Ophthalmology, University Hospitals Birmingham NHS FT, Birmingham, 2IIH UK, Newcastle, 3Institute of Clinical Sciences, 4Metabolic Neurology, University of Birmingham, Birmingham, United Kingdom

Introduction: Idiopathic Intracranial Hypertension (IIH) which causes debilitating headaches and in some permanent visual loss is under-researched. The current Cochrane review highlighted only two clinical trials in IIH.

Objectives: This James Lind Alliance Priority Setting Partnership (PSP) was commissioned by IIH UK, a patient charity, to encourage people with direct and personal experience of IIH to collectively identify and prioritise the top 10 uncertainties that impact on everyday clinical practice for the management IIH.

Methods: A modified nominal group technique was used to engage participants who had experience of IIH including: people with IIH, carers, family and friends, healthcare professionals. They were invited to participate in two rounds of surveys to identify what issues they deemed should be prioritised for research in IIH. Unique research questions unanswered by current evidence were identified for the interim survey and participants were asked to identify their top 10 research priorities from this list. The top 26 uncertainties were presented to a consensus meeting with key stakeholders then agreeing the top 10 research priorities.

Results: 356 participants provided 2405 responses, 140 were deemed to be out of scope. 2,265 were grouped into 64 indicative questions. 14 were deemed to be already known or they would be unanswerable by research. 48 questions were then presented in the interim prioritisation survey. 512 people took part (401 with IIH, friends or carers and 111 healthcare professionals). The most popular 26 were then taken for the final workshop. 24 stakeholders, these included patients, carers, neurologists, ophthalmologists, radiologists, neurosurgeons, and nurses took part in the consensus workshop. They agreed the top 10 research priorities. The overarching research aspiration was to understand the aetiology and management of IIH. The top 10 research priorities for IIH included aetiology of IIH; the pathological mechanisms of headache in IIH; new treatments in IIH; the difference between acute and gradual visual loss; the best ways to monitor visual function; biomarkers of the disease; hormonal causes of IIH; drug therapies for treatment of headache; weight loss and its role in IIH; and finally, the best intervention to treat IIH and when should surgery be performed.

Conclusion: These research priorities identify crucial gaps in the existing evidence for those who develop and those who manage IIH.
**Secondary headaches**

**MTIS2018-185**

HEADACHE CURED BY HEPATIC TRANSPLANT: A CASE REPORT

D. Moreno Ajona 1,*, P. Irimia 1

1Neurology, University of Navarre Clinic, Pamplona, Spain

**Introduction:** Intracranial hypertension related to cerebral edema may occur in up to 80% of cases fulminant hepatic failure. Cerebral edema, however, is usually not associated with intracranial hypertension in chronic liver disease. Headache is not considered a common symptom in these patients.

**Objectives:** The purpose of this report is to describe a single case of a patient with intracranial hypertension headache caused by liver disease.

**Methods:** The patient was a 52-year-old man who was previously diagnosed of porto-mesenteric venous thrombosis due to antiphospholipid syndrome, treated by placing transjugular intrahepatic porto-sistemic shunt (TIPS). He reported headache episodes for approximately 2 years. He started with bi-occipital pressure-like pain that clearly worsened with the Valsalva manoeuvre, and also with physical activity. Progressively, the episodes became more frequent, until pain was constant throughout the day.

**Results:** Neurological examination showed dysarthria, right facial paresis and postural hands tremor. Brain MRI and MRV showed no signs of venous thrombosis. Several lumbar punctures were performed, obtaining CSF opening pressure, ranging 25-32 cm of CSF. Treatment with acetazolamide (up to 750 mg / 12 hours) as well as topiramate (25 mg OD) obtained only partial relief. Following a confusion state, blood analysis showed hyperammonaemia (305 µg/dL) with normal liver enzymes. Symptoms persisted until hepatic transplant was performed 3 years later. Since then, the patient obtained complete relief of his headache.

**Conclusion:** Hyperammonaemia can lead to cerebral edema which, if maintained, may cause intracranial hypertension headache. High ammonium levels reaching the brain after TIPS may have been the cause for this patient’s headache.
Abstracts

Secondary headaches

MTIS2018-186

SUBCUTANEOUS ADIPOSE TISSUE FROM PATIENTS WITH IDIOPATHIC INTRACRANIAL HYPERTENSION DISPLAYS UNIQUE TRANSCRIPTOMIC AND METABOLIC FEATURES


1Institute of Metabolism and Systems Research, University of Birmingham, 2Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, 3School of Life Sciences, University of Warwick, Warwick, 4Upper GI and Minimally Invasive Unit, Heart of England NHS Foundation Trust, 5Department of Neurology, University Hospitals Birmingham, Queen Elizabeth Hospital, Birmingham, United Kingdom

Introduction: Idiopathic intracranial hypertension (IIH) is characterised by raised intracranial pressure (ICP), papilledema and chronic debilitating headache. IIH has a strong association with obesity. Over 95% of patients are obese women of reproductive age and the incidence is rising with the global epidemic of obesity. Truncal adiposity correlates with ICP and weight-loss lowers ICP and treats IIH. No mechanism explains the link between obesity and raised ICP. We hypothesise that adipose tissue from IIH patients is transcriptomically and metabolically distinct and contributes to raised ICP.

Objectives: We aimed to phenotype adipose tissue from IIH patients.

Methods: Phenotyping of subcutaneous (SC) adipose tissue from fasted female IIH patients and healthy age, BMI and gender matched controls derived from elective NHS bariatric lists, was achieved through RNA sequencing, histomorphometric analysis and nuclear magnetic resonance (NMR) metabolomics.

Results: Morphometric analysis showed that IIH and control SC adipocytes are indistinguishable in terms of size and cross-sectional area. RNA sequencing highlights that IIH SC adipose has 693 upregulated genes and 400 downregulated genes (P<0.05), where gene set enrichment analysis demonstrates a strong downregulation in ribosomal protein genes (P<0.0001) and an upregulation in genes associated with lipid biosynthesis (P<0.01). Analysis shows enrichment of genes associated with subjects gaining weight (P<0.0001).

NMR metabolomics demonstrates increased glycerol production in IIH SC adipose vs control (186±67 vs 97±25 μM; p<0.05 n=6 vs 6). Lipid generating amino acids leucine and isoleucine were preferentially consumed by IIH SC adipose vs control. IIH SC adipose leptin secretion was elevated compared to controls (8309±1593 vs 2366±431 pg/24h/100mg; p<0.01, n=11-12). Together, these data are indicative of altered lipid metabolism and function in IIH SC adipose tissue.

Conclusion: These data suggest that IIH SC adipose tissue is both transcriptomically and metabolically distinct from matched controls. We propose that SC adipose derived factors, such as leptin, coupled with changes in lipid turnover may mechanistically contribute to raised ICP and warrants further investigation.
EVALUATING THE BENEFITS OF MORE FREQUENT NON-INVASIVE VAGUS NERVE STIMULATION (NVNS) FOR PATIENTS WITH CHRONIC CLUSTER HEADACHE: A POST HOC ANALYSIS OF THE PREVA TRIAL

C. Gaul 1,*, E. Liebler 2, C. McClure 3, A. Andersson 2, A. Straube 4

1Migraine and Headache Clinic, Königstein, Germany, 2electroCore, LLC, Basking Ridge, New Jersey, 3North American Science Associates Inc., Minneapolis, Minnesota, United States, 4Ludwig Maximilian University of Munich, Munich, Germany

Introduction: Results from the randomised controlled PREVention and Acute treatment of chronic cluster headache (PREVA) study demonstrated a greater preventive effect on weekly attack frequency with the use of non-invasive vagus nerve stimulation plus standard of care (nVNS+SoC) than with SoC alone.

Objectives: We conducted a post hoc analysis to evaluate whether more frequent use of nVNS (as acute treatment) beyond the preventive regimen further contributes to the preventive effect of nVNS+SoC.

Methods: PREVA comprised a 2-week baseline period of individualised SoC therapy, a 4-week period of randomised treatment with nVNS+SoC or SoC alone, and an optional 4-week extension period of nVNS+SoC therapy. One preventive nVNS treatment consisted of three 2-minute stimulations to the right vagus nerve of the neck and was administered twice daily, for a total of 6 stimulations per day. Patients in the nVNS+SoC group were also allowed to use up to 3 stimulations to acutely treat an attack. Further examination of acute treatment use showed median values of 76.9% for the percentage of attacks per patient that were acutely treated with nVNS and 8.2 for the average number of daily acute nVNS stimulations per patient. For this post hoc analysis, we used subgroups that fell above and below these median values to evaluate patients who used nVNS more and less frequently, respectively. To provide insight into an optimal treatment paradigm, the mean reduction in weekly attack frequency from baseline to the randomised period for the 4 subgroups was compared with that of the SoC alone group. Linear regression with adjustment for multiple comparisons using the Bonferroni method was used to derive p values.

Table:

Results: The mean reduction in weekly attack frequency was significantly higher for patients who used nVNS to treat ≥76.9% of their attacks (−8.5 attacks per week; n=22) than for the SoC alone group (−2.1 attacks per week; n=47; p<0.01). The reduction observed for patients who used nVNS to treat <76.9% of their attacks was less pronounced (mean, −3.7 attacks per week; n=22; p=1.00). The mean decrease in weekly attack frequency was higher for patients who used ≥8.2 daily stimulations (−6.3 attacks per week; n=23) than for those who used <8.2 daily stimulations (−5.9 attacks per week; n=21); compared with the SoC alone group, these differences did not reach significance after adjustment for multiple comparisons (p=0.15 and p=0.25, respectively).

Conclusion: Patients who used nVNS more frequently (for ≥76.9% of attacks) demonstrated a significantly better response than those who used nVNS less frequently. Effects of nVNS on overall attack prevention appeared to be more closely related to the frequent treatment of attacks than to the use of more (≥8.2) stimulations per day. This post hoc analysis provides a clinical rationale for considering more frequent acute treatment of attacks with nVNS to enhance its preventive effects for patients with chronic cluster headache.
Disclosure of Interest: C. Gaul Conflict with: Honoraria from Allergan; Bayer; Boehringer Ingelheim; Desitin Arzneimittel; electroCore, LLC; Eli Lilly and Company; Grünenthal; Hormosan Pharma; Novartis; Ratiopharm; Reckitt Benckiser Group; and Teva Pharmaceuticals. He has no ownership interests and does not own any pharmaceutical company stocks., E. Liebler Conflict with: Employee of electroCore, LLC, and receives stock ownership., C. McClure Conflict with: Employee of North American Science Associates Inc., A. Andersson Conflict with: Employee of electroCore, LLC, and receives stock ownership., A. Straube Conflict with: Honoraria from Allergan plc; Berlin-Chemie AG; Boehringer Ingelheim GmbH; Desitin Arzneimittel GmbH; electroCore, LLC; Hormosan Pharma GmbH; Medical Specialties Distributors, LLC; Novartis Pharma AG; and Teva GmbH. He has also received research grants from the Else Kröner-Fresenius Foundation; the German Council of Science and Humanities; the German Secretary of Education; and Ludwig-Maximilian University.
 IMAGES DEPICTING PAIN - A SCREENING TOOL FOR CLUSTER HEADACHE
A. Buture 1*, L. Dikomitis 2, J. W. Boland 3, F. Ahmed 1
1Neurology Department, Hull & East Yorkshire Hospitals NHS Trust, Hull, 2Keele University, School of Medicine and Research Institute Primary Care and Health Sciences, Keele, 3Hull York Medical School, University of Hull, Hull, United Kingdom

Introduction: Cluster headache (CH), the most common of the trigeminal autonomic cephalalgias (TAC) is a rare, severe condition. CH is characterized by unilateral V1 trigeminal distribution pain, ipsilateral cranial autonomic features and tendency to circadian and circannual periodicity. Although CH has very distinct features the patients face delays in diagnosis, misdiagnosis and mismanagement.

Objectives: The project aims to pilot a new diagnostic tool to help primary care doctors and physicians in emergency departments to correctly diagnose CH. The new diagnostic tool will include: visual and verbal component that will facilitate differentiation of CH and other primary headache disorders; in addition a few key questions that differentiate CH from migraine will be included in the diagnostic to

Methods: Patients will be recruited from the Hull Headache Clinic. A cohort of CH patients will be invited to participate and patients with migraine will be used as control group. The diagnosis will be based on the International Headache Society Criteria. We aim to apply the new diagnostic tool on 100 participants in each group for validation and the sensitivity and specificity for each component will be evaluated.

Results: We aim to produce an A4 sheet for the new diagnostic tool to be available at the GP practices and emergency departments to assist in diagnosing CH.

Conclusion: The new tools of diagnosis have the potential to improve the delays in diagnosis, misdiagnosis and mismanagement.
**MTIS2018-144**

**MELATONIN IN CHRONIC CLUSTER HEADACHE: A CLINICAL AUDIT FROM 23 PATIENTS**

N. Vandenbussche 1,*, P. J. Goadsby 1,2

1Headache Group, Department of Basic and Clinical Neurosciences, King’s College London, 2NIHR Wellcome Trust Clinical Research Facility, King’s College Hospital, London, United Kingdom

**Introduction:** Melatonin has been found to play a role in the pathophysiology of cluster headache (1). The literature on the therapeutic use of melatonin in chronic cluster headache (CCH) is sparse but has shown a potential benefit for attack frequency and pain intensity (2,3).

**Objectives:** To evaluate the therapeutic efficacy in a clinic-based audit in patients with CCH. To distinguish the difference in clinical characteristics between responders to treatment with melatonin compared to non-responders.

**Methods:** We performed a retrospective clinical audit of adult patients with CCH (n = 23) treated with melatonin from our practice. Clinical data of these patients was collected, i.e. year of disease onset, number of treatments failed, dose, response to treatment, side effects and duration of treatment.

**Results:** 23 patients (10 females) had a median age in clinic of 45 (interquartile range (IQR) 39-52) and a median age of disease onset of 32 years (IQR 22-39). The median number of failed preventive treatments was 6 (IQR 5-10). The median maximum number of attacks per day was 6 (IQR 5-9). 18 patients were previously prescribed melatonin (78.3%), 5 were prescribed melatonin by our clinic (21.7%). Melatonin provided remission of CCH in zero patients, partial benefit in 7/23 (30.4%) and no effect in 16/23. When comparing melatonin responders to non-responders, responders had failed less preventive treatments (median 5, IQR 4-5) than non-responders (median 8.5, IQR 5.8-10.3) (p=0.007). Furthermore, responders used higher doses than non-responders (median 15mg vs 10mg, p=0.02). Melatonin prescribed by our clinic resulted in more responders (3/4) than previous use (1/15 patients, p=0.017). 4 patients presented side-effect (17.4%). Side effects were mostly mild with drowsiness as the most common side-effect.

**Conclusion:** Melatonin is partially effective in around 30% of our CCH patients, with efficacy potentially dose-related and a favourable side effect profile.

**References:**


**DELAYS IN THE DIAGNOSIS AND MISDIAGNOSIS OF CLUSTER HEADACHE – A SYSTEMATIC LITERATURE REVIEW**

A. Buture 1,*, J. W. Boland 2, L. Dikomitis 3, F. Ahmed 1

1Neurology Department, Hull & East Yorkshire Hospitals NHS Trust, 2Hull York Medical School, University of Hull, Hull, 3Keele University, School of Medicine and Research Institute Primary Care and Health Sciences, Keele, United Kingdom

**Introduction:** Patients with cluster headache (CH), the most common trigeminal autonomic cephalalgia, often face delayed diagnosis, misdiagnosis and mismanagement.

**Objectives:** To identify, appraise and synthesise clinical studies on the delays in diagnosis and misdiagnosis of 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. Both patient and physician factors account for the delays in diagnosis.

**Conclusion:** Diagnostic delays and misdiagnosis of CH is a worldwide problem and both patients and clinicians are responsible for the delays in diagnosis.
TACs

MTIS2018-187

PREMONITORY AND POSTDROME SYMPTOMS IN 28 CLUSTER HEADACHE PATIENTS IN A REFERRAL PRACTICE

M. Khalil 1,*, D. Wei 1, P. Goadsby 1

1Institute of Psychiatry, Psychology & Neuroscience, King’s College London, London, United Kingdom

Introduction: Premonitory and postdrome symptoms in cluster headache are not well understood. It is important to elucidate their character in order to improve our understanding of the condition.

Objectives: To characterise the clinical phenotype and evolution of the “premonitory” and “postdrome” phases in a cluster headache attack.

Methods: This retrospective study was conducted as an audit in a tertiary headache centre. We identified cluster headache patients as per the International Classification of Headache Disorders 3rd edition (ICHD-3) from 2014 until 2017

Table:

Results: We identified 28 cluster headache patients. The majority were males (n=18, 64%), with a median age of 48 (interquartile range of 40 to 56). Twenty-six patients (93%) had migraine biology. The median delay to diagnosis was 1 year and on average, a patient saw 4 clinicians before being diagnosed. Premonitory and postdrome symptoms were described 96%, with the median number of symptoms being 3. The commonest symptoms in the “premonitory” phase were, cranial autonomic symptoms, mood changes, neck stiffness and concentration difficulties with median duration before onset of pain of 10 minutes. The commonest postdrome symptoms were lethargy, cranial autonomic features, mood disturbance and poor concentration with median duration after the attack of 45 minutes

Conclusion: Premonitory and postdrome symptoms are common in cluster headache patients; however, their durations are markedly shorter than those in migraine headache. Further studies are needed to compare the difference in those symptoms across the two condition and whether having migraine biology has an impact on their character and the duration

Disclosure of Interest: M. Khalil: None Declared, D. Wei: None Declared, P. Goadsby Conflict with: Already submitted for this conference, Conflict with: Already submitted for this conference
Author Index
<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
<th>Abstract Programme N°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abagnale</td>
<td>Chiara</td>
<td>MTIS2018-052, MTIS2018-054</td>
</tr>
<tr>
<td>Abuoras</td>
<td>Yasmine</td>
<td>MTIS2018-125</td>
</tr>
<tr>
<td>Abu-Rumeileh</td>
<td>Samir</td>
<td>MTIS2018-055</td>
</tr>
<tr>
<td>Abuukar-Abdullahi</td>
<td>Ramla</td>
<td>MTIS2018-022</td>
</tr>
<tr>
<td>Adderley</td>
<td>Nicola</td>
<td>MTIS2018-150</td>
</tr>
<tr>
<td>Agati</td>
<td>Raffaele</td>
<td>MTIS2018-055</td>
</tr>
<tr>
<td>Aguiar</td>
<td>M</td>
<td>MTIS2018-132</td>
</tr>
<tr>
<td>Ailani</td>
<td>Jessica</td>
<td>MTIS2018-065, MTIS2018-066</td>
</tr>
<tr>
<td>Akerman</td>
<td>Ildem</td>
<td>MTIS2018-186</td>
</tr>
<tr>
<td>Al-Kaisy</td>
<td>Adnan</td>
<td>MTIS2018-179</td>
</tr>
<tr>
<td>Alina</td>
<td>Marta</td>
<td>MTIS2018-034, MTIS2018-128</td>
</tr>
<tr>
<td>Al-Mahdi-Al-Karagholi</td>
<td>Mohammad</td>
<td>MTIS2018-076</td>
</tr>
<tr>
<td>Almuayqil</td>
<td>Taim</td>
<td>MTIS2018-125</td>
</tr>
<tr>
<td>Alnafsah</td>
<td>Mohammed</td>
<td>MTIS2018-125</td>
</tr>
<tr>
<td>Alonso</td>
<td>Isabel</td>
<td>MTIS2018-033</td>
</tr>
<tr>
<td>Alpuente</td>
<td>Alicia</td>
<td>MTIS2018-030</td>
</tr>
<tr>
<td>Alvaro</td>
<td>Luis Carlos</td>
<td>MTIS2018-002</td>
</tr>
<tr>
<td>Alves-Ferreira</td>
<td>Miguel</td>
<td>MTIS2018-033</td>
</tr>
<tr>
<td>Ambrosini</td>
<td>Anna</td>
<td>MTIS2018-059, MTIS2018-060</td>
</tr>
<tr>
<td>Ameijeira</td>
<td>Pablo</td>
<td>MTIS2018-003</td>
</tr>
<tr>
<td>Andersson</td>
<td>Annelie</td>
<td>MTIS2018-142</td>
</tr>
<tr>
<td>Andreou</td>
<td>Anna</td>
<td>MTIS2018-022</td>
</tr>
<tr>
<td>Andreou</td>
<td>Anna</td>
<td>MTIS2018-179</td>
</tr>
<tr>
<td>Ashina</td>
<td>Messoud</td>
<td>MTIS2018-076, MTIS2018-099</td>
</tr>
<tr>
<td>Ashina</td>
<td>Messoud</td>
<td>MTIS2018-080</td>
</tr>
<tr>
<td>Asskour</td>
<td>Laila</td>
<td>MTIS2018-030</td>
</tr>
<tr>
<td>Ayer</td>
<td>David</td>
<td>MTIS2018-073, MTIS2018-097</td>
</tr>
<tr>
<td>Azimova</td>
<td>Julia</td>
<td>MTIS2018-099</td>
</tr>
<tr>
<td>Bahra</td>
<td>Anish</td>
<td>MTIS2018-162</td>
</tr>
<tr>
<td>Barbanti</td>
<td>Piero</td>
<td>MTIS2018-059, MTIS2018-060</td>
</tr>
<tr>
<td>Bardos</td>
<td>Jennifer</td>
<td>MTIS2018-176</td>
</tr>
<tr>
<td>Barrera-Barrera</td>
<td>Silvia</td>
<td>MTIS2018-151</td>
</tr>
<tr>
<td>Basarir</td>
<td>Ilker</td>
<td>MTIS2018-159, MTIS2018-161</td>
</tr>
<tr>
<td>Bassez</td>
<td>lege</td>
<td>MTIS2018-061</td>
</tr>
<tr>
<td>Battistella</td>
<td>Pier Antonio</td>
<td>MTIS2018-177</td>
</tr>
<tr>
<td>Baumgartner</td>
<td>Christoph</td>
<td>MTIS2018-167</td>
</tr>
<tr>
<td>Beato-Coelho</td>
<td>José</td>
<td>MTIS2018-118</td>
</tr>
<tr>
<td>Belin</td>
<td>Andrea</td>
<td>MTIS2018-029</td>
</tr>
<tr>
<td>Beltran</td>
<td>Amada Eloisa</td>
<td>MTIS2018-041</td>
</tr>
<tr>
<td>Belvis</td>
<td>Roberto</td>
<td>MTIS2018-002</td>
</tr>
<tr>
<td>Benchiheub</td>
<td>Anissa</td>
<td>MTIS2018-173</td>
</tr>
<tr>
<td>Bhattacharya</td>
<td>Suman</td>
<td>MTIS2018-099</td>
</tr>
<tr>
<td>Bhola</td>
<td>Ria</td>
<td>MTIS2018-162</td>
</tr>
<tr>
<td>Biondi</td>
<td>David</td>
<td>MTIS2018-099</td>
</tr>
<tr>
<td>Bitetto</td>
<td>Vito</td>
<td>MTIS2018-064, MTIS2018-128</td>
</tr>
<tr>
<td>Blanco</td>
<td>Juan</td>
<td>MTIS2018-002, MTIS2018-003</td>
</tr>
<tr>
<td>Blatchley</td>
<td>Chris</td>
<td>MTIS2018-175</td>
</tr>
<tr>
<td>Blixt</td>
<td>Frank</td>
<td>MTIS2018-044</td>
</tr>
<tr>
<td>Bogers</td>
<td>Ad J. c</td>
<td>MTIS2018-041</td>
</tr>
<tr>
<td>Boland</td>
<td>Jason</td>
<td>MTIS2018-143, MTIS2018-145</td>
</tr>
<tr>
<td>Bonner</td>
<td>Jo</td>
<td>MTIS2018-074</td>
</tr>
<tr>
<td>Bose</td>
<td>Pyari</td>
<td>MTIS2018-051</td>
</tr>
<tr>
<td>Bottfield</td>
<td>Hannah</td>
<td>MTIS2018-131, MTIS2018-186</td>
</tr>
<tr>
<td>Bottiroli</td>
<td>Sara</td>
<td>MTIS2018-128</td>
</tr>
<tr>
<td>Boyd</td>
<td>James</td>
<td>MTIS2018-068</td>
</tr>
<tr>
<td>Bozdag</td>
<td>Mumune</td>
<td>MTIS2018-149</td>
</tr>
<tr>
<td>Brin</td>
<td>Mitchell</td>
<td>MTIS2018-092</td>
</tr>
<tr>
<td>Brink</td>
<td>Antoinette</td>
<td>MTIS2018-041</td>
</tr>
<tr>
<td>Brössner</td>
<td>Gregor</td>
<td>MTIS2018-074</td>
</tr>
<tr>
<td>Bullock</td>
<td>Hayley</td>
<td>MTIS2018-124</td>
</tr>
<tr>
<td>Burk</td>
<td>Caroline</td>
<td>MTIS2018-005</td>
</tr>
<tr>
<td>Buyukgol</td>
<td>Huseyin</td>
<td>MTIS2018-160</td>
</tr>
<tr>
<td>Cady</td>
<td>Roger</td>
<td>MTIS2018-099, MTIS2018-107</td>
</tr>
<tr>
<td>Cala</td>
<td>Mary Lynn</td>
<td>MTIS2018-005</td>
</tr>
<tr>
<td>Calistrri</td>
<td>Valentina</td>
<td>MTIS2018-056</td>
</tr>
<tr>
<td>Camiña Muñiz</td>
<td>Javier</td>
<td>MTIS2018-011, MTIS2018-117</td>
</tr>
<tr>
<td>Campbell</td>
<td>Karen</td>
<td>MTIS2018-006</td>
</tr>
<tr>
<td>Camporeale</td>
<td>Angela</td>
<td>MTIS2018-072</td>
</tr>
<tr>
<td>Capone</td>
<td>Fioravante</td>
<td>MTIS2018-054</td>
</tr>
<tr>
<td>Caramia</td>
<td>Francesca</td>
<td>MTIS2018-056</td>
</tr>
<tr>
<td>Carmine Belin</td>
<td>Andrea</td>
<td>MTIS2018-031</td>
</tr>
<tr>
<td>Caronna</td>
<td>Edoardo</td>
<td>MTIS2018-180</td>
</tr>
<tr>
<td>Carter</td>
<td>Jeffrey</td>
<td>MTIS2018-072, MTIS2018-097</td>
</tr>
<tr>
<td>Cartocci</td>
<td>Gaia</td>
<td>MTIS2018-056</td>
</tr>
<tr>
<td>Case</td>
<td>Michael</td>
<td>MTIS2018-075</td>
</tr>
<tr>
<td>Centurioni</td>
<td>Clarissa</td>
<td>MTIS2018-052, MTIS2018-054</td>
</tr>
<tr>
<td>Cevoli</td>
<td>Sabina</td>
<td>MTIS2018-055</td>
</tr>
<tr>
<td>Chakhava</td>
<td>George</td>
<td>MTIS2018-107</td>
</tr>
<tr>
<td>Charles</td>
<td>Andrew</td>
<td>MTIS2018-020</td>
</tr>
<tr>
<td>Chen</td>
<td>Shih-Pin</td>
<td>MTIS2018-035</td>
</tr>
<tr>
<td>Last Name</td>
<td>First Name</td>
<td>Abstract Programme N°</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Cheng</td>
<td>Sunfa</td>
<td>MTIS2018-066, MTIS2018-110</td>
</tr>
<tr>
<td>Chung</td>
<td>Chinn-Sang</td>
<td>MTIS2018-049</td>
</tr>
<tr>
<td>Chung</td>
<td>Ming-Yi</td>
<td>MTIS2018-035</td>
</tr>
<tr>
<td>Cirillo</td>
<td>Luigi</td>
<td>MTIS2018-055</td>
</tr>
<tr>
<td>Clarke</td>
<td>Carl</td>
<td>MTIS2018-087</td>
</tr>
<tr>
<td>Conley</td>
<td>Robert</td>
<td>MTIS2018-176</td>
</tr>
<tr>
<td>Conway</td>
<td>Charles</td>
<td>MTIS2018-171</td>
</tr>
<tr>
<td>Coric</td>
<td>Vladimir</td>
<td>MTIS2018-170, MTIS2018-171</td>
</tr>
<tr>
<td>Correia</td>
<td>Pedro</td>
<td>MTIS2018-118</td>
</tr>
<tr>
<td>Cortelli</td>
<td>Pietro</td>
<td>MTIS2018-055</td>
</tr>
<tr>
<td>Cortese</td>
<td>Francesca</td>
<td>MTIS2018-053</td>
</tr>
<tr>
<td>Cowan</td>
<td>Robert</td>
<td>MTIS2018-006</td>
</tr>
<tr>
<td>Croop</td>
<td>Robert</td>
<td>MTIS2018-170, MTIS2018-171</td>
</tr>
<tr>
<td>Cuadrado</td>
<td>Maria Luz</td>
<td>MTIS2018-002</td>
</tr>
<tr>
<td>Dabbous</td>
<td>Firas</td>
<td>MTIS2018-006</td>
</tr>
<tr>
<td>D’Alito</td>
<td>Francesco</td>
<td>MTIS2018-002, MTIS2018-003</td>
</tr>
<tr>
<td>Danno</td>
<td>Daisuke</td>
<td>MTIS2018-046</td>
</tr>
<tr>
<td>Danser</td>
<td>Jan</td>
<td>MTIS2018-041, MTIS2018-062, MTIS2018-164</td>
</tr>
<tr>
<td>Day</td>
<td>Kathleen</td>
<td>MTIS2018-072, MTIS2018-081</td>
</tr>
<tr>
<td>de Boer</td>
<td>Irene</td>
<td>MTIS2018-163</td>
</tr>
<tr>
<td>De Llco</td>
<td>Roberto</td>
<td>MTIS2018-064</td>
</tr>
<tr>
<td>de la Red</td>
<td>Renar</td>
<td>MTIS2018-127</td>
</tr>
<tr>
<td>de la Torre</td>
<td>Elena</td>
<td>MTIS2018-012, MTIS2018-016</td>
</tr>
<tr>
<td>de Tommaso</td>
<td>Marina</td>
<td>MTIS2018-059, MTIS2018-060, MTIS2018-061</td>
</tr>
<tr>
<td>Deger</td>
<td>Kristen</td>
<td>MTIS2018-089</td>
</tr>
<tr>
<td>DeGryse</td>
<td>Ronald</td>
<td>MTIS2018-091</td>
</tr>
<tr>
<td>Demartini</td>
<td>Chiara</td>
<td>MTIS2018-034, MTIS2018-043</td>
</tr>
<tr>
<td>Denton</td>
<td>Amanda</td>
<td>MTIS2018-184</td>
</tr>
<tr>
<td>Derici Yildirim</td>
<td>Didem</td>
<td>MTIS2018-149</td>
</tr>
<tr>
<td>Desai</td>
<td>Pooja</td>
<td>MTIS2018-065, MTIS2018-066</td>
</tr>
<tr>
<td>Di Lazzaro</td>
<td>Vincenzo</td>
<td>MTIS2018-054</td>
</tr>
<tr>
<td>Di Lenola</td>
<td>Davide</td>
<td>MTIS2018-053</td>
</tr>
<tr>
<td>Di Lorenzo</td>
<td>Cherubino</td>
<td>MTIS2018-052, MTIS2018-053, MTIS2018-056</td>
</tr>
<tr>
<td>Di Piero</td>
<td>Vittorio</td>
<td>MTIS2018-056</td>
</tr>
<tr>
<td>Di Pino</td>
<td>Giovanni</td>
<td>MTIS2018-054</td>
</tr>
<tr>
<td>Di Renzo</td>
<td>Antonio</td>
<td>MTIS2018-056</td>
</tr>
<tr>
<td>Diaz de Teran Velasco</td>
<td>Javier</td>
<td>MTIS2018-011</td>
</tr>
<tr>
<td>Dikomitis</td>
<td>Lisa</td>
<td>MTIS2018-143, MTIS2018-145</td>
</tr>
</tbody>
</table>
## Author Index

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
<th>Abstract Programme N°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galina</td>
<td>Corcea</td>
<td>MTIS2018-129</td>
</tr>
<tr>
<td>Gallego de la Sacristana</td>
<td>Mercedes</td>
<td>MTIS2018-127</td>
</tr>
<tr>
<td>Gantenbein</td>
<td>Andreas</td>
<td>MTIS2018-057, MTIS2018-167</td>
</tr>
<tr>
<td>García López</td>
<td>David</td>
<td>MTIS2018-147</td>
</tr>
<tr>
<td>García Ull</td>
<td>Jessica</td>
<td>MTIS2018-147</td>
</tr>
<tr>
<td>Garza</td>
<td>Ivan</td>
<td>MTIS2018-134</td>
</tr>
<tr>
<td>Gaul</td>
<td>Charly</td>
<td>MTIS2018-076, MTIS2018-142, MTIS2018-172</td>
</tr>
<tr>
<td>Gens</td>
<td>Helena</td>
<td>MTIS2018-139, MTIS2018-140</td>
</tr>
<tr>
<td>Geppetti</td>
<td>Pierangelo</td>
<td>MTIS2018-059, MTIS2018-060</td>
</tr>
<tr>
<td>Gil-Gouveia</td>
<td>Raquel</td>
<td>MTIS2018-026</td>
</tr>
<tr>
<td>Gokhale</td>
<td>Krishna</td>
<td>MTIS2018-150</td>
</tr>
<tr>
<td>Gómez Galván</td>
<td>Juan</td>
<td>MTIS2018-030</td>
</tr>
<tr>
<td>Gómez Pilar</td>
<td>Javier</td>
<td>MTIS2018-113</td>
</tr>
<tr>
<td>Gonzalez García</td>
<td>Nuria</td>
<td>MTIS2018-011</td>
</tr>
<tr>
<td>Gonzalez Martínez</td>
<td>Alicia</td>
<td>MTIS2018-127</td>
</tr>
<tr>
<td>González Quintanilla</td>
<td>Vicente</td>
<td>MTIS2018-011</td>
</tr>
<tr>
<td>González-Oria</td>
<td>Carmen</td>
<td>MTIS2018-002</td>
</tr>
<tr>
<td>Gouveia</td>
<td>Raquel</td>
<td>MTIS2018-130</td>
</tr>
<tr>
<td>Govindan</td>
<td>Srima</td>
<td>MTIS2018-069</td>
</tr>
<tr>
<td>Graeter</td>
<td>Heidemarie</td>
<td>MTIS2018-172</td>
</tr>
<tr>
<td>Graham</td>
<td>Christina</td>
<td>MTIS2018-005</td>
</tr>
<tr>
<td>Grazzi</td>
<td>Licia</td>
<td>MTIS2018-059, MTIS2018-060</td>
</tr>
<tr>
<td>Greco</td>
<td>Rosario</td>
<td>MTIS2018-034, MTIS2018-043</td>
</tr>
<tr>
<td>Guaschino</td>
<td>Elena</td>
<td>MTIS2018-128</td>
</tr>
<tr>
<td>Gupta</td>
<td>Shalo</td>
<td>MTIS2018-070, MTIS2018-083</td>
</tr>
<tr>
<td>Haaker</td>
<td>Jan</td>
<td>MTIS2018-045</td>
</tr>
<tr>
<td>Haanes</td>
<td>Kristian Agmund</td>
<td>MTIS2018-044, MTIS2018-062</td>
</tr>
<tr>
<td>Haghdooost</td>
<td>Faraidoon</td>
<td>MTIS2018-120</td>
</tr>
<tr>
<td>Hall</td>
<td>Olivia</td>
<td>MTIS2018-124</td>
</tr>
<tr>
<td>Hebenstreit</td>
<td>Daniel</td>
<td>MTIS2018-186</td>
</tr>
<tr>
<td>Hemmings</td>
<td>Krystal</td>
<td>MTIS2018-184</td>
</tr>
<tr>
<td>Herd</td>
<td>Clare</td>
<td>MTIS2018-087</td>
</tr>
<tr>
<td>Herd</td>
<td>Clare</td>
<td>MTIS2018-184</td>
</tr>
<tr>
<td>Hernández-Beltrán</td>
<td>Natalia</td>
<td>MTIS2018-180</td>
</tr>
<tr>
<td>Hicka</td>
<td>Toshiyuki</td>
<td>MTIS2018-032</td>
</tr>
<tr>
<td>Hill</td>
<td>Bethany</td>
<td>MTIS2018-179</td>
</tr>
<tr>
<td>Hirman</td>
<td>Joe</td>
<td>MTIS2018-107</td>
</tr>
<tr>
<td>Hoffmann</td>
<td>Jan</td>
<td>MTIS2018-076</td>
</tr>
<tr>
<td>Holland</td>
<td>Philip</td>
<td>MTIS2018-036, MTIS2018-037, MTIS2018-039</td>
</tr>
<tr>
<td>Hoogeveen</td>
<td>Evelien</td>
<td>MTIS2018-163</td>
</tr>
<tr>
<td>Hornby</td>
<td>Catherine</td>
<td>MTIS2018-113</td>
</tr>
<tr>
<td>Hornero</td>
<td>Roberto</td>
<td>MTIS2018-113</td>
</tr>
<tr>
<td>Hould</td>
<td>Jennifer</td>
<td>MTIS2018-170</td>
</tr>
<tr>
<td>Hours-Zesiger</td>
<td>Peggy</td>
<td>MTIS2018-077, MTIS2018-106</td>
</tr>
<tr>
<td>Hurst</td>
<td>Susan</td>
<td>MTIS2018-135</td>
</tr>
<tr>
<td>Ijaz</td>
<td>Aamir</td>
<td>MTIS2018-027</td>
</tr>
<tr>
<td>Ilik</td>
<td>Falk</td>
<td>MTIS2018-159, MTIS2018-160, MTIS2018-161</td>
</tr>
<tr>
<td>Imai</td>
<td>Noboru</td>
<td>MTIS2018-048</td>
</tr>
<tr>
<td>Imre László</td>
<td>Vecsei</td>
<td>MTIS2018-021</td>
</tr>
<tr>
<td>Ion</td>
<td>Moldovanu</td>
<td>MTIS2018-129</td>
</tr>
<tr>
<td>Irimia Sieira</td>
<td>Pablo</td>
<td>MTIS2018-079, MTIS2018-147, MTIS2018-185</td>
</tr>
<tr>
<td>Ishizaki</td>
<td>Kumiko</td>
<td>MTIS2018-046</td>
</tr>
<tr>
<td>Ivans</td>
<td>Andrea</td>
<td>MTIS2018-170</td>
</tr>
<tr>
<td>Ives</td>
<td>Natalie</td>
<td>MTIS2018-018, MTIS2018-087</td>
</tr>
<tr>
<td>Janelidze</td>
<td>Marina</td>
<td>MTIS2018-107</td>
</tr>
<tr>
<td>Jarman</td>
<td>Heather</td>
<td>MTIS2018-157</td>
</tr>
<tr>
<td>Jensen</td>
<td>Christopher</td>
<td>MTIS2018-170, MTIS2018-171</td>
</tr>
<tr>
<td>Jiang</td>
<td>Liwen</td>
<td>MTIS2018-017</td>
</tr>
<tr>
<td>Jiang</td>
<td>Yun-Jin</td>
<td>MTIS2018-035</td>
</tr>
<tr>
<td>Jin</td>
<td>Yan</td>
<td>MTIS2018-111</td>
</tr>
<tr>
<td>Johansen</td>
<td>Troels</td>
<td>MTIS2018-058</td>
</tr>
<tr>
<td>John</td>
<td>Plachrill</td>
<td>MTIS2018-119</td>
</tr>
<tr>
<td>Johnston</td>
<td>Kirk</td>
<td>MTIS2018-062</td>
</tr>
<tr>
<td>Johnston</td>
<td>Hannah</td>
<td>MTIS2018-138</td>
</tr>
<tr>
<td>Jones</td>
<td>Martyn</td>
<td>MTIS2018-022</td>
</tr>
<tr>
<td>Joshi</td>
<td>Mandeep</td>
<td>MTIS2018-126</td>
</tr>
<tr>
<td>Karsan</td>
<td>Nazia</td>
<td>MTIS2018-051</td>
</tr>
<tr>
<td>Kasch</td>
<td>Helge</td>
<td>MTIS2018-152</td>
</tr>
<tr>
<td>Kawahara</td>
<td>Steve</td>
<td>MTIS2018-006</td>
</tr>
<tr>
<td>Kechechyan</td>
<td>Gayane</td>
<td>MTIS2018-020</td>
</tr>
<tr>
<td>Kellerman</td>
<td>Donald</td>
<td>MTIS2018-063</td>
</tr>
<tr>
<td>Kielbasa</td>
<td>William</td>
<td>MTIS2018-111</td>
</tr>
<tr>
<td>Kikui</td>
<td>Shouji</td>
<td>MTIS2018-046</td>
</tr>
<tr>
<td>Last Name</td>
<td>First Name</td>
<td>Abstract Programme N°</td>
</tr>
<tr>
<td>-----------</td>
<td>------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Kim</td>
<td>Byungkun</td>
<td>MTIS2018-122</td>
</tr>
<tr>
<td>Kissoon</td>
<td>Narayan</td>
<td>MTIS2018-134</td>
</tr>
<tr>
<td>Knudsen</td>
<td>Diana</td>
<td>MTIS2018-152</td>
</tr>
<tr>
<td>Kocabiyyik</td>
<td>Nihal</td>
<td>MTIS2018-159, MTIS2018-161</td>
</tr>
<tr>
<td>Kollias</td>
<td>Spyros</td>
<td>MTIS2018-057, MTIS2018-167</td>
</tr>
<tr>
<td>Kovalchin</td>
<td>Joe</td>
<td>MTIS2018-062</td>
</tr>
<tr>
<td>Krege</td>
<td>John</td>
<td>MTIS2018-169</td>
</tr>
<tr>
<td>Krishnan</td>
<td>Anita</td>
<td>MTIS2018-018</td>
</tr>
<tr>
<td>Kronwall</td>
<td>Erik</td>
<td>MTIS2018-042</td>
</tr>
<tr>
<td>Krut</td>
<td>Mark</td>
<td>MTIS2018-163</td>
</tr>
<tr>
<td>Kuca</td>
<td>Bernice</td>
<td>MTIS2018-075</td>
</tr>
<tr>
<td>Kudrow</td>
<td>David</td>
<td>MTIS2018-107</td>
</tr>
<tr>
<td>La Morgia</td>
<td>Chiara</td>
<td>MTIS2018-055</td>
</tr>
<tr>
<td>Labastida-Ramirez</td>
<td>Alejandro</td>
<td>MTIS2018-062</td>
</tr>
<tr>
<td>Lafemme</td>
<td>Annik</td>
<td>MTIS2018-070, MTIS2018-083</td>
</tr>
<tr>
<td>Laires</td>
<td>Pedro</td>
<td>MTIS2018-086</td>
</tr>
<tr>
<td>Lakkis</td>
<td>Hassan</td>
<td>MTIS2018-174.</td>
</tr>
<tr>
<td>Labru</td>
<td>Giorgio</td>
<td>MTIS2018-179</td>
</tr>
<tr>
<td>Larouche</td>
<td>Richard</td>
<td>MTIS2018-170</td>
</tr>
<tr>
<td>Latorre</td>
<td>Germán</td>
<td>MTIS2018-002</td>
</tr>
<tr>
<td>Lavery</td>
<td>Gareth</td>
<td>MTIS2018-186</td>
</tr>
<tr>
<td>Lee</td>
<td>Chungbin</td>
<td>MTIS2018-049</td>
</tr>
<tr>
<td>Lee</td>
<td>Mi Ji</td>
<td>MTIS2018-049</td>
</tr>
<tr>
<td>Lee</td>
<td>Seung-Han</td>
<td>MTIS2018-122</td>
</tr>
<tr>
<td>Leech</td>
<td>Robert</td>
<td>MTIS2018-166</td>
</tr>
<tr>
<td>Leira</td>
<td>Yago</td>
<td>MTIS2018-002, MTIS2018-003</td>
</tr>
<tr>
<td>Leira Muñó</td>
<td>Rogelio</td>
<td>MTIS2018-147</td>
</tr>
<tr>
<td>Lemos</td>
<td>Carolina</td>
<td>MTIS2018-033</td>
</tr>
<tr>
<td>Li</td>
<td>Lily</td>
<td>MTIS2018-178</td>
</tr>
<tr>
<td>Liczkowski</td>
<td>Anthony</td>
<td>MTIS2018-024</td>
</tr>
<tr>
<td>Linstra</td>
<td>Katie</td>
<td>MTIS2018-164</td>
</tr>
<tr>
<td>Lloyd</td>
<td>Joseph</td>
<td>MTIS2018-022, MTIS2018-179</td>
</tr>
<tr>
<td>Logan</td>
<td>Anne-Marie</td>
<td>MTIS2018-157, MTIS2018-158</td>
</tr>
<tr>
<td>Lombard</td>
<td>Louise</td>
<td>MTIS2018-169</td>
</tr>
<tr>
<td>Lopez</td>
<td>J. Ivan</td>
<td>MTIS2018-093, MTIS2018-095</td>
</tr>
<tr>
<td>López Bravo</td>
<td>Alba</td>
<td>MTIS2018-147</td>
</tr>
<tr>
<td>Lopez Veloso</td>
<td>Ana</td>
<td>MTIS2018-011</td>
</tr>
<tr>
<td>Lu</td>
<td>Kaifeng</td>
<td>MTIS2018-174</td>
</tr>
<tr>
<td>Ludwig</td>
<td>Christian</td>
<td>MTIS2018-186</td>
</tr>
<tr>
<td>Luechinger</td>
<td>Roger</td>
<td>MTIS2018-057</td>
</tr>
<tr>
<td>Luvsannorov</td>
<td>Otgonbayar</td>
<td>MTIS2018-004</td>
</tr>
<tr>
<td>Lyn</td>
<td>Nicole</td>
<td>MTIS2018-005</td>
</tr>
<tr>
<td>Maassen Van Den Brink</td>
<td>Antoinette</td>
<td>MTIS2018-062, MTIS2018-164, MTIS2018-168</td>
</tr>
<tr>
<td>MacGregor</td>
<td>Anne</td>
<td>MTIS2018-025</td>
</tr>
<tr>
<td>MacGregor</td>
<td>E. Anne</td>
<td>MTIS2018-146</td>
</tr>
<tr>
<td>Machado</td>
<td>Rita</td>
<td>MTIS2018-137</td>
</tr>
<tr>
<td>Machado</td>
<td>Sara</td>
<td>MTIS2018-026</td>
</tr>
<tr>
<td>Magis</td>
<td>Delphine</td>
<td>MTIS2018-076</td>
</tr>
<tr>
<td>Main</td>
<td>Sophie</td>
<td>MTIS2018-138</td>
</tr>
<tr>
<td>Maniyar</td>
<td>Farooq</td>
<td>MTIS2018-089</td>
</tr>
<tr>
<td>Mankad</td>
<td>Kshitij</td>
<td>MTIS2018-183</td>
</tr>
<tr>
<td>Marfil</td>
<td>Alejandro</td>
<td>MTIS2018-151</td>
</tr>
<tr>
<td>Marques</td>
<td>Ines</td>
<td>MTIS2018-026</td>
</tr>
<tr>
<td>Martin</td>
<td>Vincent</td>
<td>MTIS2018-008</td>
</tr>
<tr>
<td>Martinelli</td>
<td>Daniele</td>
<td>MTIS2018-064</td>
</tr>
<tr>
<td>Martinez</td>
<td>Blanca</td>
<td>MTIS2018-112</td>
</tr>
<tr>
<td>Martinez</td>
<td>James</td>
<td>MTIS2018-176</td>
</tr>
<tr>
<td>Martinez Fernandez</td>
<td>Elvira</td>
<td>MTIS2018-121</td>
</tr>
<tr>
<td>Martinez Pias</td>
<td>Enrique</td>
<td>MTIS2018-121</td>
</tr>
<tr>
<td>Martins</td>
<td>Isabel</td>
<td>MTIS2018-026, MTIS2018-130</td>
</tr>
<tr>
<td>Maruta</td>
<td>Carolina</td>
<td>MTIS2018-130</td>
</tr>
<tr>
<td>Mas Sala</td>
<td>Natalia</td>
<td>MTIS2018-011</td>
</tr>
<tr>
<td>Matthews</td>
<td>Tim</td>
<td>MTIS2018-018</td>
</tr>
<tr>
<td>Matza</td>
<td>Louis</td>
<td>MTIS2018-089</td>
</tr>
<tr>
<td>Mavor</td>
<td>Ale_</td>
<td>MTIS2018-141</td>
</tr>
<tr>
<td>McCann</td>
<td>Fionnuala</td>
<td>MTIS2018-028</td>
</tr>
<tr>
<td>McClure</td>
<td>Candace</td>
<td>MTIS2018-142</td>
</tr>
<tr>
<td>McCorkell</td>
<td>Laura</td>
<td>MTIS2018-173</td>
</tr>
<tr>
<td>McCormack</td>
<td>Timothy</td>
<td>MTIS2018-171</td>
</tr>
<tr>
<td>McGinley</td>
<td>James</td>
<td>MTIS2018-182</td>
</tr>
<tr>
<td>McMahon</td>
<td>Stephen</td>
<td>MTIS2018-022</td>
</tr>
</tbody>
</table>
### Author Index

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
<th>Abstract Programme Nº*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menz</td>
<td>Mareike</td>
<td>MTIS2018-045</td>
</tr>
<tr>
<td>Messia</td>
<td>Monica</td>
<td>MTIS2018-055</td>
</tr>
<tr>
<td>Messina</td>
<td>Roberta</td>
<td>MTIS2018-166</td>
</tr>
<tr>
<td>Mestre</td>
<td>António</td>
<td>MTIS2018-137</td>
</tr>
<tr>
<td>Michalska</td>
<td>Julia</td>
<td>MTIS2018-031</td>
</tr>
<tr>
<td>Michels</td>
<td>Lars</td>
<td>MTIS2018-057, MTIS2018-167</td>
</tr>
<tr>
<td>Middelkoop</td>
<td>Hubertus</td>
<td>MTIS2018-163</td>
</tr>
<tr>
<td>Milen</td>
<td>Brian</td>
<td>MTIS2018-098, MTIS2018-176</td>
</tr>
<tr>
<td>Milocchi</td>
<td>Anna Carlotta</td>
<td>MTIS2018-177</td>
</tr>
<tr>
<td>Minguez Olaondo</td>
<td>Ane</td>
<td>MTIS2018-147</td>
</tr>
<tr>
<td>Mitchell</td>
<td>James</td>
<td>MTIS2018-018, MTIS2018-131</td>
</tr>
<tr>
<td>Mitsikostas</td>
<td>Dimos</td>
<td>MTIS2018-076</td>
</tr>
<tr>
<td>Miyahara</td>
<td>Junichi</td>
<td>MTIS2018-046</td>
</tr>
<tr>
<td>Moeller</td>
<td>Maike</td>
<td>MTIS2018-165</td>
</tr>
<tr>
<td>Molina</td>
<td>Francisco José</td>
<td>MTIS2018-117</td>
</tr>
<tr>
<td>Mollan</td>
<td>Susan</td>
<td>MTIS2018-019</td>
</tr>
<tr>
<td>Monzón</td>
<td>Maria José</td>
<td>MTIS2018-002</td>
</tr>
<tr>
<td>Moreno Ajona</td>
<td>David</td>
<td>MTIS2018-185</td>
</tr>
<tr>
<td>Moriya</td>
<td>Asami</td>
<td>MTIS2018-048</td>
</tr>
<tr>
<td>Morris</td>
<td>Beth</td>
<td>MTIS2018-170, MTIS2018-171</td>
</tr>
<tr>
<td>Mortimer</td>
<td>Joanne</td>
<td>MTIS2018-124</td>
</tr>
<tr>
<td>Moulin</td>
<td>Julie-Alexandra</td>
<td>MTIS2018-170</td>
</tr>
<tr>
<td>Murray</td>
<td>Sharron</td>
<td>MTIS2018-009</td>
</tr>
<tr>
<td>Musumeci</td>
<td>Gabriella</td>
<td>MTIS2018-054</td>
</tr>
<tr>
<td>Myers Oakes</td>
<td>Tina</td>
<td>MTIS2018-176</td>
</tr>
<tr>
<td>Nadir</td>
<td>Syed</td>
<td>MTIS2018-136</td>
</tr>
<tr>
<td>Nagy</td>
<td>Abraham</td>
<td>MTIS2018-081</td>
</tr>
<tr>
<td>Nappi</td>
<td>Giuseppe</td>
<td>MTIS2018-128</td>
</tr>
<tr>
<td>Nativi</td>
<td>Cristina</td>
<td>MTIS2018-043</td>
</tr>
<tr>
<td>Neto</td>
<td>João</td>
<td>MTIS2018-033</td>
</tr>
<tr>
<td>Nichols</td>
<td>Russell</td>
<td>MTIS2018-169, MTIS2018-073</td>
</tr>
<tr>
<td>Nightingale</td>
<td>Helen</td>
<td>MTIS2018-183</td>
</tr>
<tr>
<td>Nightingale</td>
<td>Peter</td>
<td>MTIS2018-131</td>
</tr>
<tr>
<td>Nirantharakumar</td>
<td>Krishnaraj</td>
<td>MTIS2018-150</td>
</tr>
<tr>
<td>Nirmalananthan</td>
<td>Niranjana</td>
<td>MTIS2018-157, MTIS2018-158</td>
</tr>
<tr>
<td>Nosadini</td>
<td>Margherita</td>
<td>MTIS2018-177</td>
</tr>
<tr>
<td>Notting</td>
<td>Irene</td>
<td>MTIS2018-163</td>
</tr>
<tr>
<td>O’Gorman</td>
<td>Ruth</td>
<td>MTIS2018-057</td>
</tr>
<tr>
<td>Ohlsson</td>
<td>Lena</td>
<td>MTIS2018-042</td>
</tr>
<tr>
<td>Öksüz</td>
<td>Nevra</td>
<td>MTIS2018-149</td>
</tr>
<tr>
<td>Onderwater</td>
<td>Gerrit</td>
<td>MTIS2018-168</td>
</tr>
<tr>
<td>Orejudos</td>
<td>Amelia</td>
<td>MTIS2018-090, MTIS2018-092, MTIS2018-094</td>
</tr>
<tr>
<td>Orlandi</td>
<td>Marco</td>
<td>MTIS2018-002</td>
</tr>
<tr>
<td>Ottridge</td>
<td>Ryan</td>
<td>MTIS2018-018, MTIS2018-131</td>
</tr>
<tr>
<td>Oxana</td>
<td>Grosu</td>
<td>MTIS2018-129</td>
</tr>
</tbody>
</table>

---

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
<th>Abstract Programme Nº*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ozge</td>
<td>Aynur</td>
<td>MTIS2018-149</td>
</tr>
<tr>
<td>Park</td>
<td>Bo-Yong</td>
<td>MTIS2018-049</td>
</tr>
<tr>
<td>Park</td>
<td>Hyunjin</td>
<td>MTIS2018-049</td>
</tr>
<tr>
<td>Parker</td>
<td>Catriona</td>
<td>MTIS2018-138</td>
</tr>
<tr>
<td>Parreira</td>
<td>Elsa</td>
<td>MTIS2018-026</td>
</tr>
<tr>
<td>Pascual</td>
<td>Julio</td>
<td>MTIS2018-065</td>
</tr>
<tr>
<td>Patel</td>
<td>Atul</td>
<td>MTIS2018-007</td>
</tr>
<tr>
<td>Pavlovic</td>
<td>Jelena</td>
<td>MTIS2018-006, MTIS2018-116</td>
</tr>
<tr>
<td>Pazzi</td>
<td>Stefania</td>
<td>MTIS2018-128</td>
</tr>
<tr>
<td>Pedraza Hueso</td>
<td>Maria Isabel</td>
<td>MTIS2018-113</td>
</tr>
<tr>
<td>Pelzer</td>
<td>Nadine</td>
<td>MTIS2018-163</td>
</tr>
<tr>
<td>Pereira-Monteiro José</td>
<td>MTIS2018-053</td>
<td></td>
</tr>
<tr>
<td>Peterlin</td>
<td>Borut</td>
<td>MTIS2018-141</td>
</tr>
<tr>
<td>Petolicchio</td>
<td>Barbara</td>
<td>MTIS2018-056</td>
</tr>
<tr>
<td>Picard</td>
<td>Hernan</td>
<td>MTIS2018-065, MTIS2018-074</td>
</tr>
<tr>
<td>Pierangeli</td>
<td>Giulia</td>
<td>MTIS2018-055, MTIS2018-059, MTIS2018-060</td>
</tr>
<tr>
<td>Piomelli</td>
<td>Daniele</td>
<td>MTIS2018-034</td>
</tr>
<tr>
<td>Piretti</td>
<td>Elena</td>
<td>MTIS2018-177</td>
</tr>
<tr>
<td>Prabhakar</td>
<td>Prab</td>
<td>MTIS2018-124, MTIS2018-183</td>
</tr>
<tr>
<td>Prieto</td>
<td>Pablo</td>
<td>MTIS2018-012, MTIS2018-016</td>
</tr>
<tr>
<td>Puledda</td>
<td>Francesca</td>
<td>MTIS2018-153</td>
</tr>
<tr>
<td>Pulicharam</td>
<td>Riya</td>
<td>MTIS2018-006</td>
</tr>
<tr>
<td>Quadros</td>
<td>Maria</td>
<td>MTIS2018-130</td>
</tr>
<tr>
<td>Rainero</td>
<td>Innocenzo</td>
<td>MTIS2018-059, MTIS2018-060</td>
</tr>
<tr>
<td>Ramirez</td>
<td>Alejandro</td>
<td>MTIS2018-041</td>
</tr>
<tr>
<td>Ramji</td>
<td>Saipriya</td>
<td>MTIS2018-183</td>
</tr>
<tr>
<td>Ran</td>
<td>Caroline</td>
<td>MTIS2018-029, MTIS2018-031</td>
</tr>
<tr>
<td>Ranieri</td>
<td>Federico</td>
<td>MTIS2018-054</td>
</tr>
<tr>
<td>Rankin</td>
<td>Christine</td>
<td>MTIS2018-173</td>
</tr>
<tr>
<td>Reed</td>
<td>Michael</td>
<td>MTIS2018-006, MTIS2018-008, MTIS2018-009</td>
</tr>
<tr>
<td>Reid</td>
<td>India</td>
<td>MTIS2018-157</td>
</tr>
<tr>
<td>Ricci</td>
<td>Katia</td>
<td>MTIS2018-061</td>
</tr>
<tr>
<td>Rick</td>
<td>Caroline</td>
<td>MTIS2018-018, MTIS2018-087</td>
</tr>
<tr>
<td>Riederer</td>
<td>Franz</td>
<td>MTIS2018-057, MTIS2018-167</td>
</tr>
<tr>
<td>Ritter</td>
<td>Shannon</td>
<td>MTIS2018-074, MTIS2018-110</td>
</tr>
<tr>
<td>Robbins</td>
<td>Lawrence</td>
<td>MTIS2018-094</td>
</tr>
<tr>
<td>Last Name</td>
<td>First Name</td>
<td>Abstract Programme N°</td>
</tr>
<tr>
<td>---------------</td>
<td>------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Roberto</td>
<td>De Icco</td>
<td>MTIS2018-128</td>
</tr>
<tr>
<td>Robertson</td>
<td>Carrie</td>
<td>MTIS2018-134</td>
</tr>
<tr>
<td>Rodriguez</td>
<td>Eva</td>
<td>MTIS2018-127</td>
</tr>
<tr>
<td>Rosen</td>
<td>Noah</td>
<td>MTIS2018-081</td>
</tr>
<tr>
<td>Rossaro</td>
<td>Maria Paola</td>
<td>MTIS2018-177</td>
</tr>
<tr>
<td>Rubio-Beltrán</td>
<td>Eloisa</td>
<td>MTIS2018-062, MTIS2018-164</td>
</tr>
<tr>
<td>Ruffing</td>
<td>Kelsey</td>
<td>MTIS2018-010</td>
</tr>
<tr>
<td>Ruiz Piñero</td>
<td>Marina</td>
<td>MTIS2018-011, MTIS2018-112</td>
</tr>
<tr>
<td>Saadatnia</td>
<td>Mohammad</td>
<td>MTIS2018-120</td>
</tr>
<tr>
<td>Saengjaroentham</td>
<td>Chonlawan</td>
<td>MTIS2018-036</td>
</tr>
<tr>
<td>Saleeon</td>
<td>Manita</td>
<td>MTIS2018-040</td>
</tr>
<tr>
<td>Sanches</td>
<td>Grazia</td>
<td>MTIS2018-034, MTIS2018-064, MTIS2018-128</td>
</tr>
<tr>
<td>Sánchez del Río</td>
<td>Margarita</td>
<td>MTIS2018-013, MTIS2018-014</td>
</tr>
<tr>
<td>Sandor</td>
<td>Peter</td>
<td>MTIS2018-057, MTIS2018-167</td>
</tr>
<tr>
<td>Sanguanrangsirkul</td>
<td>Sompol</td>
<td>MTIS2018-040</td>
</tr>
<tr>
<td>Santos</td>
<td>Sonia</td>
<td>MTIS2018-002</td>
</tr>
<tr>
<td>Santos Lasaosa</td>
<td>Sonia</td>
<td>MTIS2018-147</td>
</tr>
<tr>
<td>Saper</td>
<td>Joel</td>
<td>MTIS2018-107</td>
</tr>
<tr>
<td>Sarchielli</td>
<td>Paola</td>
<td>MTIS2018-059, MTIS2018-060</td>
</tr>
<tr>
<td>Sartori</td>
<td>Stefano</td>
<td>MTIS2018-177</td>
</tr>
<tr>
<td>Schaeffler</td>
<td>Barbara</td>
<td>MTIS2018-099, MTIS2018-107</td>
</tr>
<tr>
<td>Schankin</td>
<td>Christoph</td>
<td>MTIS2018-153</td>
</tr>
<tr>
<td>Schmidt</td>
<td>Pete</td>
<td>MTIS2018-063</td>
</tr>
<tr>
<td>Schroeder</td>
<td>Celina</td>
<td>MTIS2018-019, MTIS2018-165</td>
</tr>
<tr>
<td>Schulte</td>
<td>Laura</td>
<td>MTIS2018-045</td>
</tr>
<tr>
<td>Scotton</td>
<td>Sangeeta</td>
<td>MTIS2018-024</td>
</tr>
<tr>
<td>Seglah</td>
<td>Oliver</td>
<td>MTIS2018-138</td>
</tr>
<tr>
<td>Selvarajah</td>
<td>Johann</td>
<td>MTIS2018-138</td>
</tr>
<tr>
<td>Selzler</td>
<td>Katherine</td>
<td>MTIS2018-075, MTIS2018-111</td>
</tr>
<tr>
<td>SEQUEIROS</td>
<td>Jorge</td>
<td>MTIS2018-033</td>
</tr>
<tr>
<td>Serraio</td>
<td>Mariano</td>
<td>MTIS2018-052, MTIS2018-053, MTIS2018-056</td>
</tr>
<tr>
<td>Shah</td>
<td>Pushkar</td>
<td>MTIS2018-018</td>
</tr>
<tr>
<td>Sharma</td>
<td>Chandra</td>
<td>MTIS2018-119</td>
</tr>
<tr>
<td>Sharma</td>
<td>Neha</td>
<td>MTIS2018-119</td>
</tr>
<tr>
<td>Sheykizade</td>
<td>Majid</td>
<td>MTIS2018-044</td>
</tr>
<tr>
<td>Sides</td>
<td>Ryan</td>
<td>MTIS2018-111</td>
</tr>
<tr>
<td>Sierra Mencia</td>
<td>Alvaro</td>
<td>MTIS2018-112, MTIS2018-113, MTIS2018-121</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
<th>Abstract Programme N°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silva</td>
<td>Alexandra</td>
<td>MTIS2018-139, MTIS2018-140</td>
</tr>
<tr>
<td>Silva</td>
<td>Bruno</td>
<td>MTIS2018-118</td>
</tr>
<tr>
<td>Silva</td>
<td>Catarina</td>
<td>MTIS2018-086</td>
</tr>
<tr>
<td>Silver</td>
<td>Nicholas</td>
<td>MTIS2018-076</td>
</tr>
<tr>
<td>Sinclair</td>
<td>Alex</td>
<td>MTIS2018-132, MTIS2018-133, MTIS2018-184</td>
</tr>
<tr>
<td>Singhal</td>
<td>Rishi</td>
<td>MTIS2018-186</td>
</tr>
<tr>
<td>Sjöstrand</td>
<td>Christina</td>
<td>MTIS2018-029, MTIS2018-031</td>
</tr>
<tr>
<td>Skjarevski</td>
<td>Vladimir</td>
<td>MTIS2018-097</td>
</tr>
<tr>
<td>Smith</td>
<td>Gabriele</td>
<td>MTIS2018-186</td>
</tr>
<tr>
<td>Smith</td>
<td>Jeff</td>
<td>MTIS2018-099, MTIS2018-107</td>
</tr>
<tr>
<td>Snelman</td>
<td>Josefin</td>
<td>MTIS2018-041, MTIS2018-042</td>
</tr>
<tr>
<td>Sotnikov</td>
<td>Dmytro</td>
<td>MTIS2018-082</td>
</tr>
<tr>
<td>Sousa</td>
<td>Alda</td>
<td>MTIS2018-033</td>
</tr>
<tr>
<td>Srikkathachorn</td>
<td>Anan</td>
<td>MTIS2018-040</td>
</tr>
<tr>
<td>Starling</td>
<td>Amaal</td>
<td>MTIS2018-065, MTIS2018-066</td>
</tr>
<tr>
<td>Stauffer</td>
<td>Virginia</td>
<td>MTIS2018-067, MTIS2018-072, MTIS2018-111</td>
</tr>
<tr>
<td>Steenmeijer</td>
<td>Sylvie</td>
<td>MTIS2018-163</td>
</tr>
<tr>
<td>Steinberg</td>
<td>Anna</td>
<td>MTIS2018-031, MTIS2018-029</td>
</tr>
<tr>
<td>Steiner</td>
<td>Timothy</td>
<td>MTIS2018-004</td>
</tr>
<tr>
<td>Stepanchenko</td>
<td>Kostiantyn</td>
<td>MTIS2018-123</td>
</tr>
<tr>
<td>Stock</td>
<td>David</td>
<td>MTIS2018-170, MTIS2018-171</td>
</tr>
<tr>
<td>Stock</td>
<td>Elyse</td>
<td>MTIS2018-171</td>
</tr>
<tr>
<td>Straube</td>
<td>Andreas</td>
<td>MTIS2018-142</td>
</tr>
<tr>
<td>Stringfellow</td>
<td>Joseph</td>
<td>MTIS2018-170</td>
</tr>
<tr>
<td>Subramanian</td>
<td>Anuradha</td>
<td>MTIS2018-150</td>
</tr>
<tr>
<td>Supronsinchai</td>
<td>Weera</td>
<td>MTIS2018-038</td>
</tr>
<tr>
<td>Sureda</td>
<td>Gilbert</td>
<td>MTIS2018-057</td>
</tr>
<tr>
<td>Szegedi</td>
<td>Armin</td>
<td>MTIS2018-174</td>
</tr>
<tr>
<td>Takeshima</td>
<td>Takao</td>
<td>MTIS2018-046</td>
</tr>
<tr>
<td>Talib</td>
<td>Sophie</td>
<td>MTIS2018-183</td>
</tr>
<tr>
<td>Tanguay</td>
<td>Mario</td>
<td>MTIS2018-170</td>
</tr>
<tr>
<td>Tanveer</td>
<td>Sarah</td>
<td>MTIS2018-001</td>
</tr>
<tr>
<td>Tardioli</td>
<td>Stefano</td>
<td>MTIS2018-056</td>
</tr>
<tr>
<td>Tasdelen</td>
<td>Bahar</td>
<td>MTIS2018-149</td>
</tr>
<tr>
<td>Tinelli</td>
<td>Emanuele</td>
<td>MTIS2018-056</td>
</tr>
</tbody>
</table>
## Author Index

<table>
<thead>
<tr>
<th>Last Name First Name</th>
<th>Abstract Programme N°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tockhorn-Heidenreich Antje</td>
<td>MTIS2018-073</td>
</tr>
<tr>
<td>Tolo Irene</td>
<td>MTIS2018-177</td>
</tr>
<tr>
<td>Tomlinson Claire</td>
<td>MTIS2018-087</td>
</tr>
<tr>
<td>Toni Francesco</td>
<td>MTIS2018-055</td>
</tr>
<tr>
<td>Tonsi Germana</td>
<td>MTIS2018-043</td>
</tr>
<tr>
<td>Torphy Brad</td>
<td>MTIS2018-010</td>
</tr>
<tr>
<td>Trigo López Javier</td>
<td>MTIS2018-121</td>
</tr>
<tr>
<td>Trochet Jérôme</td>
<td>MTIS2018-013, MTIS2018-014</td>
</tr>
<tr>
<td>Trugman Joel</td>
<td>MTIS2018-174</td>
</tr>
<tr>
<td>Tsenddorj Byambasuren</td>
<td>MTIS2018-004</td>
</tr>
<tr>
<td>Tyagi Alok</td>
<td>MTIS2018-173</td>
</tr>
<tr>
<td>Uyar Mehmet</td>
<td>MTIS2018-160</td>
</tr>
<tr>
<td>van Casteren Daphne</td>
<td>MTIS2018-168</td>
</tr>
<tr>
<td>van den Berg Jeffrey</td>
<td>MTIS2018-164</td>
</tr>
<tr>
<td>Vandenbussche Nicolas</td>
<td>MTIS2018-144</td>
</tr>
<tr>
<td>Vandervorst Fenne</td>
<td>MTIS2018-181</td>
</tr>
<tr>
<td>Vanniasegaram Divyen</td>
<td>MTIS2018-155</td>
</tr>
<tr>
<td>Vecchio Eleonora</td>
<td>MTIS2018-061</td>
</tr>
<tr>
<td>Verhagen Iris</td>
<td>MTIS2018-168</td>
</tr>
<tr>
<td>Viana Michele</td>
<td>MTIS2018-034</td>
</tr>
<tr>
<td>Viguera Romero Francisco Javier</td>
<td>MTIS2018-147</td>
</tr>
<tr>
<td>Vila-Pueyo Marta</td>
<td>MTIS2018-039</td>
</tr>
<tr>
<td>Villalón Carlos</td>
<td>MTIS2018-062</td>
</tr>
<tr>
<td>Villanueva Jeanette</td>
<td>MTIS2018-057</td>
</tr>
<tr>
<td>Virre Erik</td>
<td>MTIS2018-156</td>
</tr>
<tr>
<td>Viswanathan Hema</td>
<td>MTIS2018-005, MTIS2018-006</td>
</tr>
<tr>
<td>Waldenlind Elisabet</td>
<td>MTIS2018-029, MTIS2018-031</td>
</tr>
<tr>
<td>Walsh Mark</td>
<td>MTIS2018-186</td>
</tr>
<tr>
<td>Wang Minyan</td>
<td>MTIS2018-017</td>
</tr>
<tr>
<td>Wang Shuu-Jyun</td>
<td>MTIS2018-035</td>
</tr>
<tr>
<td>Wang Yen-Feng</td>
<td>MTIS2018-035</td>
</tr>
<tr>
<td>Warfvinge Karin</td>
<td>MTIS2018-044</td>
</tr>
<tr>
<td>Weatherall Mark</td>
<td>MTIS2018-155</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Last Name First Name</th>
<th>Abstract Programme N°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wei Diana</td>
<td>MTIS2018-047, MTIS2018-166, MTIS2018-187</td>
</tr>
<tr>
<td>Weiser Thomas</td>
<td>MTIS2018-172</td>
</tr>
<tr>
<td>Wermer Marieke</td>
<td>MTIS2018-164</td>
</tr>
<tr>
<td>Westgate Connar</td>
<td>MTIS2018-186</td>
</tr>
<tr>
<td>Watteca Linda</td>
<td>MTIS2018-075</td>
</tr>
<tr>
<td>Wilkins Arnold</td>
<td>MTIS2018-175</td>
</tr>
<tr>
<td>Williams Helen</td>
<td>MTIS2018-124</td>
</tr>
<tr>
<td>Williamson Shelly</td>
<td>MTIS2018-184</td>
</tr>
<tr>
<td>Wilson Maria-Carmen</td>
<td>MTIS2018-090</td>
</tr>
<tr>
<td>Winner Paul</td>
<td>MTIS2018-092, MTIS2018-099</td>
</tr>
<tr>
<td>Wolf Johanna</td>
<td>MTIS2018-046</td>
</tr>
<tr>
<td>Woolley Rebecca</td>
<td>MTIS2018-018</td>
</tr>
<tr>
<td>Xu Cen</td>
<td>MTIS2018-041, MTIS2018-042</td>
</tr>
<tr>
<td>Yang Jyun</td>
<td>MTIS2018-176</td>
</tr>
<tr>
<td>Yang Ronghua</td>
<td>MTIS2018-079, MTIS2018-080</td>
</tr>
<tr>
<td>Yeh Christopher</td>
<td>MTIS2018-020</td>
</tr>
<tr>
<td>Yangou Andreas</td>
<td>MTIS2018-131, MTIS2018-150</td>
</tr>
<tr>
<td>Yogarajah Mahinda</td>
<td>MTIS2018-157</td>
</tr>
<tr>
<td>Yoshikawa Hiroo</td>
<td>MTIS2018-046</td>
</tr>
<tr>
<td>Young William</td>
<td>MTIS2018-093, MTIS2018-095</td>
</tr>
<tr>
<td>Yu Justin</td>
<td>MTIS2018-005, MTIS2018-006</td>
</tr>
<tr>
<td>Zaidi Adil</td>
<td>MTIS2018-027</td>
</tr>
<tr>
<td>Zanaboni Anna Maria</td>
<td>MTIS2018-034, MTIS2018-043</td>
</tr>
<tr>
<td>Zandifar Alireza</td>
<td>MTIS2018-120</td>
</tr>
<tr>
<td>Zelaya Fernando</td>
<td>MTIS2018-051, MTIS2018-153, MTIS2018-166</td>
</tr>
<tr>
<td>Zesiger Peggy Hours</td>
<td>MTIS2018-078</td>
</tr>
<tr>
<td>Zhang Feng</td>
<td>MTIS2018-065, MTIS2018-066, MTIS2018-110</td>
</tr>
<tr>
<td>Zhou Chunmel</td>
<td>MTIS2018-176</td>
</tr>
<tr>
<td>Zick Bart</td>
<td>MTIS2018-164</td>
</tr>
<tr>
<td>Ziegeler Christian</td>
<td>MTIS2018-148</td>
</tr>
</tbody>
</table>
We are absolutely delighted to invite you back to London for the

18th Biennial Migraine Trust International Symposium

10 – 13 September 2020
Hilton London Metropole

www.mtis2020.org
mtis2020@mci-group.com