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ePosters

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Ageing and dementia 1

EPO-001

Epilepsy in Alzheimer's disease associated with Down syndrome. Experience in real-life clinical practice.

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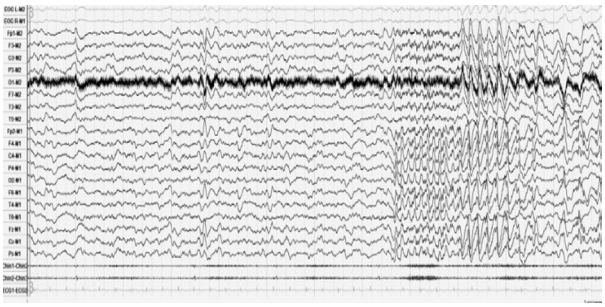
Background and aims: Down syndrome(DS) is a genetically determined form of Alzheimer's Disease(AD). AD is a risk factor for epilepsy, mainly genetic forms of AD, including DS (DSAD). Our objective is to present real-life data on clinical and electrophysiological characterization of DSAD-associated epilepsy.
Methods: A multicentric cross-sectional study in adults with DS (January 2015-January 2023). All participants were assessed by neurologists and neuropsychologists and classified into asymptomatic-aDS-, prodromal-pAD- and dementia AD-dAD- in a consensus meeting based on objective criteria. Personal history of epilepsy for all and for a subgroup routine EEG and/or 21 channel video-polysomnography(v-PSG) were performed.
Results: We recruited 966 adults with DS, 45.9% women, mean age 44.3y(+/-11.6). Of these 36.3% were symptomatic for DSAD. Frequency of untriggered seizures increased in AD continuum (7.6% aDS, 19.4% pAD, 54.7% dAD). The most frequent were bilateral tonic-clonic(BTCS) and the coexistence with myoclonic seizures was especially frequent in dAD (57.1%). The prevalence of both interictal epileptiform (short paroxysms of generalized polyspike-waves) and non-epileptiform abnormalities (slowing of background activity) increased significantly in the AD continuum and in relation to epilepsy. Most frequently used ASM was levetiracetam (61.5%), removed in 1/5 of the cases due to behavioral adverse effects and 48% of them tolerated brivaracetam. Seizures freedom for ≥1year was achieved in 65.9% of DSAD patients, with better response for BTCS.



Slow wave sleep recording (Phase N3) in DSAD patient with critical and interictal epileptiform activity.

Conclusion: The development of symptomatic AD is strongly associated with epileptic seizures in adults with Down syndrome. The good tolerance to ASMs and their good ability to control BTCs supports their use after the first untriggered seizure.
Disclosure: The authors have no relevant financial or non-financial interests to disclose.

EPO-002

Dysautonomia in the differential diagnosis of Dementia with Lewy Bodies and Alzheimer's Disease

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Background and aims: Dementia with Lewy bodies (DLB) is the second most common degenerative dementia in the elderly. Despite their differences in clinical presentation, DLB misdiagnosis as Alzheimer's disease (AD) remains frequent. Autonomic dysfunction is a known supportive clinical feature of DLB but is often overlooked in dementia evaluation. The aim of this work is to evaluate the role of dysautonomia in the differential diagnosis between DLB and AD.
Methods: We selected a convenience sample of 40 patients divided into 2 equal groups, matched for sociodemographic data and neuropsychological scores. Dysautonomia was assessed with Scales for Outcomes in Parkinson's Disease-Autonomic Questionnaire (P-SCOPA-AUT). Core clinical features were assessed with motor score of Unified Parkinson's Disease Rating Scale (mUPDRS), Rapid Eye Movement Sleep Behaviour Disorder Screening Questionnaire (RBD-SQ), Clinician Assessment of Fluctuation (CAF) and hallucination score of Neuropsychiatry Inventory (hNPI).

Results: We enrolled 40 patients, 21 women, with a mean age of 77.9±5.0 years. P-SCOPA-AUT scores correlated with mUPDRS (r=0.632; p<0.001), RBD-SQ (r=0.613; p<0.001), CAF (r=0.49; p=0.001) and hNPI (r=0.397; p=0.012). DLB patients presented higher P-SCOPA-AUT scores compared to AD patients (p<0.001). P-SCOPA-AUT showed a high diagnostic accuracy in differentiating DLB from AD (AUC = 0.845; p<0.001).
Conclusion: Dysautonomia seems to be associated with all four core clinical features of DLB and may help differentiate between DLB and AD. P-SCOPA-AUT may be a reliable tool to define patients for a detailed investigation of DLB symptoms.
Disclosure: Nothing to disclose.

EPO-003

Abstract withdrawn

EPO-004

Using a PET atlas to probe neurotransmitter-disease associations in Mild Cognitive Impairment and Alzheimer's disease

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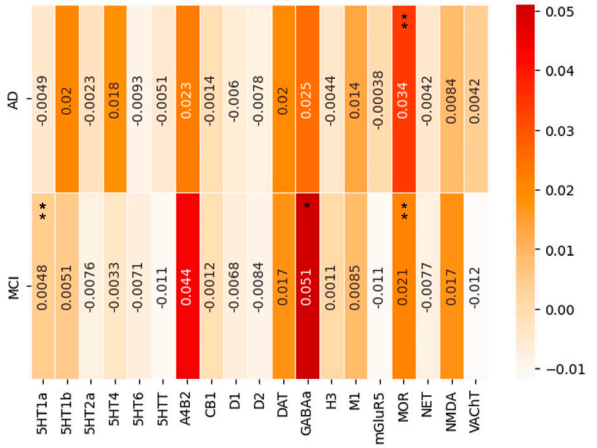
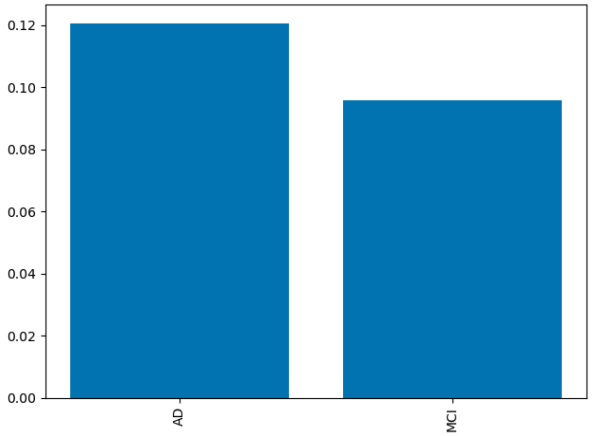
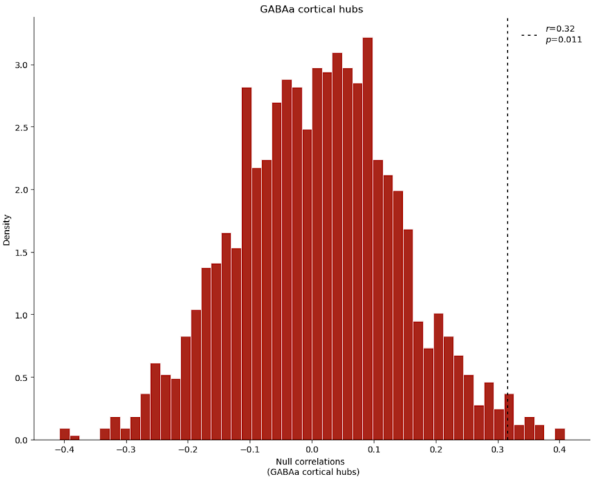
Background and aims: Disease-neurotransmitter associations may identify druggable pathways in Mild cognitive impairment (MCI) and Alzheimer's disease (AD). Current symptomatic treatments target receptor systems. Disease PET can measure neurotransmitter activity but is difficult to scale to multiple systems. Hansen et al (2022) have created an atlas of 19 neurotransmitter systems in healthy subjects. We examined associations between disease cortical atrophy with PET. The MCI-AD biological gradient enables testing of methodological validity.
Methods: We used MRI data from ADNI (457 AD, 713 MCI, 881 controls). Cortical thickness values were derived with FreeSurfer v7.1.1. These were processed in R to generate Cohen's d values, and then with the ENIGMA toolbox. PET maps were averaged from 1200 healthy subjects. Associations were analysed with dominance analysis (contribution to regression model fit). Output was a heatmap of relative dominance (Figure). Spin test generated p-values adjusting for spatial autocorrelation.
Results: For MCI, GABAa (p=0.011) and MOR receptors (p = 0.021) showed significant association, with 5HT1A (p=0.066), approaching significance. In AD, MOR receptor was significant (p=0.045). AD total dominance (0.12) was greater than MCI (0.095). There was progression in receptor dominance values from MCI to AD.



Heat map of dominance analysis. Contribution of each variable can be assessed and compared to other input variables normalised by the total fit. ** means p value <=0.05 * means discussed in abstract for ease of reference.



Total dominance from AD greater than MCI: a validation of biological gradient. Total dominance is average of the relative increase in R^2 when adding a single input variable of interest to a submodel, across all 2p − 1 submodels.



Example output of spin test to determine statistical significance of cortical atrophy – GABAa neurotransmitter receptor/transporter system distribution on PET map. Associations are made to maps created through map rotation.

Conclusion: We did not demonstrate differences in the cholinergic system or the NMDA receptor system. There are multiple possible explanations. The GABAa receptor is perturbed in AD imaging studies. The opioid system has known associations with amyloid beta. Further target research is warranted. The increase in total dominance values from MCI to AD suggests a biological gradient.
Disclosure: No competing interests.

EPO-005

Meta-analysis of cerebrospinal fluid immune markers in frontotemporal dementia patients compared to healthy controls

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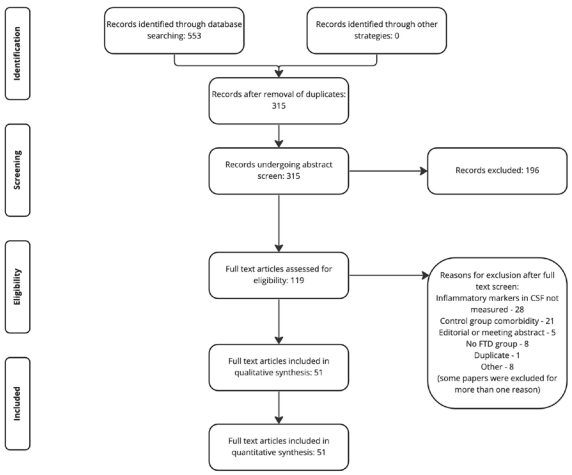
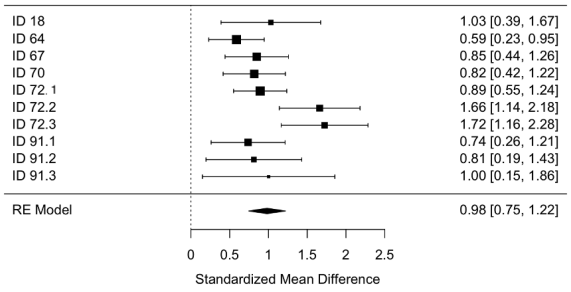
Background and aims: There is pleiotropy between frontotemporal dementia (FTD) and immune related conditions, within the Chromosome 6 HLA region, related to microglial function. PET studies with a marker of activated microglia demonstrate increased binding in frontotemporal regions across FTD pathologic and genetic subtypes. We aimed to identify perturbations in cerebrospinal fluid cytokines and chemokines in FTD versus healthy controls.
Methods: See also Prospero Protocol (ID: 212528). Databases searched were MEDLINE, Web of Science, and EMBASE. For immune markers where two or more papers were identified, a random effects model was used to calculated standardized mean difference (Hedge's g) between FTD and controls. Heterogeneity was assessed by funnel plot, Cochran Q-test and I^2 statistic. Data analysis was in R using Estmeansd and Metafor packages.

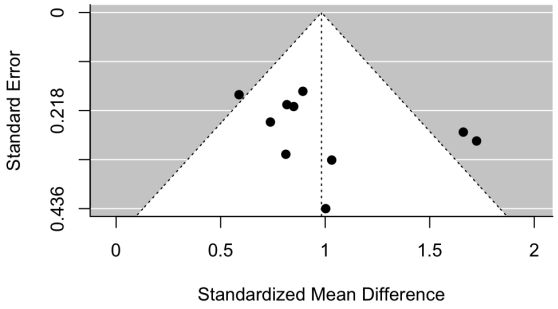


PRISMA flowchart of study selection. Abstract and full text screen and data extraction were carried out by two researchers (SB and YA) independently.

Results: The following immune markers were raised in FTD versus controls: Neurofilament light chain (NfL), standard mean difference (SMD) of 1.46 (1.26-1.66); CHI3L1, SMD of 0.98 (0.75-1.22); CHIT1, SMD of 0.50 (0.26-0.73). There was significant heterogeneity in NfL values (I^2 93%). The following immune markers were decreased in FTD versus controls: progranulin, SMD of -0.59 (-1.06– -0.12). Results from the following immune markers were obtained from two of more papers, without statistically significant differences found: CCL2, IL-6, MCP1, MIP1-alpha, TGF-beta, TNF-alpha.



Example forest plot of studies measuring CHI3L1 (YKL-40)



Example funnel plot of studies measuring CHI3L1 (YKL-40), enabling visual inspection of heterogeneity. I^2 for CHI3L1 was 54%

Conclusion: The perturbations detected in FTD replicate findings from the literature in plasma immune markers, and studies of brain transcriptomics. Findings suggest macrophage and microglial activation. Therapies targeting progranulin are in development. These findings may serve to identify additional targets.
Disclosure: No conflicts of interest to disclose.

EPO-006

Repetitive Transcranial Magnetic Stimulation of Dorsolateral Prefrontal Cortex in MCI

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Background and aims: Repetitive transcranial magnetic stimulation (rTMS), a non-invasive neuromodulation technique rTMS has been shown to modify cognitive performances and brain functional connectivity (FC) in neurological and psychiatric diseases. In this preliminary study, we evaluated the possible effects of rTMS of the bilateral dorsolateral prefrontal cortex (DLPFC) in patients with mild cognitive impairment (MCI).

Methods: 27 MCI patients were randomly assigned to two groups: one received high-frequency (10 Hz) rTMS for four weeks (MCI-TMS, n=11), and the other received sham stimulation (MCI-C, n=16). Cognitive and psycho-behavioral scores, brain FC analyzed by resting state functional MRI (RS-fMRI) networks, and regional atrophy measures, were evaluated at baseline (T0), after five weeks (T1), and six months after rTMS stimulation (T2). Neuropsychological and MRI measures were compared with 15 healthy controls (HC).

Results: MCI-TMS scored higher than MCI-C on semantic fluency and visuo-spatial subtests, in T1. Longitudinal analysis of brain FC in MCI-TMS showed increased FC within the salience network (SLN), in the left superior temporal gyrus and in the left parahippocampal gyrus at T1 and within the left fronto-parietal network (L-FPN), in the supramarginal gyrus, prefrontal cortex, and middle frontal gyrus, at T2. No FC differences were observed in MCI-C. Conversely, regional atrophy measures did not show significant longitudinal changes between the two groups across six months.

Conclusion: Our findings suggest that targeting DLPFC by rTMS application may lead to a long-term increase in FC in MCI patients in RS network associated with executive functions. This process might counteract the progressive cortical dysfunction affecting this domain.

Disclosure: I have no disclosure.

EPO-007

EEG correlates in the three variants of Primary Progressive Aphasia

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Background and aims: The analysis of EEG cortical sources is promising for the investigation of neurodegenerative disorders. The aim of this study is to explore its value in the characterization of the three clinical presentations of primary progressive aphasia (PPA).

Methods: A resting-state 19-channel EEG was obtained in 48 patients diagnosed with PPA (21 nonfluent/agrammatic variant PPA [nfv-PPA], 18 logopenic variant PPA [lv-PPA], 9 semantic variant PPA [sv-PPA]) and in 21 matched healthy controls. Using eLORETA, EEG current source density (CSD) values were estimated at voxel-level and compared among groups of patients and controls.

Results: Patients showed a low-to-moderate cognitive impairment. Lv-PPA cases showed a higher delta density over the left frontal and temporal regions when compared to sv-PPA subjects, and in left precuneus and posterior cingulate when compared to nfv-PPA patients. They also displayed a higher delta density in left frontal, parietal and temporal regions than healthy subjects, and lower alpha1 density in left occipital regions compared with other patient groups. Lv-PPA patients also showed reduced alpha2, beta1 and beta2 density over the left occipital regions when compared to healthy subjects. No significant differences were found in terms of CSD among sv-PPA, nfv-PPA and healthy subjects.

Conclusion: Consistently with our previous studies, findings in PPA patients suggest that Alzheimer's disease (AD), but not fronto-temporal degeneration (FTD), might induce a characteristic disruption of the cortical electrical activity, detectable by EEG. EEG might thus help in the differential diagnosis between AD-related and FTD-related PPA variants.

Disclosure: The authors have nothing to disclose.

EPO-008

A Systematic Review of Pharmacological Treatments for Neuropsychiatric Symptoms in Creutzfeldt Jakob Disease (CJD)

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Background and aims: Creutzfeldt-Jakob Disease (CJD) is a rare but important cause of rapidly progressive dementia with challenging symptomatology and significant public health implications. Whilst neuropsychiatric symptoms form a large burden of care, evidence-based approaches to pharmacological treatments are lacking. We aimed to investigate the evidence base for pharmacological management of neuropsychiatric symptoms in CJD using a rigorous, systematic, and unbiased approach to identify treatment approaches that can be recommended in clinical practice. We also aimed to evaluate administration routes and reported side effects.
Methods: We completed a systematic review of the literature using MeSH terms derived from the Neuropsychiatric Inventory (NPI) and classes of commonly prescribed medications, interrogating Embase, Medline, Pubmed, and Web of Science. There were no language or date restrictions (searches completed 1st September 2022). Inclusion-criteria applied using COVIDENCE software.
Results: 47 studies including over 300 participants were included, detailing medications for the 12 NPI domains. Atypical antipsychotics were reported to have benefit in management of agitation, and cholinesterase inhibitors for hallucinations. Antidepressants were reported to lack efficacy for mood disturbance. Benzodiazepines have utility for multiple symptoms. Quality of evidence is hampered by small study size, variability in dosing and administration routes, and separating side effects from disease progression. Evidence available ranges from class 3 to 4.
Conclusion: Studies dedicated to evaluation of symptomatic control of neuropsychiatric symptoms in CJD are limited and have methodological flaws. However, atypical antipsychotics seem to be of benefit for agitation and cholinesterase inhibitors for hallucinations. There is need for larger prospective longitudinal studies for these challenging symptoms.
Disclosure: Nothing to disclose.

EPO-009

Longitudinal Quantification of Hippocampal Amyloid-Beta Burden from the AppNL-G-F Mouse Model of Alzheimer's Disease

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Background and aims: Amyloid-beta (Aβ) pathology is suggested to precede the onset of clinical Alzheimer's disease symptoms by up to two decades. The humanised AppNL-G-F knock-in model of amyloidopathy has accelerated pathogenesis and is used here to quantify the temporal and spatial characteristics of Aβ accumulation as it first appears in the hippocampus.
Methods: AppNL-G-F and wild-type mice are transfused and sliced for immunohistochemistry analysis, incubated with neuronal marker (NeuN), anti-Aβ antibody (6E10), and DAPI. Fiji was used to quantify Aβ plaques in regions of interest, representative of sub-hippocampal regions (CA1, CA3, DG), in left/right hemispheres, and ventral/dorsal segments.
Results: We found age to be a significant factor on determining area density, with hippocampal deposition observed by 3 months. Bin analysis showed a near-exponential reduction in plaque number with increasing plaque size, increasing with age. Regionally, there was an increase in plaque density in CA3, with non-linear regression analysis indicating area density for CA3 is most strongly correlated with age. Within the CA1 region, the densest plaque formation was in the pyramidal cell layer. The aged 9-month time point suggested a differential pathology across the axial plane and hemispheric lateralisation.
Conclusion: This data provides further evidence for the protracted timeline to which AppNL-G-F mice recapitulate AD neuropathologies including insoluble amyloidosis beginning before 3 months in the hippocampus. It also indicates potentially novel differential sub-regional Aβ accumulation patterns, axial variations, and hemispheric asymmetries, offering mechanistic insights for plaque localisation and differential susceptibility to Aβ. This could aid advancement of Aβ-targeting therapies.
Disclosure: Nothing to disclose.

EPO-010

Orexin-A determination in different biological fluids in neurodegenerative dementias

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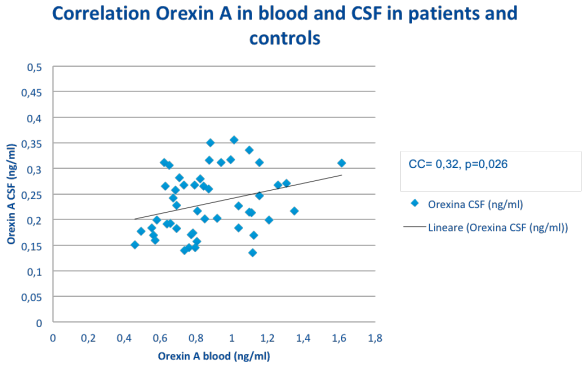
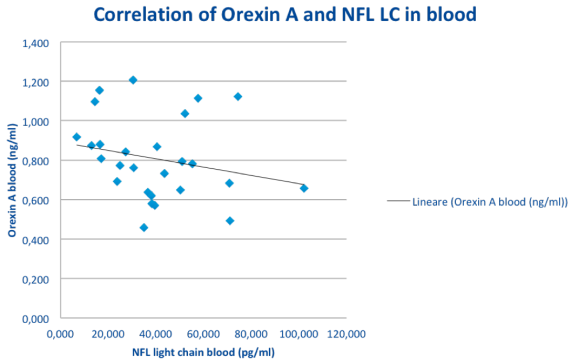
Background and aims: The main aim of this study is to evaluate correlations of Orexin-A (OXA) in different biological fluids, such as blood and CSF, in patients affected by several neurodegenerative dementias (ND). The secondary aim is to evaluate OXA concentration compared to other neurodegeneration associated peptides.

Methods: ND considered were the following: Alzheimer disease and its logopenic variant patients (AD/ADlv), non-logopenic primary progressive aphasia and behavioural variant of Fronto-Temporal Dementia (PPA/bvFTD). A group of patients with no evidence of ND served as controls. Both patients and controls underwent OXA determination in CSF and blood (ELISA). Other neurodegeneration associated peptides measured were: serum neurofilament light chain (NFL, SIMOA), CSF total-tau (t-tau, ELISA), CSF phospho-tau (p-tau, ELISA), CSF Amyloid beta 1-40 (Abeta 1-40) and Amyloid beta 1-42 (Abeta 1-42, ELISA).

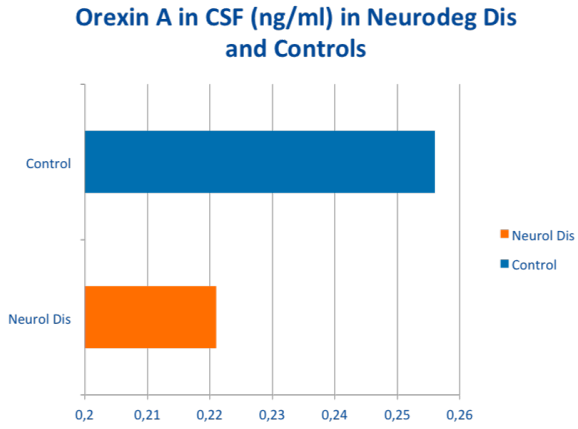
Results: Sample size was the following: 10 AD/ADlv patients (pts), 19 PPA/bvFTD pts, 21 controls. Gender and age did not statistically differ between groups (p=0.6067; p=0.147). We found a positive correlation between OXA levels in CSF and blood in the whole group of subjects (CC= 0,32, p=0,026) with a stronger correlation in controls (CC= 0,74) than in ND (CC= 0,29). Mean OXA concentration in CSF was significantly reduced in ND than controls (p=0,04). We also found an inverse correlation between OXA and NFL in ND group (CC= -0,37, p=0,04).



Correlation of Orexin A in blood and CSF in patients and controls.



Correlation between Orexin A and NFL LC in blood



Orexin A levels in CSF in patients and controls.

Conclusion: Despite the small sample size, our results suggest that OXA level in different biological fluids may represent a biomarker of degeneration in ND, especially when correlated to NFL.

Disclosure: The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work.

EPO-011

Abstract withdrawn

EPO-012

Dementia care in Italy in the era of anti-amyloid agents for AD: an Expert Opinion and practical guideline

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Background and aims: Current evidence from clinical trials testing anti-beta amyloid (Aβ) monoclonal antibodies (mAbs) in patients with early Alzheimer's disease (AD) suggests a likely authorization in Europe in the next years, requiring a huge change of dementia care in all countries.
Methods: A group of prominent AD clinical experts in Italy met to discuss patients' selection for immunotherapies and management strategies. The current diagnostic-therapeutical standards in Italy were taken as the starting-point.
Results: Immunotherapies' prescription must follow a biological diagnosis of AD, defined through the assessment of both amyloidopathy and tauopathy biomarkers. Their high risk/benefit ratio, moreover, needs a highly specialized diagnostic assessment, which should be dispensed by a neurologist. The Expert Panel suggests a reorganization of dementia and cognitive decline centers (CDCD) for the diagnosis of AD in Italy into 3 levels of increasing complexity, with specific tasks and requirements/resources: 1) community centers, with at least 1 neurologist / geriatrician / psychiatrist, with global screening purposes; 2) first-level centers, deputed to biological diagnosis; and 3) second-level centers, requiring the presence of on-site facilities for the biological diagnosis and of at least one neurologist with expertise also in rarer neurodegenerative syndromes. Finally, specific characteristics of a center deputed to prescribe anti-Aβ mAbs were discussed, highlighting the need for clinical and neuroradiological management protocols.
Conclusion: The number of potentially treatable patients in Italy will be tens of thousands. To successfully face such a breakthrough, a quick reorganization of Italian CDCDs will be required, together with the allocation of the necessary resources.
Disclosure: Funding: Unrestricted grants from Biogen.

EPO-013

Differentiation between frontotemporal dementia and primary psychiatric disorder using visual rating scales of atrophy

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Background and aims: Frontotemporal dementia (FTD) and primary psychiatric disorders (PPD) may overlap in terms of clinical presentations with behavioral change and altered executive functioning, however the role of brain atrophy in differentiating the two conditions has not been thoroughly investigated. The aim of the study is to identify the discriminative pattern of brain atrophy between FTD and PPD.
Methods: Among the patients followed in Neurology and Psychiatry departments of Ospedale Maggiore Policlinico of Milan, we retrospectively selected subjects with frontal lobe symptoms with an age at onset between 40 and 75 and with mild severity at the time of MRI. All the subjects underwent extensive neuropsycological testing, neurological and psychiatric examination. Two rater, blind for all the clinical infomations, applied a protocol of 6 visual rating scales of atrophy and 2 of white matter hyperintensities.
Results: A total of 52 subjects were recruited for the study: 15 FTD, 22 PPD and 15 controls. Compared to PPD, FTD cases showed higher degree of atrophy in left orbitofrontal, anterior cingulate and fronto insula, bilateral anterior and medial temporal and parietal areas. ROC curve analysis showed that left orbitofrontal scale was the most useful in the differentiation between FTD and PPD (AUC 0.88) while left anterior temporal better discriminated between FTD and controls (AUC 0.873). No differences between PPD and controls was found.
Conclusion: Visual rating scales can be useful to discriminate FTD and PPD and the left orbitofrontal showed the highest accuracy.
Disclosure: Nothing to disclose.

EPO-014

Differences and Similarities in Empathy Deficit and Its Neural Basis between Logopenic and Amnesic Alzheimer's Disease

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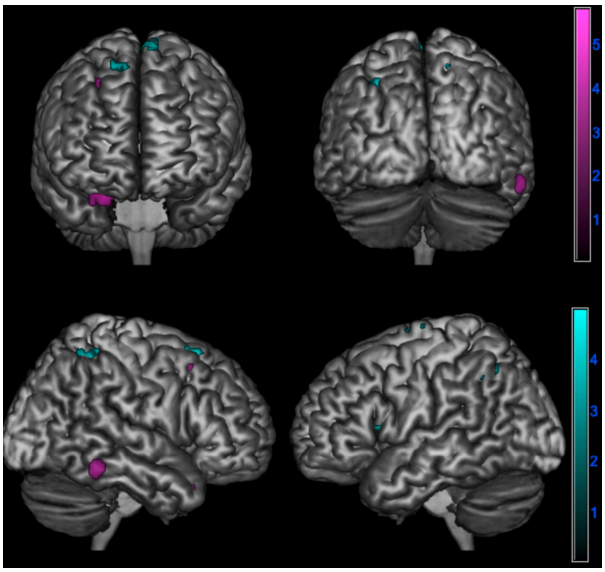
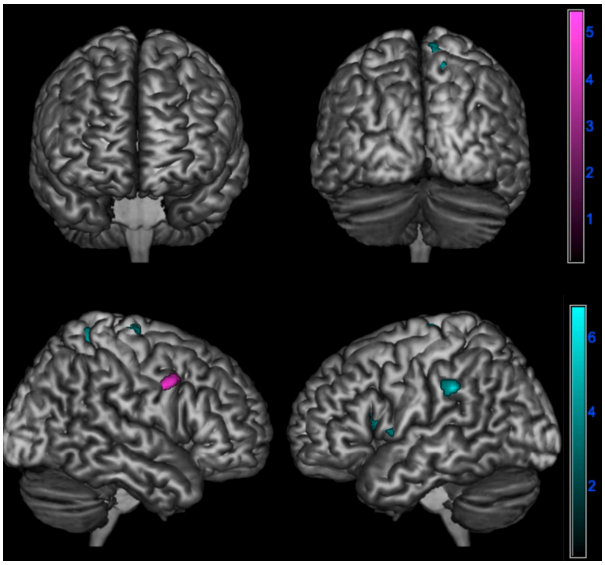
Background and aims: Empathy represents the ability to both feel and comprehend what others feel. The aims of the study were to assess empathy deficit and its neuronal correlates in logopenic primary progressive aphasia (lv-PPA) and amnesic Alzheimer's disease (a-AD).
Methods: Empathy was assessed in eighteen lv-PPA and thirty-eight a-AD patients by Informer-rated Interpersonal Reactivity Index (perspective taking, PT, and fantasy, FT, for cognitive domain; empathic concern, EC, and personal distress, PD, for affective domain) before (T0) and after (T1) cognitive symptoms' onset. Neural correlates of empathy were explored using cerebral FDG-PET.
Results: From T0 to T1, PT decreased, and PD increased in both lv-PPA (PT $z = -3.43$, $p = 0.001$; PD $z = -3.62$, $p < 0.001$) and a-AD (PT $z = -4.57$, $p < 0.001$; PD $z = -5.20$, $p < 0.001$). Delta PT (T0–T1) negatively correlated with metabolic disfunction of the right superior temporal gyrus, fusiform gyrus, and middle frontal gyrus (MFG) in a-AD and of the left inferior parietal lobule (IPL), insula, MFG, and bilateral superior frontal gyrus (SFG) in lv-PPA ($p < 0.005$). Delta PD (T0-T1) positively correlated with metabolic disfunction of the right inferior frontal gyrus in a-AD ($p < 0.001$) and of the left IPL, insula, and bilateral SFG in lv-PPA ($p < 0.005$).



Negative correlation between changes in ΔPT (PT-T0 - PT-T1) and brain metabolism in lv-PPA and a-AD patients at 18F-FDG-PET SPM analysis. Color grading: cyan, lv-PPA; violet, amnesic AD.



Positive correlation between changes in ΔPD (PD-T0 - PD-T1) and brain metabolism in lv-PPA and a-AD patients at 18F-FDG-PET SPM analysis. Color grading: cyan, lv-PPA; violet, amnesic AD.

Conclusion: Lv-PPA and a-AD share the same empathic changes, with damage of cognitive empathy and heightening of personal distress over time. The corresponding metabolic disfunctions' differences might be due to a different vulnerability of specific brain regions in the two AD clinical presentations.
Disclosure: The authors have nothing to disclose.

EPO-015

Novel pathogenic variants in frontotemporal dementia: whole exome sequencing monocentric cohort study.

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Background and aims: Frontotemporal dementia (FTD) etiology has an important genetic component, the three most frequently involved genes (MAPT, GRN and C9orf72) are implicated in about 5-10% of cases. In recent years, other causative genes were discovered opening new ethyologic and therapeutic perspectives. The present study aims to identify gene variations by WES (whole exome sequencing) in a cohort of FTD patients.

Methods: 78 patients (38 female, 40 male) were involved. They received a diagnosis included in FTD spectrum. The most frequent genetic variants known at the time of the diagnosis (MAPT, GRN and C9orf72) resulted negative. Investigation was then expanded using WES focused on unknown variants in already evaluated genes and on sixteen genes responsible for rare forms of familial FTD.

Results: Seven novel variants classified as pathogenic (ACMG guidelines) were detected: six frameshift mutations (two in GRN, two in CHMP2B, one in UBQLN2 and one in FUS) and one splice site variant of TBK1. Other three variants were classified as likely pathogenic: one in FUS and two in UBQLN2. There were also thirty one variants of uncertain significance (VUS), affecting MAPT, C9orf72, SQSTM1, VCP, OPTN, TARDBP, CHCHD10, CCNF, TIA1, DCTN1.

Conclusion: Investigating genes responsible for rare forms could have a significant diagnostic impact in FTD. In this study, 15% of cases are carriers of mutations classified as pathogenic or likely pathogenic. VUS emerged in one third of cases. Finally, WES will allow to search for variants in new candidate genes or for genetic risk factors for FTD.

Disclosure: No disclosures to declare.

	Total variants	Variants of interest	VUS	Pathogenic + likely pathogenic
MAPT	163	3	3	-
GRN	33	7	4	3
C9orf72	33	4	4	-
SQSTM1	25	3	3	-
TBK1	43	3	2	1
CHMP2B	25	2	-	2
VCP	35	1	1	-
OPTN	41	2	2	-
TARDBP	29	1	1	-
CHCHD10	9	1	1	-
UBQLN2	6	3	-	1 + 2
FUS	22	2	-	1 + 1
TUBA4A	14	-	-	-
CCNF	32	2	2	-
TIA1	36	3	3	-
DCTN1	53	5	5	-
Total	**599**	**42**	**31**	**11**

Synopsis of identified variants.

Autonomic nervous system diseases; Peripheral nerve disorders

EPO-016

Clinical and genetic features of congenital myasthenic syndrome in adult patients from Serbia

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Background and aims: Congenital myasthenic syndrome (CMS) is a group of inherited disorders of the neuromuscular junction (NMJ). The study aimed to characterize the clinical and genetic features of Serbian patients with CMS from the largest national neuromuscular center.
Methods: We retrospectively evaluated nine patients diagnosed with CMS at the Neurology Clinic, University Clinical Center of Serbia in the last ten years. Clinical symptoms and signs, electrophysiological findings, and genetic analysis were evaluated.
Results: We found mutations in four genes in our cohort. RAPSN gene mutation was the most prevalent discovered in 4 patients. These patients presented with facial and limb muscle weakness and fatigability and skeletal abnormalities, usually with head drop. Homozygous c.1327delG mutation in CHRNE gene was found in two patients of Roma origin with ptosis, facial and proximal limb muscle weakness and fatigability. One patient had p.Thr265Ser mutation in CHRNB1 gene presenting as a slow channel disease responding flunirine. DOK7 gene mutations were identified in one patient with ptosis, limb muscle weakness, and fatigue. COLQ gene mutations c.1228C>T and c.109del were identified in one patient. She had more proximal limb muscle weakness and fatigability with hyperelastic skin and joints. All patients had a decremental response to repetitive nerve stimulation (RNS).
Conclusion: Our findings contribute to the clinical and genetic spectrum of congenital myasthenic syndrome in Serbia. Neurologists should consider this rare disorder in the differential diagnosis of myasthenia gravis, congenital myopathies, and even limb-girdle muscular dystrophies.
Disclosure: Nothing to disclose.

EPO-017

Multidisciplinary care approach in familial dysautonomia – a single centre experience

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Background and aims: Familial dysautonomia is a rare, multi-systemic genetic syndrome caused by the impaired development of sensory and afferent autonomic nerves. We aimed to describe the phenotype of the FD cohort in the UK, its multidisciplinary approach, and treatment.
Methods: Data regarding autonomic function, ophthalmological, cardiovascular, respiratory, gastrointestinal, renal, behavioural, psychological, and orthopaedic involvement were collected retrospectively, as well as the number of specialists involved, and the medication regimen. All results are presented as average ± SD.
Results: Our cohort included 11 FD patients (5 females), aged 34 ± 11 years old (range 19-50). 2 patients died at 26 and 48 years of age. AFT was available for 8 patients, showing evidence of baroreflex failure. Autonomic crises were daily in 2, frequent in 2, and rare in 5 patients respectively. 2 patients had a diagnosis of epilepsy, 4 had evidence of optic atrophy, 6 had pulmonary involvement (bronchiectasis), 3 were on nocturnal NIV for SDB. Echocardiograms were available and normal in 5 patients. 6 patients had a PEG, 1 had an NGT, 2 had previous fundoplication. Average weight was 48.8 ± 9.64 kg. 1 patient had CKD and underwent transplantation and haemodialysis. Spinal surgery for scoliosis was performed in 4 patients, mostly wheelchair bound. 12 specialists were involved in the care of FD patients, who used an average of 15 ± 9 (range 4-29) medications daily.
Conclusion: Patients with FD require a multidisciplinary management including several specialists and carers. Yearly monitoring is recommended to increase life expectancy and quality of life.
Disclosure: Nothing to disclose.

EPO-018

An induced pluripotent stem cell-based model to study neurodegeneration in RFC1 disease

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Background and aims: Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) is a late-onset ataxia associated with biallelic AAGGG expansions in RFC1. The disease mechanisms of this disorder remain elusive and previous studies on patients' cell lines (i.e., fibroblasts, lymphoblasts) did not show a reduction of RFC1 RNA or protein. Induced pluripotent stem cells (iPSCs) have been proposed as a powerful experimental model for several diseases, as they allow to generate patient-specific cell lines from different sources. As sensory system is constantly involved in RFC1 disease, we generated IPSC-derived sensory neurons to investigate the pathomechanisms of this disorder.
Methods: We used Chamber's modified protocol to differentiate sensory neurons from IPSC lines derived from patients' and controls' fibroblasts. We assessed morphological parameters such as neurite outgrowth and number of branching points. We compared the transcriptome profile of CANVAS and control lines by RNAseq. Finally, we quantified markers of DNA and axonal damage in basal conditions and after pharmacological stress.
Results: We generated mature colonies of sensory neurons derived from IPSCs lines (3 CANVAS and 3 controls). No significant difference in neurite outgrowth and branching points was observed between patients and controls. Transcriptomic analyses revealed unchanged RFC1 transcription and splicing. Quantification of DNA and axonal damage markers is ongoing.
Conclusion: The study confirmed no overt reduction of RFC1 transcript or abnormal splicing in a disease relevant model as IPSCs-sensory neurons. Future studies on long-term cultures of IPSCs-derived neurons will provide a better insight into the mechanisms underlying neurodegeneration in this disorder.
Disclosure: Nothing to disclose.

EPO-019

Will all Axonal forms of Guillain-Barré syndrome have poor prognosis? A serial nerve conduction study can help to answer

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Background and aims: Electrodiagnostic (EDx) studies play a crucial role in subtypes classification of Guillain-Barré syndrome (GBS). It provides diagnostic and prognostic information. However, initial EDx findings may change because of the reversible conduction failure (RCF).
Methods: In a prospective study, we included all patients admitted with a diagnosis of GBS in two general referral hospitals in Tehran in 2021. We performed two serial NCSs in admission time and after 2-4 weeks. The Uncini criteria were applied to the NCSs, and subtype classification and changes on serial NCS were determined.
Results: This study included fifty-four patients. The mean age of the patients was 45.9±20.39 years, and 67 percent of patients were male. The patients were treated with intravenous immunoglobulin (IVIg) or plasma exchange (PLEX). The serial NCSs were performed on 26 patients. In seven patients (26.9%), variant changes were seen. In four of these patients, initial AMAN variants changed to AIDP due to distal RCF, And in three patients, the initial AIDP variant changed to Axonal variants due to Length-dependent conduction failure. Response to treatment in distal RCF was good similar to AIDP variants.
Conclusion: For the dynamic pathophysiology of GBS, only serial studies allow an accurate diagnosis of subtypes. The pathophysiology in axonal GBS differs from functional axonal involvement manifesting as RCF to axonal degeneration appearing as distal CMAP reduction or as a length-dependent conduction failure pattern.
Disclosure: Nothing to disclose.

EPO-020

Abstracts withdrawn

EPO-021

NERVE ULTRASOUND AND MRI FINDINGS IN NODO-PARANODOPATHIES: CORRELATION WITH CLINICAL AND NEUROPHYSIOLOGICAL EXAMINATIONS

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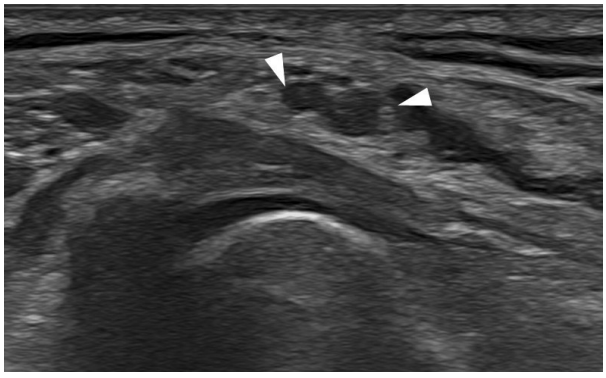
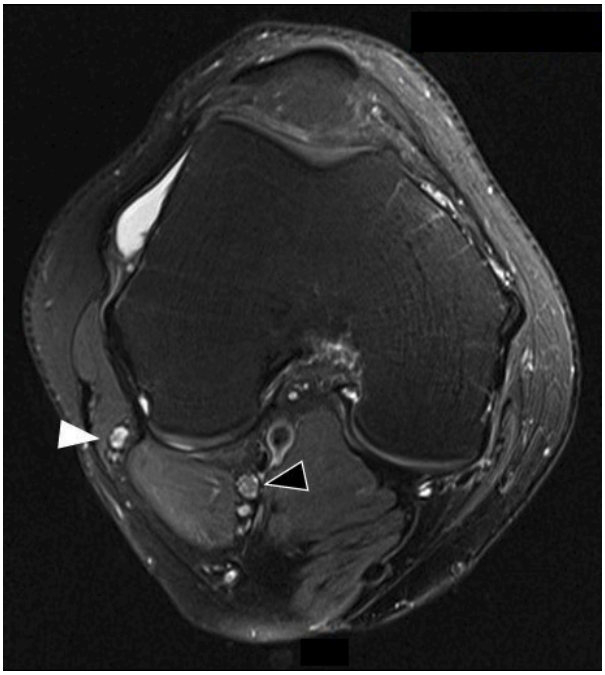
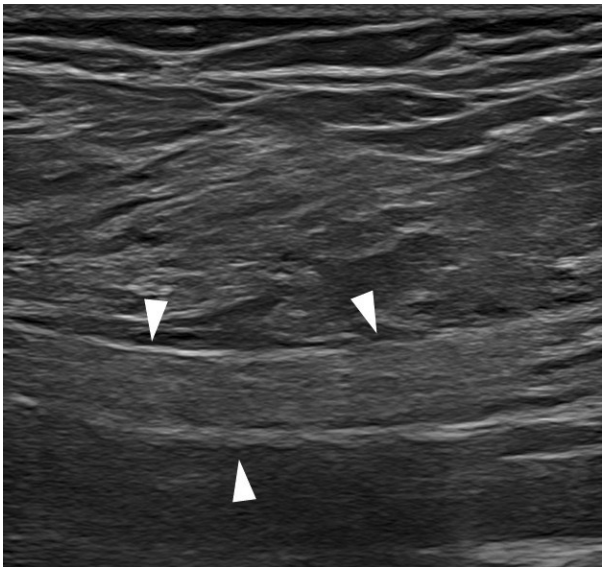
Background and aims: Immune-mediated neuropathies with anti-nodal/paranodal antibodies are rare polyneuropathies that have been increasingly identified within the last decade. Six patients with inflammatory nodo-paranodopathies were evaluated by use of nerve ultrasound and nerve 3T-MRI, comparing imaging with clinical and neurophysiological examinations.
Methods: Five patients tested positive for anti contactin-1 and one positive for anti-NF155 were included in the series. Clinical evaluation, motor/sensory nerve conduction study and nerve ultrasound of the four limbs were performed. The nerve cross sectional area (CSA) and the nerve echotexture were analyzed with qualitative (according to a modified Padua et.al. classification) and quantitative methods (using an automatic software). A 3-Tesla-system MRI was performed in the most affected limb on nerve conduction study.
Results: In the patients with a short duration of disease or worsening of symptoms we observed heterogeneous enlarged hypo and hyperechoic fascicles with different distributions: moderate/diffuse or multifocal. The MRI confirmed ultrasound abnormalities with a particular pattern: only part of the nerve fascicles was hyperintense and swollen with a multifocal distribution. Curiously, despite the presence of an altered sural nerve conduction study in most patients, no sural nerve ultrasound abnormalities were seen in all patients except one.



Nerve ultrasound: Linear probe 18-5 MHz, Short-axis section of common peroneal nerve (arrow head) with enlarged fascicles.



Nerve MRI: T2-weighted sequences with fat signal saturation technique. Common peroneal nerve (white arrow head) hyperintense with some fascicles enlarged Tibial nerve (black arrow head) with some hyperintense fascicles



Nerve ultrasound: Linear probe 18-5 MHz, Long-axis section of hyperechoic sciatic nerve (arrowheads) with loss of fascicular structure.

Conclusion: These data suggest that nerve ultrasound and MRI abnormalities could reflect an active phase of disease and can be used for diagnosis/evaluation/prognosis even in patients affected by nodo-paranodopathies. A larger sample of patients is needed to provide information about the ultrasound pattern in nodo-paranodopathies and the absence of sural nerve ultrasound alterations.
Disclosure: Nothing to disclose.

EPO-022

Polyneuropathy: the role of peripheral nerve biopsy in the clinical decision

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Background and aims: Peripheral nerve biopsy (PNB) is a complementary mean of diagnosis used in the investigation of patients with peripheral neuropathy of undetermined aetiology. The increasing use of non-invasive/minimally invasive complementary means, such as neurophysiological studies and imaging studies by ultrasound and MRI, may impose new challenges to its diagnostic relevance. This study aims to evaluate the results of PNB in the diagnostic definition and therapeutic decision in patients with peripheral neuropathy of undetermined etiology.
Methods: Retrospective study including adult patients who underwent a peripheral nerve biopsy at the Centro Hospitalar e Universitário de Coimbra (CHUC) since 2010. Clinical, laboratory, neurophysiological and histopathological information was obtained. The presence of neurophysiological criteria of polyneuropathy, associated with clinical and laboratory manifestations concordant with a diagnosis of peripheral neuropathy, was defined as a probable etiological diagnosis.
Results: From a total of 46 peripheral nerve biopsies, we obtained complete information from 40 patients (60% female). The mean age at the time of the biopsy was 56.9 years. In 26.7% of patients, a probable etiological diagnosis was obtained with the information provided by PNB (p=0.435).
Conclusion: PNB continues to be an important complementary diagnostic tool in the etiological clarification of peripheral neuropathy, and strict criteria should be followed in patient selection to optimize its results.
Disclosure: Nothing to disclose.

EPO-023

Case series of pyridoxine-induced neuropathy

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Background and aims: Vitamin B6 in the form of pyridoxine is commonly used by the general population. The use of pyridoxine-containing supplements had gained lots of attention over the past years as they have been related to the development of peripheral neuropathy. In the light of this, the number of reported cases of adverse health effects due to the use of vitamin B6 have increased.
Methods: We described eight cases of peripheral neuropathy associated with pyridoxine supplements.
Results: Nerve conduction study revealed axonal sensorimotor polyneuropathy in 6 patients and demyelinating sensorimotor polyneuropathy in 2 patients. Extensive diagnostic work-up was without any etiological clue. Measurement of blood levels of vitamin B6 (normal range; 15-73 nmol/L) showed increased levels (mean; 397.3 nmol/L, range 163.8 – 623.5). We advised the patients to immediately stop vitamin B6 administration.
Conclusion: Based on the current limited data, it can be concluded that very low doses of daily pyridoxine are required to prevent peripheral neuropathy. There is inadequate evidence to support routine pyridoxine supplementation in patients with disorders of peripheral nervous system. Supplementation with pyridoxine at doses greater than 50 mg/d for extended duration may be harmful and should be discouraged.
Disclosure: Nothing to disclose.

EPO-024

Changes of neurophysiological and nerve ultrasound characteristics in CIDP over time: follow-up period more than 5 years

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Background and aims: Diagnosis of Chronic inflammatory demyelinating polyneuropathy (CIDP) is made by demonstrating peripheral nerve demyelination, commonly by electrophysiological testing. It remains unclear whether the neurophysiological and ultrasound signs characteristic of demyelination in the long-term clinical remission and absence of motor deficits. We evaluate changes of neurophysiological and nerve ultrasound characteristics in CIDP over time: follow-up period ≥ 5 years.
Methods: We included 45 adult patients that fulfilled EAN/PNS diagnostic criteria for CIDP 2021 at onset and have follow-up period ≥ 5 years. Disease activity status (CDAS, Gorson 2010), electrophysiological examination (4 motor and 4 sensory nerves), needle EMG of tibialis anterior muscle and nerve ultrasound (UPPS, Grimm 2015) were performed.
Results: Median follow-up period was 10 [7; 14], average age 47.6±13.6 years. There were 33 (73,3%) typical CIDP patients and 12 (26,7%) multifocal CIDP. 34% had CDAS 1 (≥5 years off treatment), 13,3% - CDAS 5 (unstable active disease). 82,2% of patients had neurophysiological signs of demyelination, fulfilled criteria of EAN/PNS 2021 and 50% had nerve enlargement in proximal ulnar and median nerves segments and brachial plexus. 42% had electrophysiological signs of axonal degeneration.
Conclusion: In the long-term follow-up of CIDP (≥5 years) in spite of treatment neurophysiological and ultrasound signs of peripheral nerve damage are persistent and do not completely regress, there is clinical and neurophysiological dissociation.
Disclosure: The authors have nothing to disclose.

EPO-025

Axonal Guillain-Barre Syndrome variants: analysis of clinical features and prognosis of patients in a tertiary hospital

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Background and aims: Axonal variants of Guillain-Barré syndrome (GBS) mainly include acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN). Our aim was to describe the epidemiological, clinical presentation and outcomes of axonal variant of Guillain-Barré syndrome in a tertiary university hospital in Córdoba, Spain.
Methods: An observational, retrospective and descriptive study was performed. We obtained 81 patients with the diagnosis of GBS from the Neurology department between 2015 and 2022. Finally, we included 21 cases of axonal variant of GBS: 8 cases of AMAN and 13 of AMSAN. Clinical presentation, electrophysiological pattern, cerebrospinal fluid (CSF) findings, as well as final clinical outcomes were collected using the modified Hughes Functional Grading Scale.
Results: In our series, 12 patients (57.1%) were male. Mean age at presentation was 62.9 years (range 39-80). Most cases (61.9%) debuted in winter and spring. 15 patients (71.4%) had gastroenteritis before onset. 16 patients (76%) had an abnormal CSF biochemical pattern (hyperproteinorrachia in the first 24h). 6 patients suffered from respiratory failure (RF) and 5 of them were admitted to the Intensive Care Unit. All of them were treated with IVIG and 8 required plasmapheresis in addition. The mean number of days of hospitalization was 31.4. 66.6% were confined to a wheelchair at discharge and all of them had residual impairment after 6 months (85.7%: Hughes 2-3).
Conclusion: We observed clinical features and outcomes similar to those described in the current literature, including RF and residual disability.
Disclosure: Nothing to disclose.

EPO-026

Phenotypical and Genotypical Variability of Patients with Charcot-Marie-Tooth Disease at Charité Berlin, Germany

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Background and aims: Charcot-Marie-Tooth disease (CMT) is the most frequent hereditary peripheral neuropathy. Symptoms often start in early childhood and progress over time, leading to disability and loss of self-sufficiency. There are over 100 known mutations known but no causal therapy available up to now. The characterization of phenotypical variability and natural disease history is essential for present and future therapy development and clinical trial preparation.
Methods: At Charité Berlin, we used an extensive battery of clinical scores, laboratory examinations, and electrophysiological examinations to characterize patients with CMT during 2022. Furthermore, we established a biobank for skin biopsies as well as fibroblast cultures for future genomic, proteomic, and morphological analyses.
Results: We collected over 40 patients with clinical diagnosis of CMT, out of which about 70% received a genetic diagnosis. Variants of 11 causal genes were identified, including 6 variants of unknown significance. The average age of onset was 19 years with a range from 0 to 55 years, and clinical severity as well as phenotypes varied greatly even within single mutations.
Conclusion: CMT is a genetically and phenotypically diverse disorder. There is an urgent need to better understand this variability in order to predict disease course, identify possible modifiers of disease severity, and prepare for clinical studies.
Disclosure: This project was supported by financial reimbursement/travel support by Alnylam Pharmaceuticals Inc, research funding by Alnylam Pharmaceuticals Inc., and Pfizer Pharmaceuticals, and research funding by Deutsche Gesellschaft für Muskelkranke (DGM)

Cerebrovascular diseases 1

EPO-027

The relationship between vascular risk factors and white matter hyperintensities in patients with lacunar stroke.

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Background and aims: The purpose of the study was to determine association between the severity of WMH and vascular risk factors in lacunar ischemic stroke.
Methods: 62 patients with lacunar IS were enrolled in this study. Brain MRI and CT scans were performed within 7 days after stroke onset. Periventricular WMH(P-WMH) and deep WMH(D-WMH) were assessed independently by Fazekas scale. Patients were divided into two groups according to Fazekas scores: Group I participants with a P-WMH/ D-WMH Fazekas score of 0–1 and Group II patients with a P-WMH/ D-WMH Fazekas score of 2 and 3.
Results: The severe P-WMH group had higher age (p=0.028) and higher proportion of hypertension (p=0.038) compared to mild P-WMH group, while percent of smoking was higher in P-WMH group. The results of binary logistic regression analyses(BLRA) showed that there were a significant association between higher age (OR=1.048, 95% CI, 1.032-1.086, p=0.001) and the recurrent stroke (OR=4.892, 95%CI, 2.456-9.216 p<0.001) with severe degree of P-WMH after adjusting for sex and vascular risk factors. The severe D-WMH group also had higher age (p<0.001), and higher proportion of hyperlipidemia (p=0.008) and stroke (p<0.001) in comparison with mild D-WMH group. BLRA demonstrated that there were a significant relationship between higher age and the recurrent stroke with the severity of D-WMH after adjusting for sex and vascular risk factors.
Conclusion: The results of our study showed that there are relationship between age and recurrent stroke with the severity of P-WMH and D-WMH in patients with lacunar IS.
Disclosure: Nothing to disclose.

EPO-028

Outcomes of intravenous (IV) thrombolysis in acute ischemic stroke in Albania

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Background and aims: Stroke is a leading cause of disability worldwide. IV thrombolysis represents a mainstay therapy that can improve neurological deficits in patients with acute ischemic stroke. However, there are some factors that influence the outcome in those who receive alteplase.
Methods: We included data of the patients hospitalized in the Neurovascular Service of "Mother Teresa" University Hospital during the year 2022, who met the criteria for thrombolytic treatment. Demographic data, stroke risk factors, time window of alteplase administration, National Institutes of Health Stroke Scale (NIHSS) before thrombolysis and in the discharge from hospital were analyzed.
Results: IV alteplase was administered in 87 patients aged from 46 to 95 years. 35 were male sex with a mean age of 69.6 and 52 were female with a mean age of 71.12. 90.8% of patients had hypertension, 19.5% diabetes mellitus, 30% hypercholesterolemia and 40.2% had atrial fibrillation, of which 6.9% were under treatment with anticoagulants. 19 patients (21.8%) had intracranial hemorrhage. 37 patients had good outcome, defined as Modified Rankin Scale (mRS) score at discharge of 0-2 and NIHSS of 0-5 points. There was no significant difference in the outcome between male and female sex (p<0.594) in terms of mRS. We found a statistically significant correlation between NIHSS before treatment and outcome (p<0.001), hemorrhagic transformation and advanced age and poor outcome [mRS score of 5-6 points] (p<0.001).
Conclusion: The best predictor of outcome after thrombolysis is the NIHSS before treatment. Hemorrhagic transformation and advanced age are predictors for poor outcome.
Disclosure: Nothing to disclose.

EPO-029

The opacification time of ascending aorta during CT angiography as a predictor of heart failure.

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Background and aims: Heart failure (HF) represent the second most frequent cause of cardioembolic (CE) stroke. Brain CT angiography is routinely performed in the suspect of a large vessel occlusion. Placing a region of interest (ROI) at the level of the ascending aorta, the opacification of the vessel is monitored until a threshold value of Hounsfield Unit (HU) is reached, starting images acquisition. The opacification time of the ascending aorta may be affected by heart ejection fraction (EF). We evaluated the existence of a correlation between these parameters and tried to identify a cut-off value able to predict a diagnosis of heart failure.
Methods: We screened all patients discharged from the Fondazione Policlinico Gemelli in Rome between December 2019 and June 2021, with a CT angiography of cerebral vessel and an echocardiographic evaluation of the

EF. The opacification time of the ascending aorta was calculated as the time needed to reach a threshold of 40 Hounsfield Unit (T40HU) in the ROI.
Results: We enrolled 366 patients and found an inverse correlation between the EF and the T40HU, indicating longer time for aorta opalization as the EF decreases. Through a receiver operating characteristic (ROC) curve analysis we identified a cut-off value of 16,8 seconds for the T40HU as able to predict with good sensitivity (81%) and specificity (61%) a diagnosis of heart failure with EF <40%.
Conclusion: The T40HU is a reliable indicator of HF with reduced EF, allowing to esteem heart function already in the emergency department even in the setting of an acute stroke.
Disclosure: The authors declare no conflict of interest.

EPO-030

Early plasma YKL40 level predicts 3-month functional outcome after ischemic stroke treated with endovascular therapy

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Background and aims: More than 40% or large vessel occlusion ischemic stroke patients remain disabled at 3 months despite successful reperfusion therapies including intravenous thrombolysis and endovascular therapy (EVT). This neurological disability is mainly due to sensori-motor sequelae and post-stroke cognitive impairment (PSCI). Glycoprotein YKL40 is a biomarker of microglial activation. It is elevated in plasma in numerous neurodegenerative disorders but also in acute ischemic stroke. We hypothesized that acute microglial inflammation plays a key role in PSCI and that plasma levels of YKL40 could be a predictive biomarker of future cognitive and functional outcomes.
Methods: Monocentric prospective study included patients treated with EVT, for whom 3 blood samples (before, within 1h, 24h post-EVT) were drawn to measure plasma YKL40 concentration as a marker of microglial activation. Excellent outcome was defined as a modified Rankin scale (mRS) 0 or 1 at 3 months.
Results: We included 120 patients between 2016 and 2020. Median NIHSS was 17 and median ASPECT score was 7. Repercussion was achieved at mean delay of 5h44. After 3 months, median mRS was 3 and 25% of patients with pre-stroke mRS< 2 had excellent outcome. Excellent clinical outcome was significantly associated with lower plasma YKL40 levels (p= 0,001) after adjustment on age, NIHSS and delay since onset.
Conclusion: Plasma YKL40 levels is a candidate predictor of functional outcome at 3 months in ischemic stroke treated by EVT. This novel biomarker of stroke could allow optimizing rehabilitation strategies and give new insight on pathophysiology of PSCI.
Disclosure: INSERM U1144 INSERM U1148

EPO-031

Glycemic variability after mechanical thrombectomy for acute ischemic stroke is associated with increased mortality

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Background and aims: Acute ischemic stroke (AIS) is a leading cause of death and disability. Mechanical thrombectomy (MT) is standard of care for patients with large vessel occlusion. Even with effective recanalization morbidity remains high. Therefore, it is important to recognize modifiable risk factors for adverse outcomes after MT. Glycemic variability (GV) has been related to poor outcomes in critically ill patients, but conflicting data exist on whether it affects prognosis after MT for AIS. Thus, we aimed to clarify how GV after MT impacts functional outcome and survival of AIS patients.
Methods: This was a single-center retrospective study. We included AIS patients who received MT for anterior circulation vessel occlusion between January 2015 and December 2019 at our stroke center. Demographic, clinical and paraclinical data were recorded. We used standard deviation (SD) of the mean blood glucose for the first 24 hours post MT as a measure of GV. Outcomes were modified Rankin Scale (mRS) score and mortality at 3 months follow-up. Univariate and multivariate analyses were performed.
Results: We included 657 patients (43.5% males; median age 77 years). In univariate analysis, patients with unfavorable functional outcome (mRS score 3-6; 42.5%) and patients that died (14.8%) had significantly higher SD. When adjusting for confounders, SD remained statistically significant for mortality (adjusted OR for unfavorable functional outcome: 1.007 [95% CI 0.990-1.025]; adjusted OR for mortality: 1.020 [95% CI 1.001-1.040]).
Conclusion: Our results suggest GV as a relevant and targetable risk factor for mortality in AIS stroke patients treated with MT.
Disclosure: The authors have nothing to declare.

EPO-032

Juvenile arterial ischemic stroke due to focal cerebral arteriopathy: a case-based approach

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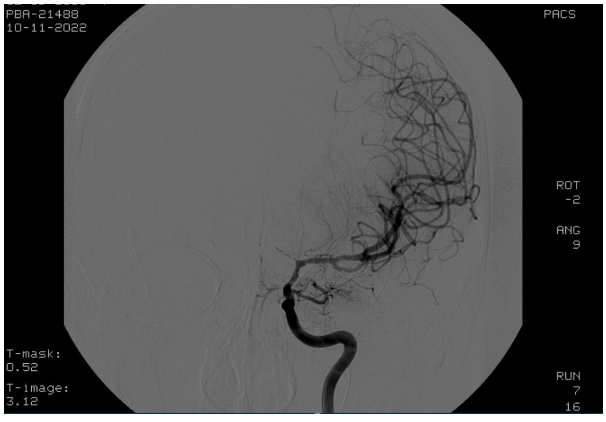
Background and aims: Focal cerebral arteriopathy (FCA) is one of the most common causes and strongest risk factor of recurrence of childhood arterial ischemic stroke (AIS), involving large vessels of the anterior cerebral circulation.
Methods: Diagnostic work-up included brain MRI and DSA, ECG monitoring, transesophageal echocardiography for PFO, TCCD, CSF and serological evaluation for infections, autoimmunity, coagulopathy.
Results: A 17-year-old woman with unremarkable medical history except for obesity was admitted to emergency department for aphasia and right hemiplegia due to left M2 dominant branch occlusion(NIHSS 21). She was treated with intravenous rt-PA only, with early neurological improvement(NIHSS 1). TCCD highlighted moderate stenosis of the proximal segment of left carotid syphon, while cerebral DSA showed banded appearance of left M1 segment suggestive for FCA (FCA Severity Score –FCASS 6). CSF analysis excluded infective and autoimmune vasculitis. Other tests were unremarkable. The patient received aspirin 100 mg daily and high dose of intravenous methylprednisolone(ivMP), followed by tapering at discharge. Three weeks later, the patient experienced right leg paresis due to left A1 occlusion. TCCD revealed early A1 recanalization but progressing M1 stenosis involving proximal M2 segment. IvMP and DAPT for 21 days was administrated with neurological improvement(NIHSS 1). Monthly follow-up demonstrated TCCD stability.



Cerebral DSA showed banded appearance of left M1 segment suggestive for focal cerebral arteriopathy.

Conclusion: FCA ranges from stabilization to improvement or resolution although arteriopathy caused a 5-fold increase of recurrence compared to idiopathic AIS. Predictive markers of recurrence and outcome, such as FCASS, are on-going validation. Use of steroid with or without antiviral therapy (hypothetical post-infectious pathophysiology) are commonly used although lack of interventional trial results.
Disclosure: All the authors have no disclosure.

EPO-033

The presence of pre-diabetes predicts the early neurologic deterioration in acute ischemic stroke using IV thrombolysis

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Background and aims: Pre-diabetes is an intermediate state between normal glucose metabolism and diabetes. However, there has been debated whether pre-diabetes might influence on short and long-term outcomes after AIS. In this study, we investigated the association between the presence of pre-diabetes and the early neurologic deterioration (END) in AIS using IV thrombolysis.
Methods: We recruited patients with AIS using IV thrombolysis prospectively registered CRCS-K database in Dong-A university stroke center from 2016 into 2020. According to their HbA1C levels, patients were divided into three groups: normal, pre-diabetes, and diabetes. We assessed the occurrence of END after using IV thrombolysis in AIS.
Results: Total 661 AIS patients using IV thrombolysis enrolled in this study. Among those subjects, pre-diabetes was diagnosed in 197 patients (29.8%) and diabetes in 210 patients (31.8%). In multiple logistic regression analysis, pre-diabetes was an independent predictor of END (OR, 1.79; 95% CI, 1.01 to 3.22; $p<0.05$) and of in-hospital death (OR, 3.31; 95% CI, 1.12 to 9.80; $p=0.03$).
Conclusion: Pre-diabetes influences on the occurrence of END in AIS with IV thrombolysis.
Disclosure: Nothing to disclose.

EPO-034

Outcome Determinants in Patients with Acute Mild Ischemic Stroke

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Background and aims: This study was conducted to clarify the risk factors of unfavorable early outcomes (UEO) in acute mild ischemic stroke (AMIS).
Methods: Patients with AMIS, defined as a National Institute of Health Stroke Score (NIHSS) <4 and admission within 48 hours after symptoms onset, were prospectively registered. A favorable outcome was defined as a modified Rankin Scale (mRS) or 1 or lower. Risk factors of UEO were analyzed.

Results: Among the 832 patients with AMIS, 174 patients had unfavorable outcomes (modified Rankin Score 2-6) at 3 months. Older age and higher initial NIHSS score are more common among those with poor outcome. On the contrary, antithrombotics given within 48 hours after stroke onset, and dual antiplatelet use among patients indicated, are associated with better outcome.

	Total (n=832)	Initial MRS 0-1 (n=610)	Initial MRS >1 (n=222)	P value
Age (years)	67.0 (57-76)	65.0 (56-74)	72.0 (62-82)	<0.001
Male, n (%)	572 (68.8%)	422 (69.2%)	150 (67.6%)	0.719
Body mass index (kg/m²)(n=787)	25.0 (22.8-27.5)	24.9 (22.9-27.4)	25.2 (22.7-27.6)	0.852
Hypertension, n (%)	612 (73.6%)	433 (71.0%)	179 (80.6%)	0.007
Diabetes, n (%)	341 (41.0%)	238 (39.0%)	103 (46.4%)	0.067
Atrial fibrillation, n (%)	131 (15.7%)	86 (14.1%)	45 (20.3%)	0.040
Heart failure, n (%)	29 (3.5%)	22 (3.6%)	7 (3.2%)	0.919
Ischemic heart disease, n (%)	83 (10.0%)	54 (8.9%)	29 (13.1%)	0.097
Total cholesterol, mg/dL (n=809)	174.0 (148-205)	174.0 (147-204)	176.0 (149-208)	0.601
Triglyceride, mg/dL (n=807)	111.0 (82-165)	112.0 (83-165)	105.0 (80-164)	0.264
HDL cholesterol, mg/dL (n=807)	44.0 (37-52)	44.0 (37-52)	43.0 (35.8-52)	0.163
LDL cholesterol, mg/dL (n=827)	108.0 (85-134)	106.0 (85-133)	111.0 (85-136)	0.431
Stroke subtype (TOAST), n (%) (n=693)				0.119
Large-artery atherosclerotic type	142 (20.5%)	87 (18.0%)	55 (26.1%)	
Cardioembolic type	190 (27.4%)	139 (28.8%)	51 (24.2%)	
Lacunar type	152 (21.9%)	103 (21.4%)	49 (23.2%)	
Undetermined type	14 (2.0%)	10 (2.1%)	4 (1.9%)	
Other determined type	195 (28.1%)	143 (29.7%)	52 (24.6%)	
Antithrombotics within 48 hours after stroke onset, n (%)	802 (96.4%)	594 (97.4%)	208 (93.7%)	0.021
Antithrombotics at discharge, n (%)	811 (97.5%)	601 (98.5%)	210 (94.6%)	0.003
No antithrombotic, n (%)	21 (2.5%)	9 (1.5%)	12 (5.4%)	0.003
Monotherapy, n (%)	361 (43.4%)	254 (41.6%)	107 (48.2%)	0.108
Dual antiplatelets, n (%)	402 (48.3%)	310 (50.8%)	92 (41.4%)	0.021
Anticoagulant, n (%)	94 (11.3%)	66 (10.8%)	28 (12.6%)	0.549
Statin use, n (%)	683 (82.1%)	504 (82.6%)	179 (80.6%)	0.575
Initial NIHSS score	2.0 (1-2)	1.0 (0-2)	2.0 (1.8-3)	<0.001

Data are expressed as median (interquartile range) for continuous variables and frequency (%) for categorical variables.
HDL, high density lipoprotein; LDL, low density lipoprotein; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institute of Health Stroke Score.

Table 1. Characteristics of patients with acute minor ischemic stroke

	Favorable early outcome (n=678)	Unfavorable early outcome (n=154)	P value
Age (years)	65.0 (56-74)	74.0 (63.8-84)	<0.001
Male, n (%)	474 (69.9%)	98 (63.6%)	0.156
Body mass index (kg/m²) (n=787)	25.0 (23-27.5)	25.0 (22.3-27.5)	0.241
Hypertension, n (%)	487 (71.8%)	125 (81.2%)	0.023
Diabetes, n (%)	272 (40.1%)	69 (44.8%)	0.329
Atrial fibrillation, n (%)	98 (14.5%)	33 (21.4%)	0.043
Heart failure, n (%)	21 (3.1%)	8 (5.2%)	0.299
Ischemic heart disease, n (%)	62 (9.1%)	21 (13.6%)	0.126
Total cholesterol, mg/dL (n=809)	177.0 (149.5-207)	169.5 (144.3-198)	0.069
Triglyceride, mg/dL (n=807)	113.0 (83-169)	100.0 (75.8-142)	0.012
HDL cholesterol, mg/dL (n=807)	45 (37-52)	44.0 (35-53)	0.577
LDL cholesterol, mg/dL (n=827)	108.0 (85-135)	107.5 (83-129)	0.259
Stroke subtype (TOAST), n (%) (n=693)			0.239
Large-artery atherosclerotic type	107 (19.4%)	35 (24.8%)	
Cardioembolic type	158 (28.6%)	32 (22.7%)	
Lacunar type	124 (22.5%)	28 (19.9%)	
Undetermined type	9 (1.6%)	5 (3.5%)	
Other determined type	154 (27.9%)	41 (29.1%)	
Antithrombotics within 48 hours after stroke onset, n (%)	662 (97.6%)	140 (90.9%)	<0.001
Antithrombotics at discharge, n (%)[f]	666 (98.2%)	145 (94.2%)	0.008
No antithrombotic, n (%)[f]	12 (1.8%)	9 (5.8%)	0.008
Monotherapy, n (%)	281 (41.4%)	80 (51.9%)	0.022
Dual antiplatelets, n (%)	346 (51.0%)	56 (36.4%)	0.001
Anticoagulant, n (%)	71 (10.5%)	23 (14.9%)	0.150
Statin use, n (%)	568 (83.8%)	115 (74.7%)	0.011
Initial NIHSS score	1.0 (0-2)	2.0 (1-3)	<0.001

Data are expressed as median (interquartile range) for continuous variables and frequency (%) for categorical variables.
Chi-Square test. [f]Fisher's Exact test.
HDL, high density lipoprotein; LDL, low density lipoprotein; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institute of Health Stroke Score.

Table 2. MRS at 3rd month

	Simple model			Multiple model		
	OR	95% CI	p value	OR	95% CI	p value
Age (years)	1.05	(1.03-1.06)	<0.001	1.04	(1.03-1.06)	<0.001
Male	0.75	(0.52-1.09)	0.130			
Body mass index (kg/m²)	0.97	(0.92-1.02)	0.170			
Hypertension	1.69	(1.09-2.62)	0.019	1.62	(0.94-2.78)	0.083
Diabetes	1.21	(0.85-1.72)	0.286			
Atrial fibrillation	1.61	(1.04-2.51)	0.033			
Total cholesterol, mg/dL	1.00	(0.99-1.00)	0.049			
Triglyceride, mg/dL	1.00	(0.99-1.00)	0.024			
HDL cholesterol, mg/dL	1.00	(1.00-1.00)	0.641			
LDL cholesterol, mg/dL	1.00	(0.99-1.00)	1.093			
Stroke subtype (TOAST)						
Large-artery atherosclerotic type	Ref.					
Cardioembolic type	0.62	(0.36-1.06)	0.081			
Lacunar type	0.69	(0.39-1.21)	0.195			
Undetermined type	1.70	(0.53-5.41)	0.370			
Other determined type	0.81	(0.49-1.36)	0.432			
Antithrombotics within 48 hours after stroke onset	0.24	(0.12-0.51)	<0.001	0.22	(0.08-0.60)	0.003
Antithrombotics at discharge	0.29	(0.12-0.70)	0.006			
No antithrombotic	3.44	(1.42-8.33)	0.006			
Monotherapy	1.53	(1.08-2.17)	0.018			
Dual antiplatelets	0.55	(0.38-0.79)	0.001	0.64	(0.41-1.00)	0.049
Anticoagulant	1.50	(0.90-2.49)	0.116			
Statin use	0.57	(0.38-0.87)	0.008			
Initial NIHSS score	1.82	(1.53-2.17)	<0.001	1.91	(1.53-2.39)	<0.001

HDL, high density lipoprotein; LDL, low density lipoprotein; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institute of Health Stroke Score.

Table 3. Logistic regression model of unfavorable outcome at 3rd month

Conclusion: Older age, presence of hypertension, and higher initial NIHSS score were associated with unfavorable early outcome. Whereas antithrombotics within 48 hours and dual antiplatelet use seemed to have protective effect.
Disclosure: Nothing to disclose.

EPO-035

Clinical profile and outcome of cerebral venous thrombosis at Oran University Hospital

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Background and aims: Cerebral venous thrombosis (CVT) is a rare but serious disease whose clinical and etiological aspects are diverse. Unlike arterial ischemic strokes, epidemiological studies are limited. This study aims to describe clinical, etiological and outcome particularities of CVT in the Algerian population.
Methods: This is a retrospective observational study conducted at the neurology department of Oran University Hospital from January 2021 to December 2022. In a clinical context suggestive of CVT, the diagnosis was provided by cerebral MRI. All subjects underwent a complete etiological assessment. Anticoagulant treatment was based on low molecular weight heparin with relay by vitamin K antagonists.
Results: 45 patients participated in the study. The mean age was 36.94 ± 9.81 years, the sex ratio F/M was 4.6 (37/8). The onset was subacute in 55% of cases. The main initial signs were headaches (88.8%), visual disturbances (50%), epileptic seizures (44.4%) and motor deficit (44.4%). Thrombosis predominated in the superior sagittal sinus and the lateral sinuses; parenchymal lesions were associated in 2/3 of the cases. Obstetrical causes were by far the most frequent. The evolution was favorable in 83.3% of cases.
Conclusion: The characteristics of CVT in the Algerian population are distinguished by a high frequency of obstetrical causes. Awareness campaigns for women of childbearing age are proving useful.
Disclosure: Nothing to disclose.

EPO-036

Clinical profile and etiology of ischemic stroke in young adults : a study from Oran, Algeria

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Background and aims: Ischemic stroke in young adults is a real diagnostic and therapeutic challenge. it differs from stroke occurring in the elderly by etiology. Despite an exhaustive assessment, a high proportion remains of unknown causes. This study aims to describe the clinical

profile and to gain further insight into the etiology of ischemic stroke in young adults in Oran.
Methods: This observational prospective study was carried out at the stroke unit of Oran University Hospital between January 1st 2021 to June 30th 2022. We included all acute ischemic stroke patients aged 18 to 44 years.
Results: Twenty one first-ever ischemic stroke patients were identified during the study period. The mean age was 36.7% and sex-ratio M/F 0.97. NIHSS at admission was 12±4.3. According to the modified TOAST criteria, spontaneous cervical arterial dissection was the leading probable etiology (19.05%). Patent foramen ovale or atrial septal aneurysm was a possible cause of stroke in 9.52% of cases, IgG anticardiolipin antibodies (4.76%), oral contraceptive use (14.3%), and migraine (4.76%). Mortality rate was 4.7% and the one year mRs 1.26.
Conclusion: The results of this study confirm the need for preventive strategies, by detecting risk factors of ischemic stroke in young adults, and early medical care of these patients in a neurovascular unit to enable the confirmation of the etiological diagnosis.
Disclosure: Nothing to disclose.

EPO-037

Predictors of good outcome after Unsuccessful Mechanical Thrombectomy in patients with hyperacute ischemic stroke

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Background and aims: The endovascular thrombectomy (EVT) has become the standard treatment for major acute anterior circulation ischemic stroke (AIS), but not all EVT guarantee successful recanalization. The predictors of good clinical outcome in patients who have experienced unsuccessful recanalization are not unknown. The study objective was to identify the predictors associated with clinical improvement after unsuccessful EVT in patients with AIS.
Methods: In this retrospective study, a total 1046 consecutive patients with AIS who underwent EVT from January 2012 to December 2021 in a single tertiary center were included. Among them, 181 patients (17.3%) had unsuccessful recanalization (modified Thrombolysis In Cerebral Infarction (mTICI) ≤2a) after EVT. Those patients with good outcomes (modified Rankin Scale [mRS], ≤2) were evaluated with clinical and procedural parameters.
Results: The 41 patients (22.7%) had good outcomes. The initial median NIHSS was 12.2 ± 5.4 and Alberta Stroke Program Early CT 7 (4-8). In multivariate analysis, predictors of good outcomes after unsuccessful EVT were age (OR, 0.937; 95% CI, 0.886-0.985, p=0.013), pre-stroke statin medication (OR, 3.145; 95% CI, 1.003-9.933, p=0.048), and total procedural time (OR, 0.973; 95% CI, 0.951–0.992, p=0.012).
Conclusion: Despite the unsuccessful recanalization after EVT, ~>20% patients with AIS showed clinical improvement. Younger age, shorter procedural time and pre-stroke statin medication were associated with good outcome after unsuccessful EVT.
Disclosure: Nothing to disclose.

EPO-038

Assessment of histological characteristics of thrombi after acute ischemic stroke

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Background and aims: Mechanical thrombectomy (MT) allows the study of acute ischemic stroke thrombi material. The aim of this study is to correlate thrombi composition and stroke aetiology, imaging, and revascularization outcomes.
Methods: Patients whose thrombus removed by TM were sent to the Neuropathology Laboratory were included. Retrospective analysis of clinical and radiological variables was performed. Three groups: 1-rich in erythrocytes (≥60% erythrocytes), 2-mixed (erythrocytes=fibrin/collagen) and 3-rich in fibrin/collagen (≥60% fibrin/collagen); presence or absence of leukocytes. Statistical analyses were performed using Fisher's exact test.
Results: 16 patients were included, 68.8% (n=11) male, median age 74 years old. 81.3% (n=13) with hypertension, 50% (n=8) with dyslipidaemia, 37.5% (n=6) with diabetes, 31.3% (n=5) were smokers, 31.3% (n=5) with atrial fibrillation/flutter, and 6.3% (n=1) with overweight/obesity. 33.3% (n=5) under antiplatelet therapy and 6.7% (n=1) under anticoagulant therapy. Median NIHSS 14.5. Median ASPECTS 8.5. 93.8% (n=15) had anterior circulation occlusion. Half had spontaneous hyperdense vessel sign on brain CT. Half underwent thrombolysis. 76.9% (n=10) underwent MT with aspiration system (global median of 2 passes). 80% (n=12) had mTICI3/2c. 43.8% (n=7) presented thrombi rich in erythrocytes and the entire sample presented leukocytes. 66.7% (n=10) had cardioembolic aetiology. There was an association between the presence of thrombi rich in erythrocytes and mRS≤3 (p=0.031).
Conclusion: Patients with less disability had thrombi rich in erythrocytes. It may be related to a higher rate of recanalization after TM in this group, previously described. Larger sample size will allow to corroborate this clinicopathological correlation.
Disclosure: Nothing to disclose.

EPO-039

Previous statins use and the risk for haemorrhagic transformation in acute ischemic stroke patients

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Background and aims: According metanalysis studies, long term statin use can slightly increase the risk for intracerebral haemorrhage, including haemorrhagic transformation (HT) of ischemic stroke. The aim of our study was to evaluate the risk for HT in acute ischemic stroke (AIS) patients with previous statin use and the correlation with the patients' outcome and recovery.
Methods: In a prospective, consecutive way, we've included patients with AIS admitted to a tertiary neurological hospital from 2018 to 2022, to evaluate possible risk factors for HT and its' impact on discharge and 3 months follow-up status by the modified Rankin Scale (mRS). The patients were grouped, based on the HT presence, into 2 cohorts: active group (with HT) and control group (without HT).
Results: From 150 patients, 55 patients presented HT during the hospitalization. The mean LDL-cholesterol level was 3.3±0.07 mmol with similar values in the compared groups (p=0.99). Up to 50% of the analysed patients presented very high cardiovascular risk prior stroke. Only 8.7% (13/150 patients) were taking high dosage statins with slightly more patients in the active cohort (11% vs 7.4%, p=0.55). The correlation analysis revealed that previous statin use didn't significantly increase the rate of HT (OR=1.62, 95% CI: 0.43-6.13, p=0.46), didn't influence the discharge mRS score (OR=0.37, 95% CI: 0.08-2.67, p=0.25), and the follow-up mRS: OR=0.46, 95% CI: 0.1-2.41, p=0.32.
Conclusion: In our study the previous statin use didn't increase the risk for HT, neither influenced the discharge or follow-up neurological functional status.
Disclosure: Nothing to disclose.

EPO-040

Stroke due to infective endocarditis treated with mechanical thrombectomy: Case Report and Literature Review.

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Background and aims: Acute ischemic stroke (AIS) due to large vessel occlusion (LVO) is a common complication of infective endocarditis. Intravenous thrombolysis is contraindicated in these patients due to risk of hemorrhagic complications. However, mechanical thrombectomy (MT) may be an effective treatment in these patients, but there is limited data on it's safety in infective endocarditis.
Methods: A case of AIS patient from infective endocarditis treated with MT was reported and literature review was performed.
Results: A 41- year-old man with infective endocarditis who developed AIS due to RICA occlusion was admitted to the comprehensive stroke center. MT was performed with successful recanalization (TICI 2B). Control CT performed after 24h revealed no hemorrhagic transformation. After 6 days from onset neurological deterioration was observed. Control CT with angiography revealed intracranial hemorrhage due to raptured mycotic aneurysm of MCA (aneurysm was not observed on the baseline cerebral arteriography). Patient underwent successful endovascular embolization. Although the patient received immediate treatment he died. 47 similar cases were identified from 16 articles. 11 patients developed hemorrhagic complications (23%). Depending on different studies functional independence (mRS 0-2) after stroke occur in 50-57% of patients.
Conclusion: MT appears to be safe and effective treatment option in patients with infective endocarditis-related AIS due to LVO, but further validation of this finding in large cohort studies is warranted.
Disclosure: The authors declare no conflict of interest.

EPO-041

Uncovering the Hallmarks of Infective Endocarditis in Retrieved Cerebral Thrombi from Acute Ischemic Stroke Patients

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Background and aims: Infective endocarditis (IE) is a major cause of ischemic stroke, and early diagnosis is crucial. The analysis of cerebral thrombi retrieved during endovascular thrombectomy in patients with large vessel occlusion acute ischemic stroke (LVO-AIS) and suspected IE may provide a diagnostic tool. The aim of this study was to identify hallmarks in the thrombus composition that could diagnose IE.
Methods: The study analyzed cerebral thrombi from patients with LVO-AIS and definite IE (n=8), cardioembolic stroke patients with concomitant acute infections (n=9), and cardioembolic stroke patients without infections (n=18). Thrombus culture, PCR, and histology were used to assess microorganisms and structural and immune components.
Results: Thrombus culture was positive in 1/2 IE thrombi, PCR and sequencing detected bacteria in 4/4 IE thrombi, and bacteria were found in 7/8 IE thrombi on histology. One IE sample displayed fungal hyphae, but no microorganisms were found in the controls. IE thrombi had lower red blood cell counts (4.8% vs. 55.5%) and macrophage counts (45.5 vs. 208.7 cells/mm2) compared to controls. No differences were found in fibrin, platelets, T- and B-lymphocytes, or neutrophils. However, IE thrombi had higher prevalence of neutrophil extracellular traps with cell-filopodia-dominant morphology.
Conclusion: The analysis of cerebral thrombi represents a useful adjunctive tool in diagnosing stroke with suspected IE.
Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 1

EPO-042

Treatments, Healthcare Utilization and Costs in Newly Diagnosed and Pre-existing Myasthenia Gravis Patients in Sweden

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune disorder characterized by muscle weakness and fatigue. This study aims to evaluate treatment use, healthcare resource utilization and costs in patients with newly diagnosed (ND) vs pre-existing (PE) MG in Sweden.
Methods: Data were linked from four Swedish nationwide population-based registries. Adults with ≥ 2 primary diagnosis of MG (ICD-10-SE: G70.0) in inpatient or outpatient specialist visits (≥ 12 months apart within 24 months, ≥ 1 MG diagnosis recorded by a neurologist) during 1/1/2010-12/31/2017; had a pharmacological treatment for MG were selected. Index date was date of first primary MG diagnosis. Patients were categorized into ND vs PE groups based on whether they had a MG diagnosis before index date (back until 2001).
Results: A total of 1,275 patients were included, of which 554 patients were ND MG. Mean (±SD) age was 61.3 (±17.4) years; 52.3% were female. During 12-month post-index period, 5.6% of patients had thymectomy and 0.7% used intubation/mechanical ventilation; ND MG had higher all-cause (70.9% vs 35.8%, p<0.01) and MG-related (62.5% vs 18.4%, p<0.01) hospitalization rates; experienced 11 more hospitalization days (p<0.01); incurred €7302 (p<0.01) higher total all-cause costs, with an incremental difference of €6275 derived from inpatient costs; incurred €6188 (p<0.01) higher total MG-related costs, of which 84% was attributable to inpatient costs.
Conclusion: MG patients incurred substantially higher economic burden in the first year compared to later years. Future research should aim to better understand potential factors (e.g., delayed diagnosis and/or treatment) associated with the increased burden.
Disclosure: Alberto E. Batista, Qian Cai, Peter Kunovszki, Qiaoyi Zhang, and Kristin Heerlein are employees of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson. Jakob Börsum and Gabriel Isheden are employees of SDS Life Science.

EPO-043

Immune-mediated necrotizing myopathies: clinical-serological features of a large Italian cohort of patients

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Background and aims: Immune-mediated necrotizing myopathies (IMNMs) represent a heterogeneous group of muscle disorders recently identified within the spectrum of idiopathic inflammatory myopathies (IIMs) by distinctive clinical, pathological, serological, and therapeutic features. Currently, three different IMNM entities have been defined: 1) anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) myopathy; 2) anti-signal recognition particle (SRP) myopathy; 3) antibody negative IMNM. An accurate diagnosis of IMNMs is relevant for prognostic purposes and to provide the best chance of treatment for patient subtypes and prevent long-term disability. We aimed to investigate clinical and histological features of different serological subgroups within an Italian cohort of IMNM patients.
Methods: We included 116 patients diagnosed with IMNM in 12 neuromuscular referral centers in Italy, relying on the 2017 European Neuromuscular Centre criteria.
Results: The study population was composed by 51 males and 65 females, with an overlapping median age at disease onset equal to 65 years old for men and 64 for women. Thirty-nine patients (33,6%) were positive for HMGCR autoantibodies (Abs), of whom 26 had a history of statin exposure (11 males, 15 females). Among anti-HMGCR Ab–positive IMNM patients naïve to statin therapy, females were more represented (61,5%). Furthermore, 33 patients (28,4%) had anti-signal recognition particle (SRP) Abs, 24 patients (20,7%) resulted seronegative, and 20 patients (17,2%) did not have a complete Ab assessment. Muscle weakness distribution at onset, myopathological features, clinical outcome after therapy, and therapeutic regimen data together with extramuscular manifestations according to serological phenotype have been reported.

Conclusion: This study provides new insights about IMNM characteristics in a large Italian cohort.
Disclosure: SB received honoraria for advisory board activities, and compensation for travel and congress participation from Sanofi Genzyme, Biogen and Roche.

EPO-044

Anxiety and depression in generalised myasthenia gravis in Europe, Middle East and Africa: A systematic review

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune disease characterised by muscle weakness and fatigue. Progression of these symptoms has a negative impact on quality of life. A systematic literature review was conducted to determine the extent of anxiety and depression in patients with generalised MG (gMG).
Methods: Electronic database searches (conducted March 2022), supplemented by interrogation of grey literature were conducted to identify studies reporting depression and/or anxiety patient reported outcomes in patients with gMG in Europe, Middle East and Africa.
Results: Of the 13 eligible studies, eight reported comparative data for anxiety using five scales and 12 reported depression using seven scales (Table 1). Where reported, data indicate that anxiety (n=3 studies) and depression (n=5) was statistically significantly worse in patients with gMG versus controls. However, while anxiety was significantly worse in gMG versus ocular MG (oMG) (n=2), no consistent difference was reported for depression (n=4). Two further studies reported a higher proportion of clinically relevant anxiety and depression in patients with gMG versus oMG; a benefit of pharmacological remission in MG was also observed (Figure 1). Finally, in patients with gMG, stage of disease (n=2) and Patient Acceptable Symptom State status (n=1) were associated with the severity of anxiety and depression whilst antibody status was not.
Conclusion: Although statistically significant differences in the extent of anxiety and depression are reported in patients with gMG compared with relevant populations and subgroups, these findings need to be confirmed in large cohorts administering consistent, validated questionnaires.

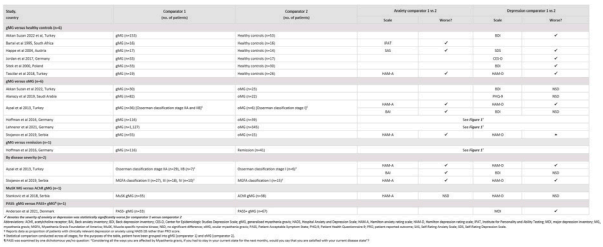
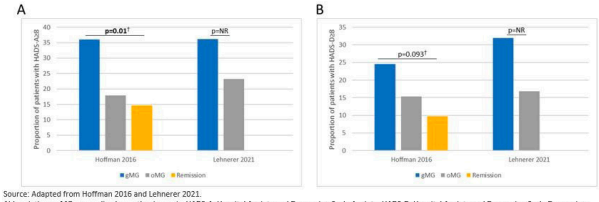


Table 1: Studies reporting anxiety and depression patient reported outcome data in patients with gMG against relevant comparators or within gMG subgroups



Source: Adapted from Hoffman 2016 and Lehnerer 2021.
Abbreviations: gMG, generalised myasthenia gravis; HADS-A, Hospital Anxiety and Depression Scale Anxiety; HADS-D, Hospital Anxiety and Depression Scale Depression; NR, not reported; oMG, ocular myasthenia gravis.
† p- value refers to overall group comparisons of patients with gMG, oMG, and pharmacological remission.

Figure 1: Proportion of patients with clinically relevant anxiety (Panel A) and depression (Panel B) by disease stage

Disclosure: This study was funded by Janssen-Cilag EMEA.

EPO-045

Matrin-3 autosomal dominant distal myopathy in Portuguese patients

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Background and aims: The nuclear matrix protein matrin-3 (MATR3) autosomal dominant distal myopathy, most commonly caused by a Ser85Cys (S85C) missense mutation, determines a heterogenous phenotype.
Methods: We present three Portuguese patients diagnosed with p.Ser85Cys MATR3-related myopathy, diagnosed by genetic assessment, using a specific gene panel dedicated to "distal myopathies".
Results: Patient no. 1 is a 57-year-old male presenting with lower leg weakness, followed by upper limb distal force loss for fine motricity gestures. Neurological examination revealed important muscle atrophy of the distal limbs and symmetrical motor deficit. The second patient, the brother of the aforementioned subject, is a 54-year-old male with similar symptoms, associated with dysphagia and dysphonia. Patient no 3 is a 58-year-old female, unrelated to previous patients, presenting with distal weakness in the upper limbs and severe Achillean contractures. All the subjects were investigated by needle electromyography and

whole-body MRI, which revealed a fatty infiltration pattern, predominantly affecting the gastrocnemius, soleus, and tibialis anterior muscles. Muscle biopsy was performed solely for patient no 1 and revealed rimmed vacuoles, consistent with previous reports. The gene analysis found the same mutation in all three cases: c.254C>G, p.Ser85Cys in the MATR3 gene.

Conclusion: Despite being a rare myopathy, with only few families reported, MATR3 gene mutations should be considered in patients with distal myopathy and rimmed vacuoles on muscle biopsy. To our knowledge, this is the first report of this phenotype in the Portuguese population.

Disclosure: Nothing to disclose.

EPO-046

Higher Need for Medical Resources in Moderate-To-Severe MG Patients: A Comparison With The General Population

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Background and aims: Myasthenia Gravis (MG) patients suffer from muscular fatigue affecting their vision, swallowing, speech, mobility, dexterity and breathing. This analysis compared the medical resource utilization (MRU) of moderate-to-severe MG (msMG) patients with the general population.

Methods: MyRealWorld-MG is an observational study conducted in the US, UK, Canada, France, Italy, Germany, Spain, and Japan among adult MG patients. Patients entered personal and disease characteristics via a smartphone application, and provided data on MRU. All patients with a self-assessed MG-Activities of Daily Living (MG-ADL) score >6 were considered as msMG. POPUP is an observational study collecting comparable data among members of the general public and was conducted in similar countries. National samples were representative of age, gender, education and region.

Results: Four times more msMG patients (N=431) took sick leave during the past month compared to POPUP (N=9000) (43.5% versus 10.2%); but the duration of sick leave did not differ (Table 1). The hospitalization rate was eighteen times higher among msMG patients (rate=0.158/month versus 0.009/month in POPUP) with three times longer length-of-stays (10.0 versus 3.4 days). Furthermore, an eleven-fold increase in ER visits (0.151 vs. 0.013/month) and a four-fold increase in specialist visits (0.811 vs. 0.184/month) were observed for msMG compared to POPUP. msMG patients had double the number of GP and physiotherapy visits per month (0.392 and 0.172 for msMG versus 0.211 and 0.092 in POPUP).

	General Population	Moderate & Severe MG patients	Relative Rate
Sick leave			
% Did take time off work / studies in the past month	**10.9%**	**43.5%**	**4.0**
Average number of days (std, range):	12.4, 11.5 (0 - 31)	14.8, 12 (1 - 31)	1.2
Use of health care services in the past month			
Had a hospitalization	0.009	0.158	18.0
Length of stay	3.4	10.0	3.0
Number of ER visits	0.013	0.151	11.6
Number of Hospital outpatient visit	0.064	0.192	3.0
Number of specialist visit	0.184	0.811	4.4
Number of GP visits	0.211	0.392	1.9
Number of Physiotherapist visit or visit to a rehabilitation cent	0.092	0.172	1.9
Number of nurse / healthcare worker visit	0.132	0.131	1.0

Table 1. Medical Resource Utilization of moderate-to-severe MG patients compared to the general population

Conclusion: Suffering from msMG was associated with a considerable impact on MRU compared to the general population, likely resulting in substantially higher health care costs.

Disclosure: EC has received public speaking honoraria and compensation for advisory boards and/or consultations fees from Argenx, UCB, Alexion and Janssen. RM has received speaking honoraria from Biomarin, Alexion and UCB, served on advisory boards for Alexion, argenx BV and UCB and received support for congress participation from Merck, Teva and Biogen FS has received public speaking honoraria from Almirall, Biogen, Mylan, Novartis, Roche, Sanofi and Teva; and served on advisory boards for Almirall, argenx BV, Avexis, Biogen, Forward Pharma, Lexeo, Merk, Novartis, Novatek, Pomona, Roche, Sanofi, and Takeda. SP is an employee of argenx BV, the sponsor of the study SD, NT and MFJ have been commissioned by argenx BV and received honoraria to design the study, analyze data and write the abstract.

EPO-047

Fatigue among generalised myasthenia gravis: real-world data from physicians and patients across 5 European countries

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Background and aims: Generalised myasthenia gravis (gMG) is a rare, chronic condition causing generalised fatigue and muscular weakness. Generalised fatigue is hard to manage, often manifesting with other symptoms. There are no objective ways to measure generalised fatigue, making the patient perspective important in understanding fatigue-related disease burden.

Methods: Data were drawn from an Adelphi Disease Specific Programme™, a point-in-time survey of physicians and MG patients in France, Germany, Italy, Spain, and the UK, between March-September 2020. Physicians reported patient demographics and symptoms from a pre-selected list. Patients separately reported their current symptoms.

Descriptive analyses were run alongside bivariate comparisons.
Results: Overall, 128 physicians reported on 554 patients with gMG. Mean age was 53.8 (Standard Deviation; SD±15.42) and 51.4% were female. Physicians reported generalised fatigue for 65.3% of patients, significantly more were female than male (55.0%, p<0.05). A higher overall number of gMG symptoms were reported in fatigued patients (mean: 7.2, SD±3.83, p<0.05) than those non-fatigued (mean: 4.2, SD±2.70). A larger proportion of fatigued patients were reported in Myasthenia Gravis Foundation of America classifications III and IV (38.1%, p<0.05) than non-fatigued patients (27.1%). Of 181 self-reporting patients, 139 (76.8%) reported fatigue. Of these 139 patients, 15.1% were not reported with fatigue, and 2.2% were reported asymptomatic, by their physicians.
Conclusion: Fatigue in gMG patients was reported in a significant number of patients, often correlated with markers of greater disease severity. Lower physician-reported, than patient-reported, fatigue may indicate a higher level of attention to fatigue is needed to understand the burden of fatigue on gMG patients.
Disclosure: This project has been funded by Janssen-Cilag EMEA.

EPO-048

Early-onset generalised myasthenia gravis in women aged 18-50: results from a real-world study in 5 European countries

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Background and aims: Generalised myasthenia gravis (gMG) is a rare, chronic condition that can present in women aged 18-50. There is a need to understand the clinical profile of early onset female (EOF) gMG patients to ensure optimal treatment outcomes.
Methods: Data were drawn from the Adelphi Myasthenia Gravis Disease Specific Programme™, a survey of gMG-treating physicians conducted in France, Germany, Italy, Spain and the United Kingdom, from March-September 2020. Physicians reported patient demographics, clinical characteristics, and treatment history including surgery. EOF was defined as females aged 18-50 at survey. Descriptive analyses were run alongside bivariate comparisons.
Results: 128 Physicians provided data for 554 gMG patients. Patients had a mean [standard deviation] age of 53.8[15.4], 51.4% were female and had been diagnosed for 48.2[63.6] months on average. Of those, 147 (26.5%) were EOF patients. EOF patients were diagnosed significantly more recently than non-EOF patients (mean [SD], 35.9[42.4] vs 52.7[69.3] months, p<0.05). 29.9% of EOF and 35.9% of non-EOF patients were in Myasthenia Gravis Foundation of America classification III or IV (p=0.22). Among EOF patients, 27.2% underwent thymectomy versus 22.9% of non-EOF patients (p=0.05). EOF patients had a mean [SD] of 1.1[0.7] myasthenic crises and 0.8[0.8] hospitalizations in the last 12 months compared to 0.9[0.7], p=0.23 and 0.6[0.7], p=0.13 in non-EOF patients, respectively.
Conclusion: The study shows that although EOF patients are earlier in their disease journey, the number of thymectomies, myasthenic crises and hospitalizations trend higher in EOF patients than in the general gMG population, potentially indicating that the unmet treatment needs of EOF patients.
Disclosure: This project has been funded by Janssen-Cilag EMEA.

EPO-049

Myotonic dystrophy type II unmasked by immune checkpoint inhibitor

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Background and aims: Although cancer immunotherapy with immune checkpoint inhibitors (ICIs) has been a milestone in cancer treatment, their increasing use has resulted in a growing number of neuromuscular adverse events, most of them immune-related (irAEs).
Methods: A 63-year-old woman, with colorectal cancer treated with pembrolizumab, presented with a 9-month history of progressive proximal lower limb weakness and minor camptocormia. Symptoms appeared 1 month after initiation of immunotherapy and progressed gradually leading to a significant motor impairment. She had marked difficulty climbing stairs and rising from sitting position. She also reported a chronic minor difficulty rising from low chairs, a symptom that was also reported by the patient's sister and father.
Results: Nerve conduction studies and 3Hz repetitive nerve stimulation were normal while electromyography revealed diffuse waning myotonic discharges and a chronic myopathic pattern. Genetic testing demonstrated a pathogenic mutation in the CNPB gene, confirming the diagnosis of type 2 myotonic dystrophy.
Conclusion: Neuromuscular toxicity induced by ICIs treatment is rare but potentially underreported. The most commonly reported irAEs are myositis, myasthenia gravis and neuropathy with several cases resulting in a fatal outcome. Due to the susceptibility of the skeletal muscle,

myotoxic drugs may unmask a primary asymptomatic or oligosymptomatic hereditary myopathy. To the best of our knowledge there are three other reported cases of hereditary neuromuscular diseases unmasked during treatment with ICIs. Patients under treatment with ICIs should be carefully evaluated for neuromuscular side-effects and the possibility of a concomitant hereditary myopathy, should also be considered.

Disclosure: I have no financial interests or relationships to disclose.

EPO-050

IgG and anti-AChR Antibody Reduction Explain Nipocalimab Effect on MG-ADL Score Improvement in Patients with gMG

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Background and aims: Nipocalimab is an anti-FcRn monoclonal antibody that lowers IgG, including anti-AChR antibodies (Ab). This analysis was conducted to quantify the relationship between IgG, anti-AChR Ab and the clinical efficacy endpoint (MG-ADL) to understand if IgG or anti-AChR Ab reduction could account for nipocalimab effect on MG-ADL.

Methods: Data from 68 patients with gMG from a Ph2 study (NCT03772587) were utilized for statistical and population modeling and simulation analyses to quantify the relationship between IgG, anti-AChR Ab and MG-ADL reduction

Results: IgG and anti-AChR Ab reduction expressed as percent change from baseline were highly correlated (R2=0.75), and correlated similarly to MG-ADL improvement. IgG was selected to quantify the relationship to MG-ADL to allow inclusion of all patients (AChR+ and AChR-). Placebo-corrected change from baseline MG-ADL (ΔΔMG-ADL) was proportional to IgG reduction. A 50% IgG reduction was estimated to lead to a median ΔΔMG-ADL reduction of 1.07 points. Subjects with higher individual baseline MG-ADL exhibited higher ΔΔMG-ADL reductions (eg a 2-fold baseline increase resulted in a 1.9-fold higher reduction). Simulations showed a that a large proportion (>80%) of the Nipocalimab-induced MG-ADL improvement could be explained by IgG reduction.

Conclusion: Serum IgG reduction explains most of the ΔΔMG-ADL change following nipocalimab treatment. Thus, IgG reduction may qualify as a biomarker for efficacy if confirmed by data from the ongoing Ph3 study. The quantitative relationship between IgG, anti-AChR Ab and MG-ADL is critical for model-informed decisions on nipocalimab development.

Disclosure: WSD is an employee of Human Predictions, LLC and a consultant for Johnson & Johnson. Other authors are employees or contractors of Janssen Pharmaceuticals any may own stock or stock options in Johnson & Johnson.

EPO-051

Cancer frequency in muscle-specific tyrosine kinase (MuSK) myasthenia gravis

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Background and aims: Cancer frequency in myasthenia gravis with anti-MuSK antibodies (MuSK-MG) has not yet been explored. The link between neurological autoimmunity and cancer is bidirectional: autoimmune diseases may increase cancer risk through long-term immunosuppression, conversely antitumor immune response may result in autoimmunity development.

Methods: In this retrospective study, we reviewed records of patients with confirmed diagnosis of MuSK-MG who had been followed for at least 1 year from disease onset in our Center. We recorded associated cancers and timing of oncological diagnosis in relation to MG onset, type and duration of immunosuppressive therapy.

Results: 94 patients were recruited, 21 males and 73 females. The median age at MG onset was 51 years [19-75]. Immunosuppressive therapy was performed in 90/94 (95.7%) cases with corticosteroids and/or immunosuppressants; 16 patients were treated with Rituximab. Fifteen cancers occurred in 13/94 patients (13.8%). Median age at cancer onset was 60 years [18-79]. Tumor detection preceded MG onset (median: 11 years, [3-17]) in 5 patients, it was concomitant in 2 and it followed MG diagnosis in 8 cases (median time from MG onset: 11.5 years, [1-32]). Six patients were on long-term immunosuppression at cancer diagnosis. Blood malignancies were the most common (N=5), all detected before MG onset. In addition, we found cancer in breast (N=3), womb (N=2), digestive organs (N=2), lung (N=1), vocal cords (N=1), skin (N=1).

Conclusion: Onco-hematological diseases, particularly mediastinal lymphoma (N=3/5, 60%), were the most common malignancy detected in MuSK-MG patients. We did not find a higher frequency of cancer occurrence in patients on long-term immunosuppression.

Disclosure: The authors declare no conflicts of interest.

EPO-052

Thymectomy in Thymomatous and Nonthymomatous Myasthenia Gravis: a 10-year follow-up cohort

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Background and aims: Thymectomy remains a mainstay of treatment in Thymomatous (T) and Nonthymomatous (nT) Myasthenia Gravis (MG). However, there is little research regarding long-term follow-up. We aim to assess the impact of surgery on the long-term outcome of patients with MG at our centre.
Methods: Retrospective analysis of MG patients submitted to thymectomy between 2007 and 2017 at the thoracic surgery department of our tertiary centre. Clinical assessment was performed according to the MG Foundation of America (MGFA) Clinical Classification (cMGFA). The follow-up was categorized according to the MGFA Post-intervention Status (MGFA-PIS) and cMGFA.
Results: Thirty-seven patients underwent extended thymectomy. Median age at diagnosis was 46.7±19.2 years. Most patients (83.8%) had anti-acetylcholine receptor antibodies and 81.1% had generalized forms of MG. Many patients (67.6%) had surgery less than 12 months after the clinical diagnosis. TMG was present in 19 (51.4%) patients. Compared to nTMG, these patients were older (54.1±17.9 vs 40.2±19.4 years) and most were men (52.9% vs 16.7%). We obtained a good outcome in most patients in the first (81.1%), second (83.3%), fifth (84.8%) and tenth (83.3%) year of follow-up. There was a shift towards better prognosis categories in the good outcome group: 11.1% complete stable remission and 61.1% minimal manifestation status in the tenth year. A shorter time to surgery (< 12 months) correlated with better outcomes.
Conclusion: Thymectomy led to a sustained clinical improvement in our cohort, allowing for a reduced need for medication. A shorter time to surgery seems to have a positive influence on long-term prognosis.
Disclosure: The authors report no disclosures relevant to this presentation.

EPO-053

Emery-Dreifuss Muscular Dystrophy type 1 (EDMD1): a phenotype characterization from a large Italian pedigree

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Background and aims: Emerin-related Emery-Dreifuss Muscular Dystrophy type 1 (EDMD1) represents an X-linked form of symmetrical humeroperoneal myopathy with almost invariable cardiac arrhythmias.
Methods: A cross-sectional evaluation of past medical history, and motor, cardiac and ventilatory assessments in 9 related individuals (5 males and 4 females) with genetically confirmed emerinopathy (exon 2 c.104_106del – p. Lys36del) was performed.
Results: Age of patients at last clinical evaluation ranged 19-82 years (57.4 + 20.1). Out of 5 males, muscular symptoms generally manifested within adolescence with scapular + axial weakness (asymmetrical winged blades, rigid spine, scoliosis – 2/9) and contractures (neck extensors, brachial biceps, finger flexors 3/9). Gardner-Medwin-Walton (GMW) graded 1 in 4/5, confirming overall favourable motor performances. From a cardiac angle, symptoms presented at 50.3 + 10.8 years in the whole cohort, with grade 1-2 atrioventricular block in 3/9, atrial fibrillation in 1/9 and ventricular extrasystoles in 2/9; 4/9 necessitated a pacemaker/implantable cardioverter. A non-ST elevation myocardial infarction (NSTEMI) occurred in one male patient at 78. Last echocardiography detected a mean ejection fraction of 58.7 + 8.1%. Spirometry, when available, revealed a mean forced vital capacity (FVC) of 101.5 + 10.6% and forced expiratory volume in the first second (FEV1) of 107 + 17%; 2/9 used nocturnal non-invasive ventilation from the 6th decade onwards.
Conclusion: Besides common neuromuscular impairment and arrhythmias, our pedigree emphasizes further and less typical complications in EDMD1, such as cardiac ischemia and sleep hypoventilation, suggesting the need for a multidisciplinary monitoring to eventually broaden the clinical spectrum.
Disclosure: Nothing to disclose.

EPO-054

Efgartigimod Demonstrates Consistent Magnitude of Response Across Subgroups of Patients With gMG

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Background and aims: Treatment with efgartigimod, a human IgG1 antibody Fc-fragment that blocks neonatal Fc receptor, resulted in clinically meaningful improvements in patients with generalised myasthenia gravis (gMG) in the ADAPT study. Efgartigimod was well tolerated and common adverse events (mostly mild or moderate) were headache, nasopharyngitis, nausea, diarrhoea, and upper respiratory/urinary tract infection. Here we assess efgartigimod efficacy in subgroups of patients with gMG.
Methods: Intravenous efgartigimod 10 mg/kg or placebo was administered in cycles of 4 weekly infusions, with subsequent cycles initiated based on clinical evaluation. Efficacy was assessed using MG-ADL and QMG scores. Here we report mean change from baseline and responder status (defined as ≥2-point [MG-ADL] and ≥3-point [QMG] improvement for ≥4 consecutive weeks, with first improvement ≤1 week after last infusion) for cycle 1 in AChR-Ab+ patients grouped according to clinical characteristics, including time since diagnosis and concomitant medications.
Results: A greater proportion of efgartigimod-treated patients were MG-ADL responders compared with those receiving placebo regardless of duration of disease (Figure 1A). Likewise, when stratified by concomitant medication use, a greater proportion of efgartigimod-treated patients were MG-ADL responders compared with those taking placebo (Figure 2A). Proportion of QMG responders was similar and consistent across subgroups (Figures 1B and 2B). Mean improvements in MG-ADL/QMG scores were also greater with efgartigimod across all subgroups (Table 1).

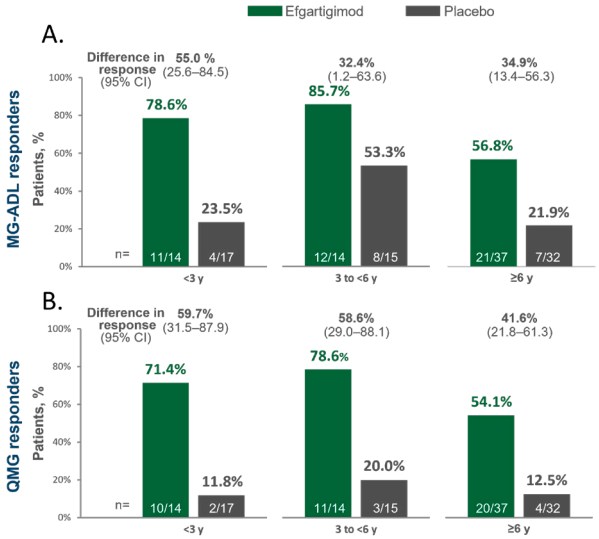

Figure 1: Proportion of MG-ADL (A) and QMG (B) responders by disease duration in AChR-Ab+ patients in cycle 1.

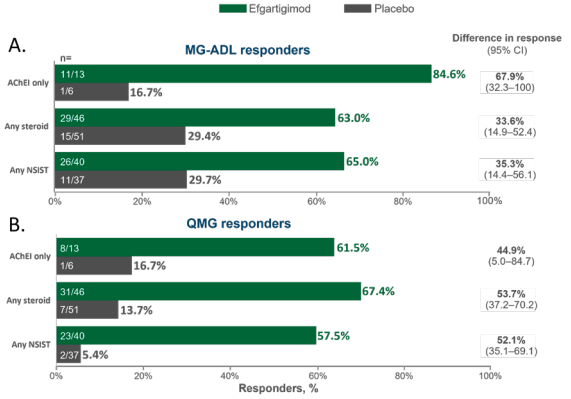

Figure 2: Proportion of MG-ADL (A) and QMG (B) responders by concomitant therapies in AChR-Ab+ patients in cycle 1.

Subgroup	Efgartigimod		Placebo	
Time since diagnosis	n	mean (SD)	n	mean (SD)
MG-ADL				
<3 y	13	-5.1 (2.63)	14	-2.0 (1.84)
≥6 y	36	-4.4 (3.47)	31	-1.4 (2.13)
QMG				
<3 y	13	-7.5 (5.41)	13	-0.6 (3.69)
≥6 y	36	-6.0 (5.39)	30	-0.9 (2.47)
Concomitant medications				
MG-ADL				
AChEI only	12	-7.4 (4.48)	5	-2.0 (1.41)
Any steroid	44	-6.3 (5.41)	47	-0.8 (3.01)
Any NSIST	39	-5.8 (5.39)	33	-0.4 (2.81)
QMG				
AChEI only	13	-5.5 (3.04)	5	-2.2 (2.17)
Any steroid	44	-4.5 (3.29)	48	-1.6 (2.28)
Any NSIST	39	-4.4 (3.11)	36	-1.5 (2.41)

Table 1: Change from baseline in MG-ADL and QMG scores by subgroup in AChR-Ab+ patients (cycle 1, week 4).

Conclusion: The proportion of responders and magnitude of response for patients treated with efgartigimod was consistent regardless of above defined subgroups, providing support for efgartigimod efficacy across a broad population of patients with gMG.
Disclosure: Multiple relationships financial and non-financial nature for authors SH, AM, SA, JLdB, JV, RK, EB, KU, NG, YL, SP, JFH Jr. and FS stated at point of presentation.

EPO-055

Gender-specific analysis of efgartigimod efficacy in patients with gMG: Subanalysis of the randomised phase3 ADAPT trial

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Background and aims: Generalised myasthenia gravis (gMG) is a rare, chronic autoimmune disease leading to potentially life-threatening muscular weakness. Efgartigimod is a human IgG1 antibody Fc-fragment that blocks the neonatal Fc receptor, leading to reduced IgG autoantibody levels. The ADAPT trial demonstrated that efgartigimod treatment resulted in clinically meaningful improvement (CMI) in gMG-specific outcome measures in the overall study population. Considering the Sex and Gender Equity in Research (SAGER) guidelines, this analysis aimed to identify potential gender-specific differences in outcomes between efgartigimod and placebo.
Methods: ADAPT (NCT03669588), a randomised, phase 3 trial included gMG patients (MG-ADL >=5: >=50% non-ocular symptoms) regardless of autoantibody-status. Efgartigimod (10 mg/kg) or matching placebo was administered as four infusions per cycle (one infusion per week), repeated as needed depending on clinical response. The primary endpoint was percentage of AChR-Ab+ patients who were MG-ADL responders (>=2 points improvement sustained for >=4 weeks) in the first treatment cycle. Secondary endpoints included Quantitative Myasthenia Gravis (QMG) responders (>=3 point QMG improvement for >=4 consecutive weeks). In this analysis, only AChR-Ab+ patients receiving a stable dose of >=1 gMG treatment were included. The outcomes were analysed by Zelen's Exact test for homogeneous odds ratio between sex subgroups.
Results: Overall, 129 patients were analysed, 86 (66.7%) were female. Differences are noted between females and males in age, disease duration, BMI and thymectomy (Table 1). There were no gender-specific treatment differences across gMG-specific outcome measures (Table 2).

Baseline characteristic	Female (n=86)	Male (n=43)
Mean age, years (SD)	42.9 (14.27)	54.8 (14.52)
Mean no. of years since diagnosis (SD)	9.95 (8.40)	8.02 (7.74)
Mean BMI, kg/m^2 (SD)	26.28 (6.13)	31.77 (7.57)
Thymectomy performed for gMG, n (%)	56 (65.1)	19 (44.2)
MGFA class at screening, n (%)		
2-2A	20 (23.3)	8 (18.6)
2-2B	15 (17.4)	10 (23.3)
3-3A	24 (27.9)	10 (23.3)
3-3B	25 (29.1)	12 (27.9)
4-4A	2 (2.3)	2 (4.7)
4-4B	0	1 (2.3)
Mean MG-ADL score at baseline (SD)	8.8 (2.19)	8.8 (2.60)
Mean QMG score at baseline (SD)	16.3 (4.83)	14.3 (4.44)

Table 1. Demographics and baseline disease characteristics in the AChR-Ab+ population, by gender

–	Overall AChR-Ab+ population			Female (n=86)		Male (n=43)		
Endpoint, n (%)	Efgartigimod (n=65)	Placebo (n=64)	Between-treatment analysis; OR (95% CI)^a	Efgartigimod (n=46)	Placebo (n=40)	Efgartigimod (n=19)	Placebo (n=24)	Between-sex subgroup analysis^b
MG-ADL responders	44 (67.7)	19 (29.7)	4.95 (2.21–11.53) p<0.0001	31 (67.4)	13 (32.5)	13 (68.4)	6 (25.0)	p=0.7014
QMG responders	41 (63.1)	9 (14.1)	10.84 (4.18–31.20) p<0.0001	26 (56.5)	7 (17.5)	15 (78.9)	2 (8.3)	p=0.1595

a. Treatment effect was tested using exact conditional logistic regression.
b. Homogeneous odds ratios were tested using Zelen's Exact test.

Table 2. MG-ADL and QMG responders during the first cycle, in the AChR-Ab+, modified intent-to-treat population and by gender

Conclusion: These analyses suggest efgartigimod results in consistent improvement across gMG-specific measures, regardless of patient gender.
Disclosure: S Hoffmann has received speaker´s honoraria from Alexion, argenx and UCB and honoraria for attendance at advisory boards from Alexion and argenx; S Zhao, F Callewaert and S Schoppe are employees of argenx, the study sponsor.

EPO-056

Retrospective Study of Select Adverse Events of Special Interest Associated With Corticosteroid Use in Myasthenia Gravis

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Background and aims: Myasthenia gravis (MG) is an autoantibody-driven disease. Oral corticosteroids (OCS) remain the initial medication for patients requiring immunotherapy despite known toxicities. The objective of the study was to assess the risk of select adverse events of special interest (AESIs) during real-world OCS use in MG patients.
Methods: US adults with newly diagnosed MG between 01/2015 and 06/2022 were identified from the Optum Clinformatics database. Periods of OCS exposure and non-exposure were defined for each patient. AESIs were identified based on the Glucocorticoid Toxicity Index using ICD codes. Frailty models were fitted to assess risks of recurrent AESIs during OCS-exposed periods compared to non-exposed periods as hazard ratios (HR). OCS dose and concomitant medications were included as time-variating covariates along with time-fixed baseline characteristics.

Results: Among the 3,839 newly diagnosed MG patients identified, 1,781 (46%) were treated with OCS after diagnosis (Table1). The patients had median 1 episode (IQR 1-3) of OCS exposure with median duration of 45 days (IQR 14-142). The crude incidence rate of any AESI was 1.57 (95%CI: 1.5-1.65) per patient-year during OCS exposure and 0.57 (0.56-0.59) during non-exposure (Table2). Adjusted frailty models identified significantly increased hazard of any AESI during OCS exposure for all OCS dosages, low: 2.45 (2.24-2.67), medium: 2.24 (2.03-2.46), high: 2.56 (2.32-2.82). Increased hazards were also observed for each of the AESIs evaluated including cardiac and bone events (Figure1).

Table 1. Myasthenia gravis patient demographic and clinical characteristics. Baseline comorbidities reported in the 1 year prior to index date. Baseline OCS patients were defined as patients who started OCS within 90 days of index date, and non-OCS patients were defined as patients not receiving OCS OR starting OCS after 90 days.

Characteristic	Overall MG N = 3,839	Baseline OCS Use* N = 1,083	No Baseline OCS Use* N = 2,756
Patient Demographics			
Age at Diagnosis (Mean, SD)	68.08 (14.62)	68.27 (13.96)	68.01 (14.87)
Female Sex (n, %)	1,922 (50%)	495 (46%)	1,427 (52%)
Follow-up Time (Years, Mean, SD)	2.06 (1.68)	2.09 (1.67)	2.05 (1.68)
Health Insurance Type (n, %)			
Commercial	1,129 (29%)	308 (28%)	821 (30%)
Medicare	2,710 (71%)	775 (72%)	1,935 (70%)
US Region (n, %)			
Midwest	749 (20%)	223 (21%)	526 (19%)
North	544 (14%)	134 (12%)	410 (15%)
South	1,956 (51%)	527 (49%)	1,429 (52%)
West	580 (15%)	197 (18%)	383 (14%)
Race (n, %)			
Asian	124 (3.4%)	33 (3.2%)	91 (3.4%)
Black	355 (9.7%)	106 (10%)	249 (9.4%)
Hispanic	396 (11%)	114 (11%)	282 (11%)
White	2,802 (76%)	779 (75%)	2,023 (76%)
Comorbidities			
Charlson Comorbidity Score (Mean, SD)	1.73 (2.24)	1.84 (2.33)	1.69 (2.20)

*OCS use includes patients who started OCS within 90 days of index date, and 'No OCS Use' includes patients not receiving OCS OR starting OCS after 90 days.

Table 2. Crude Incidence Rates and Ratios of Adverse Events of Interest. Incident rates reported as event/person-years.

Event	Incidence Rate (No OCS-exposure, 95%CI)	Incidence Rate (OCS-exposure, 95% CI)	IRR (95% CI)
Any Adverse Event	0.57 (0.56 - 0.59)	1.57 (1.50 - 1.65)	2.74 (2.59 - 2.9)
Congestive Heart Failure	0.13 (0.12 - 0.13)	0.33 (0.30 - 0.37)	2.64 (2.33 - 2.98)
Hypertension	0.02 (0.01 - 0.02)	0.02 (0.02 - 0.04)	1.57 (1.01 - 2.37)
Endocrine	0.01 (0.01 - 0.01)	0.05 (0.04 - 0.06)	4.07 (2.86 - 5.75)
Bone	0.05 (0.05 - 0.06)	0.12 (0.10 - 0.14)	2.20 (1.80 - 2.68)
Muscle and Tendon	0.06 (0.05 - 0.06)	0.09 (0.08 - 0.11)	1.70 (1.36 - 2.10)
Eye	0.22 (0.21 - 0.24)	0.45 (0.41 - 0.49)	2.01 (1.82 - 2.23)
Glucose Tolerance	0.24 (0.22 - 0.25)	0.7 (0.66 - 0.76)	2.98 (2.73 - 3.25)
Gastrointestinal	0.02 (0.02 - 0.02)	0.04 (0.03 - 0.05)	1.94 (1.34 - 2.73)
Skin	0.19 (0.18 - 0.20)	0.35 (0.31 - 0.38)	1.87 (1.66 - 2.09)
Neuropsychiatric	0.25 (0.24 - 0.27)	0.55 (0.51 - 0.59)	2.15 (1.96 - 2.36)
Infection	0.11 (0.10 - 0.12)	0.28 (0.25 - 0.31)	2.52 (2.20 - 2.88)
Other	0.12 (0.11 - 0.13)	0.26 (0.24 - 0.3)	2.17 (1.90 - 2.48)

OCS: oral corticosteroid, IRR: incidence rate ratio, CI: confidence interval.

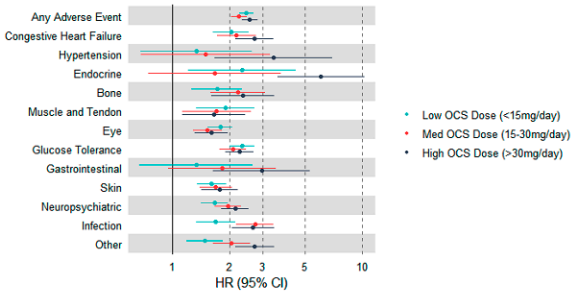

Figure 1. Adjusted frailty model results for hazard ratios of adverse events with OCS-exposure.

Reference group: Non-OCS exposed period.
OCS: oral corticosteroid.
Frailty models adjusted for time-varying OCS exposure (by prednisone equivalent daily dose) and concomitant medication (IVIg, IST, and PLEX) use as well as other fixed covariates (age, sex, race, region, payer, Charlson Comorbidity Index, and OCS use in the 1 year prior to MG diagnosis).

Conclusion: OCS exposure was associated with significantly increased hazard of AESIs in MG patients. Steroid-sparing immunotherapies for the underlying disease are needed in this population.

Disclosure: Sicong Huang, Sindhu Ramchandren, Kristin Heerlein, Hemanth Kanamedala are or were employees of Janssen Pharmaceuticals and may own stock in Johnson & Johnson. Lauren Wilson, Xin Zhao, Amanda Howarth, Carlos Flores are or were employees of Genesis Research.

Cognitive neurology/neuropsychology

EPO-057

Frequency of depressive and anxious symptoms in patients with Subjective Cognitive Complaints

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Background and aims: Subjective Cognitive Complaints (SCC) are frequent in Neurology. They may be defined as the self-perception of cognitive decline without objective deficits in neuropsychological tests. SCC have been associated with a poorer cognitive performance, a higher risk of developing Cognitive Impairment or Dementia as well as with neuropsychiatric symptoms such as depression and anxiety. Depression and anxiety are frequent mental health issues, with a remarkable impact in cognitive function. An increase in prevalence in both of them is estimated during COVID-19 pandemic. The objective is to report the frequency of depression, anxiety symptoms in a population with SCC.
Methods: We selected patients with cognitive complaints and normal neuropsychological tests. Demographic data, depressive and anxious symptoms were collected. Anxious symptoms were assessed with the Beck Anxiety Inventory-(BAI) and depressive symptoms with the Beck Depression Inventory-(BDI-II) and the Geriatric Depression Scale-(GDS-15).
Results: 166 patients were included. Mean Age was 63.13 (SD 12.2) years, Mean Education was 11.25 (SD 3.62) years. The frequency of anxiety symptoms was 44.57% (n=74). Depression symptoms were detected in 33.13% (n=55) of the patients.
Conclusion: Our study showed a significant frequency of anxiety and depression symptoms in patients with SCC. This reminds us how valuable it is to assess these symptoms in standard Neuropsychological Testing, in order to take a comprehensive approach of the patients. Future studies will help to determine dementia-developing predictors.
Disclosure: Nothing to disclose.

EPO-058

Experience and needs on social cognition measures in Italian memory clinics: a joint effort of the signature consortium

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Background and aims: Harmonisation of evidence-based neuropsychological protocols among different countries has become a priority for the benefit of researchers, clinicians and most importantly patients. The international SIGNATURE consortium has been recently established to evaluate the use of socio-cognitive measures in memory clinics and define priorities for their implementation in clinical settings.
Methods: An ad-hoc developed survey was launched through the SIGNATURE mailing list (122 members, 90 institutions, 18 countries) to evaluate state-of-the-art, experience and needs in memory clinics. Italian responses were compared to the international scenario.
Results: 406 (104 Italian) responses were collected. Italian respondents were balanced by professional background and geographic distribution. Both in Italy and abroad, all main cognitive domains are routinely assessed in the standard cognitive battery only in a quote of NCD patients. Comparably to the overall scenario, two thirds of Italian respondents use socio-cognitive measures only in selected cases both for major and minor NCDs. Insufficient time for testing is a major obstacle in Italy, while limited availability of standardised measures emerged overall. Experience and needs did not significantly differ in Northern vs Central-Southern Italy, but we found a trend to assess socio-cognitive abilities more in the North.
Conclusion: In memory clinics, social cognition assessment is usually considered in selected cases and it is expendable in case of lack of time. Despite the geographical inhomogeneity in terms of resources, there is an overall strong need for greater knowledge and availability of socio-cognitive harmonised clinical protocols in clinics.
Disclosure: Nothing to disclose.

EPO-059

Atypical onset of an atypical parkinsonism

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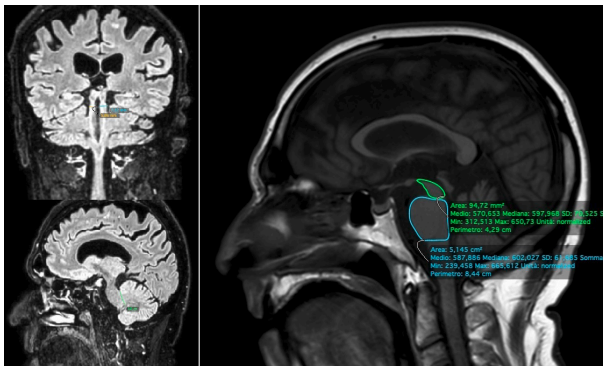
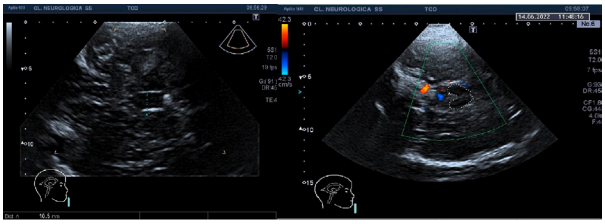
Background and aims: Progressive non-fluent aphasia is a language disorder commonly considered as a form of frontotemporal dementia, but it may also be associated with corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP). A proper differential diagnosis is important to guide treatment strategies and define a correct prognosis. In this setting, neuroimaging can help clinicians to make a more accurate diagnosis. Herein we report a case of a patient with a primary progressive motor speech disorder finally diagnosed as PSP.
Methods: A 63-year-old man with a 10-month history of gradually progressive language disturbance.
Results: Neuropsychological evaluation showed halting speech with sound errors and distortions, alteration of sentence comprehension, normal single-word comprehension and object knowledge. In addition, letter fluency and executive function were impaired, while category fluency was normal. Furthermore, memory deficit and ideomotor apraxia were absent. Neurological examination revealed hypokinetic and spastic dysarthria, up and down gaze palsy, diffuse bradykinesia with reduced right arm swing during walking and upper right limb dystonia. Brain MRI showed mild cortical atrophy and severe midbrain atrophy. Midbrain-to-pons ratio (M/P) was 0,18; Magnetic Resonance Parkinsonism Index (MRPI) was 13,81. Transcranial-ultrasound (TCS) showed absence of substantia nigra hyperechogenicity and third ventricular enlargement.



Brain MRI showed mild cortical atrophy and severe midbrain atrophy. Midbrain-to-pons ratio (M/P) was 0,18 (Cut-off <=0,215); Magnetic Resonance Parkinsonism Index (MRPI) was 13,81 (Cut-off>=13,55).



Transcranial-ultrasound showed absence of substantia nigra hyperechogenicity and third ventricular enlargement (10,5 mm).

Conclusion: Our patient met clinical criteria for diagnosis of "Possible-CBD" but also for "Probable-PSP with predominant frontal presentation" and "Possible-PSP with predominant speech/language disorder". In this case, TCS and quantitative MR planimetric measurements, like M/P ratio and MRPI, lead to a diagnosis of PSP. This case highlighted the essential role of neuroimaging in the differential diagnosis of atypical parkinsonism.
Disclosure: Nothing to disclose.

EPO-060

Accelerated hippocampal atrophy in elderly onset multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) with elderly onset (EO) has been increasingly recognized. Assessing disease-related cognitive and MRI features in elderly patients is extremely challenging, as it is necessary to consider changes due to aging. We aim to identify the distribution of recently defined cognitive phenotype in MS patients with EO and its MRI substrates.
Methods: We enrolled 159 MS patients and 80 healthy controls (HC). All patients underwent neuropsychological evaluation including Rao's brief repeatable battery and Stroop Color Word Test and were classified in cognitive phenotypes (as defined in our previous study: "preserved-cognition", "mild verbal memory/semantic fluency", "mild-multi-domain", "severe-attention/executive", and "severe-multi-domain"). Patients and HC also underwent a 3T MRI examination. Fifty-three MS patients were classified as EO, and remaining ones were equally split in disease duration-(DMS) and age-(AMS) matched groups. We compared prevalence and distribution of cognitive phenotypes across the three groups as well as their MRI features.

Results: Compared to DMS, EOMS patients showed higher frequency of "mild verbal-memory/semantic-fluency" (p=0.02) and lower frequency of "preserved-cognition" (p=0.04). Although not reaching statistical significance a similar trend was also observed when comparing EOMS with AMS patients. Compared to DMS, EOMS patients showed accelerated atrophy of the hippocampus (p=0.05), while no significant differences were observed between AMS and EOMS.
Conclusion: The distribution of cognitive phenotypes showed that EOMS had a prominent involvement of memory and linguistic abilities. These results are in line with the MRI findings of accelerated hippocampal atrophy, thus suggesting that EOMS is likely to affect more severely brain regions susceptible to aging processes.
Disclosure: The Authors report no conflict of interests related to the present manuscript.

EPO-061

Neuropsychiatric symptoms in Idiopathic Brain Calcification

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Background and aims: Idiopathic basal ganglia calcification (IBGC) is a rare neurological disease characterized by the deposition of calcium in the brain, without calcium metabolism abnormalities. Neuropsychiatric symptoms in IBGC are currently poorly defined in literature. The aim of this study is to deepen the knowledge on psychiatric disorders associated with IBGC, providing an accurate description of eleven cases and summarizing information from the review of literature.
Methods: From our clinical database, we selected patients meeting the diagnostic criteria for IBGC and collected demographic, clinical, genetic, and neuroradiological data. We also searched the PubMed database for papers dealing with psychiatric features in IBGC, and the related treatments.
Results: Eight of the eleven patients included in the study reported at least one psychiatric symptom during the course of the disease. The assessment through the HAM-D and HAM-A scale confirmed the presence of mild depression and anxiety as the main psychiatric disturbs associated with IBGC. Data from literature confirmed a significant psychiatric involvement in IBGC. Available case reports mainly concern atypical presentations of IBGC with abrupt onset psychotic symptoms. An in-depth analysis of psychiatric features associated with IBGC is lacking.

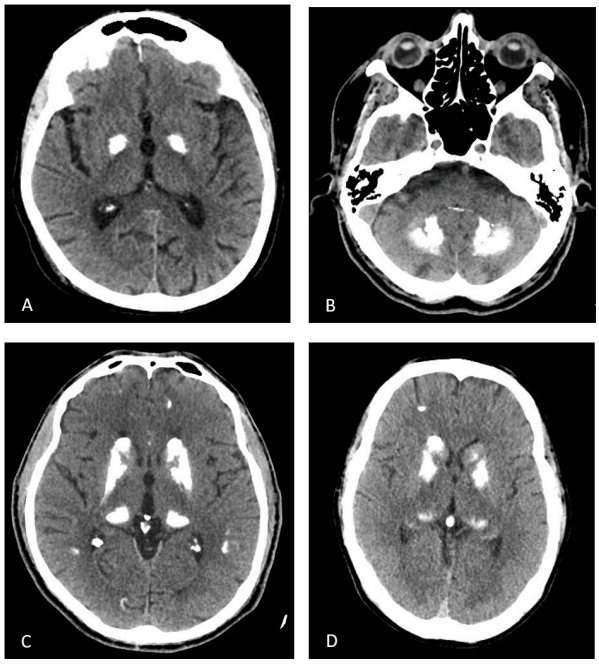

Figure 1. Brain computed tomography scan (CT scan) of PT7 (A), PT8 (B, C), and PT5 (D) showing bilateral symmetrical calcifications in the basal ganglia (A, C, D) and in the cerebellum (B).

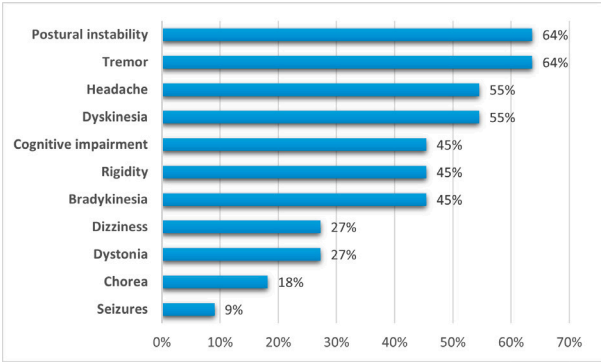

Figure 2. Histogram showing frequency of neurological clinical symptoms by percentage.

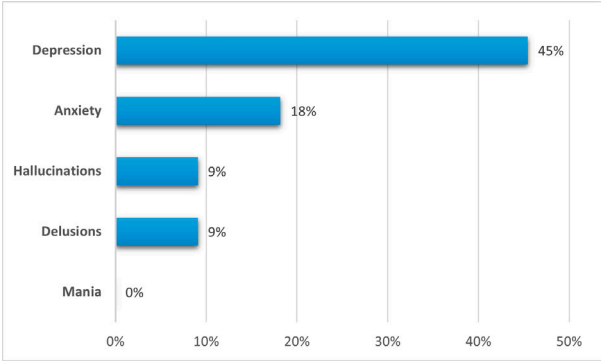

Figure 3. Histogram showing frequency of psychiatric disorders by percentage.

Conclusion: Neuropsychiatric involvement is frequent in IBGC. A neuropsychiatric evaluation is highly recommended in patients with evidence of brain calcifications. Conversely, IBGC should be considered in patients presenting with psychiatric symptoms, especially if movement disorders and neurocognitive impairment are co-existing features.
Disclosure: No conflicts of interest.

EPO-062

Testing the acute cognitive effects of tadalafil: neuropsychological outcomes from the PASTIS trial

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Background and aims: Cerebral small vessel disease (CSVD) is a major cause of cognitive impairment in older people. In a phase-2 randomised clinical trial, we tested the acute effects of a widely-used PDE5 inhibitor, tadalafil, on cognitive performance in older people with CSVD.
Methods: In a double-blinded, placebo-controlled, cross-over trial, participants received tadalafil (20mg) and placebo on two visits ≥7 days apart (randomised to order of treatment). The Montreal Cognitive Assessment (MOCA) was administered at baseline, alongside a measure to estimate optimal intellectual ability, and a battery of neuropsychological tests assessing aspects of attention, information processing speed, working memory and executive function was administered before and after treatment.
Results: Sixty-five participants were recruited and 55 completed the protocol (N=55, age: 66.8 (8.6) years, range 52-87; 15/40 female/male). Median MOCA score at baseline was 26 (IQR: 23, 27], range 15-30. No significant treatment effects were seen in any of the neuropsychological tests. However, there was a trend towards improved performance on forward digit span, a measure of immediate verbal recall considered to index attentional efficiency (treatment effect 0.37, C.I. 0.15, 0.63; P=0.052).
Conclusion: There was no significant acute treatment effect of single dose tadalafil on neuropsychological performance in older people with CSVD. The trend observed on forward digit span indicates that performance on this measure of attentional efficiency may be more malleable than previously thought and provides effect sizes useful for further research.
Disclosure: Dr Isaacs has received a speaker's fee from Biogen and consultancy fees from Roche and Nestle Health Science, all paid to his institution and unrelated to the current work. He has received conference registration and expenses from Roche. Dr Kruuse has received funding from NovoNordisk, Bayer and Bristol-Myers-Squibb, none relevant to the present trial. Dr Hainsworth has received honoraria from Eli Lilly.

EPO-063

Sensitivity of the TMA-93 for diagnosis of early Alzheimer's disease according to age and cognitive reserve

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Background and aims: TMA-93 examines relational binding by images. New norms based on age and cognitive reserve have recently been developed for the test. The aim was to analyze the sensitivity of these new norms for diagnosing early AD.
Methods: Retrospective analysis of a Biobank database associated to the Outpatient Memory Clinic of a tertiary hospital in Southern Spain. Patients' records initially consulted for memory complaints, scored MMSE≥22, and had the TMA-93 and the Cognitive Reserve Questionnarie (CRC) administered, and AD biomarker determination (Amyloid-PET or CSF) done, either positive or negative, were selected. As cutoffs, TMA-93 total scores for the 10-percentile (P10) according to the new norms were considered. Crosstabs were made up for sensitivity analysis: rows, TMA-93 positive (≤ P10) vs. negative (>P10) results; columns, positive vs. negative AD biomarkers.
Results: 188 patients were included [median age 70.5±6.4 years (range 52-84); 47.9% female; 135 (71.8%) positive AD biomarkers, 53 (28.2%) negative AD biomarkers. Tests total scores (median/interquartile range/range) were: MMSE (25/23-27/22-29), CRC (10/7-13/1-23), TMA-93: (21/14-25/0-30). The sensitivity for P10/TMA-93 was

74.1%. False negatives (25.9%) were more frequent if MMSE >24, CRC<10, age>72 and/or total TMA-93 score ≥21.
Conclusion: Sensitivity of 74.1% for diagnosing early AD in a representative but heterogeneous sample of patients referred to a Memory Clinic of a tertiary hospital is a new good result for the TMA-93. False negative are mainly distributed among less cognitively impaired elderly with lower cognitive reserve.
Disclosure: Maillet is the autohor of the TMA-93 Esteve supported the work.

EPO-064

Identification of cognitive phenotypes in pediatric multiple sclerosis using unsupervised machine learning

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Background and aims: Cognitive impairment affects approximately one-third of pediatric multiple sclerosis (PedMS) patients. Despite the high variability in neuropsychological manifestations, previous research has focused on the dichotomous classification of impairment. Aim of this study was to identify cognitive phenotypes in PedMS using an unsupervised machine learning approach and to characterize their clinical and MRI features.
Methods: Seventy-three PedMS patients and 30 healthy controls underwent 3.0T MRI and clinical examination including Expanded Disability Status Scale (EDSS). MRI analysis included quantification of T2-lesion volumes and normalized brain volumes assessment. A comprehensive neuropsychological battery (Wechsler Scale, Selective Reminding Test, Spatial Recall Test, Trail Making Test, Symbol Digit Modalities Test and Semantic and Phonemic verbal fluency test) was administered to all patients. K-means cluster analysis was used on cognitive tests z-scores to identify cognitive phenotypes.
Results: A three-clusters solution was selected including a "preserved cognition" cluster (27 patients [37%]), a "mild verbal memory/semantic fluency involvement" cluster (28 patients [38%]) and a "multidomain involvement" cluster (18 patients [25%]). Across groups, there were no significant differences in age, sex and disease duration. Compared to other groups, patients with multidomain involvement had higher EDSS scores, lower IQ, higher T2-lesion volume, lower normalized brain volume, lower normalized gray matter volume, lower normalized white matter volume and lower normalized deep gray matter volume.
Conclusion: PedMS patients present with distinct cognitive phenotypes ranging from preserved cognition to multidomain involvement. Cognitive phenotypes are not associated with age, sex and disease duration but are associated with physical disability and measures of brain structural damage.
Disclosure: The authors have nothing to disclose.

EPO-065

Encephalopathy with a reversible lesion in the splenium of the corpus callosum in adults

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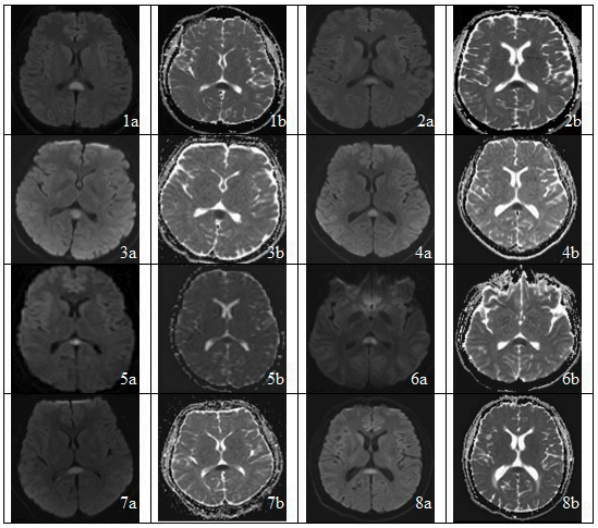
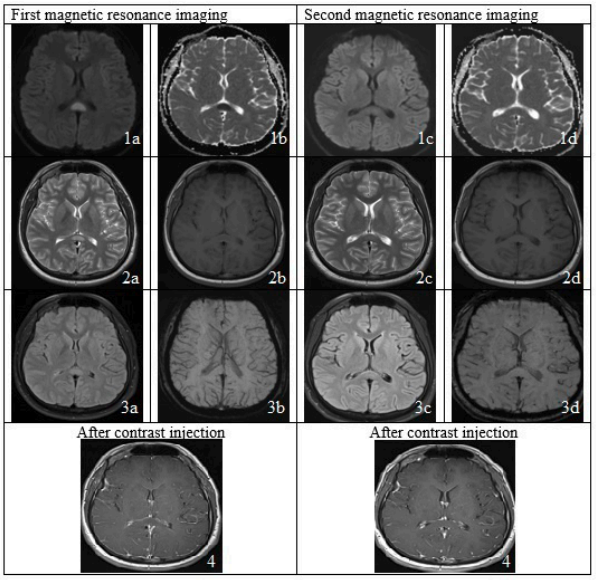
Background and aims: Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a clinico-radiological syndrome involving the splenium of the corpus callosum. This lesion is typically observed in the corpus callosum on magnetic resonance imaging (MRI) and it usually disappears in a few weeks. There are few case reports in the literature. We have reported twelve adult patients with MERS associated with infection and/or epilepsy. Also we have described the clinico-radiological features of these patients.
Methods: The patients' ages, genders, clinical and radiological features, laboratory data, treatment strategies and prognoses were demonstrated.
Results: There were seven male and five female patients in the case series. All of the patients had the fever. There was a history of upper respiratory tract infection in seven patients, visual loss episodes in three patients, epileptic seizure in two patients, arthroplasty in two patients, and cardiac arrhythmia (atrial fibrillation) in one patient.
Conclusion: Focal diffusion was restricted in the splenium of the corpus callosum on the diffusion-weighted MRI. Corpus callosum lesions resolved on diffusion MRI and clinical symptoms improved on follow-up. Thus, it is important to consider MERS as one of the differential diagnoses in adult patients with fever and cognitive changes.
Disclosure: Nothing to disclose.





EPO-066

Regression of post-stroke hemianopia with zolpidem: insights from neuropsychology, EEG, and tDCS

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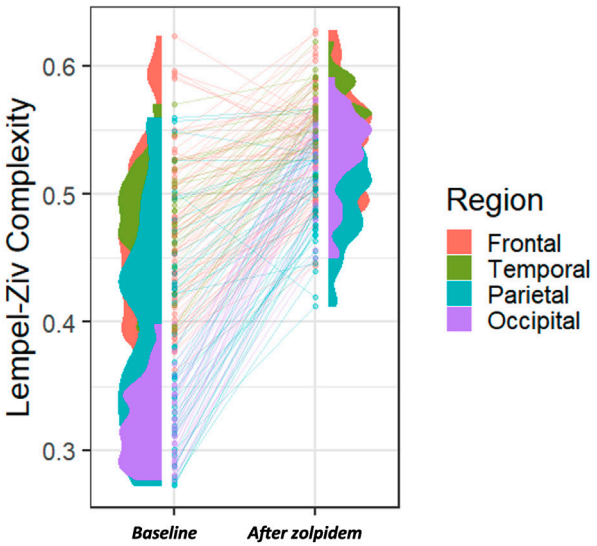
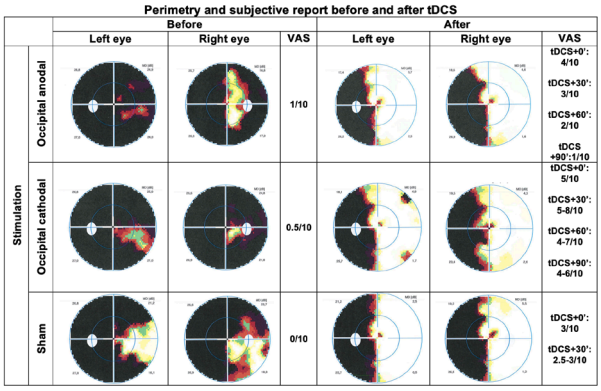
Background and aims: Humans are visual animals, and visual impairments significantly impact patients' quality of life. Here, we present the case of a patient with chronic acquired hemianopia due to occipital stroke, who demonstrates transient visual improvement after intake of zolpidem. We used neuropsychological testing, EEG, and tDCS to investigate its neural mechanisms.

Methods: We tested for neglect via a dedicated battery before and after zolpidem. High-density EEG was recorded at baseline, while taking zolpidem, when zolpidem effects were stable, and when effects started fading. We calculated regional Lempel-Ziv complexity (LZC)[1] and whole-brain alpha power. Finally, we stimulated the occipital cortex with tDCS in 3 sessions (anodal, cathodal, and sham) without zolpidem, controlling for effects with an automated static visual perimetry.

Results: The neuropsychological examination was not in favor of neglect. The post-zolpidem EEG showed decreased alpha and increased LZC compared to baseline, particularly in parietal and occipital regions. We observed a concurrent decrease of alpha while sight improved, but no effect of alpha as effects faded. The patient reported sight recovery with both anodal and cathodal occipital tDCS stimulation (strongest effects with cathodal stimulation). Nevertheless, the patient also reported visual amelioration after sham, of shorter duration.



We observed an increase of LZC all over the cortex after zolpidem compared to baseline. The effect is particularly pronounced in the occipital and the parietal cortex. LZC was calculated over time per each electrode, then averaged across trials.



Subjective effects (A) and perimetry (B) before and after the three sessions of tDCS (occipital anodal, occipital cathodal, and sham). Legend: VAS = visual analogue scale; tDCS = transcranial direct current stimulation.

Conclusion: The results suggest that zolpidem-mediated sight improvements operate on visual impairments rather than attentional deficits, in line with increased occipital metabolism previously described.[2] EEG results hinted a possible role of alpha. While tDCS partially reproduced zolpidem effects, sham stimulation demonstrated a concurrent psychological component. Future work should investigate the underlying mechanism of zolpidem-induced effects on vision.
Disclosure: The authors report no conflict of interest.

EPO-067

Altered dynamics of statistical learning due to the manipulation of rapid consolidation periods

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Background and aims: Traditionally, the time scale of hours or days has been used to study memory consolidation processes. However, the most recent advances in memory research demonstrated that memory consolidation processes could take place even within seconds, probably due to the neural replay of freshly practiced memory traces during short breaks. Here, we investigate this quick form of consolidation during statistical learning. We seek to determine (a) if general skill learning and statistical learning both benefit from this rapid consolidation and (b) whether the length of rest periods has a different impact on these two forms of learning.
Methods: Participants completed the Alternating Serial Reaction Time (ASRT) test, a commonly used statistical learning paradigm that allows us to independently measure implicit statistical and general skill acquisition. The ASRT task had rest breaks between its 25 learning blocks. In a between-subjects design, the duration of the rest periods was either set at 15 or 30 seconds, or the participants could choose their own duration.
Results: According to our findings, while the duration of rest periods does not impact the extent of statistical learning, it does alter the dynamics of learning. Shorter rest times resulted in improved learning during the learning blocks, whereas longer rest periods—possibly because of more replay—promoted learning also in the between-block rest periods. Furthermore, we found that the self-paced group learned general skills less effectively than the fixed rest period groups.
Conclusion: Our results imply that distinct learning and consolidation processes are affected differently by the length of short rest periods.
Disclosure: From a methodological perspective, our findings also demonstrate the relevance of evaluating the temporal dynamics of learning and not only giving a broad indication of the overall learning across the task.

EPO-068

High frequency multimodal training for improving motor and cognitive function in people with Parkinson's disease

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Background and aims: Cognitive decline is an important and common complication in patients with Parkinson's disease (PD) since it significantly reduces the quality of life. A breakthrough in the prevention of cognitive decline in PD remains to be achieved. This study aimed to evaluate the effectiveness of a high-frequency multimodal training in improving motor and cognitive function.
Methods: 28 patients diagnosed with idiopathic PD completed a comprehensive neuropsychological test battery and were neurologically examined. The patients of the intervention group (n=15, including 26.6% women; mean (SD) age = 63y (59y-75y)) underwent two weekly sessions of Tai Chi therapy over 4 weeks and carried out an individually tailored training program consisting of two modules: smartphone-based speech and cognitive training A matched control group consisted of n=13 patients with PD who received computer-assisted cognitive training. The data were analyzed with repeated-measures ANOVA.
Results: Four weeks of high-frequency training showed significant effects within the intervention group on verbal episodic memory: 〖ηp〗^2=.25; p=0.01 [95% CI-1.35; -0.24] and visual-spatial function: 〖ηp〗^2=0.38;p=0.00 [95% CI-0.78;-0.26]. The significant improvement was also shown in the Tinetti mobility test: r=0.85; p=0.00; [95% CI 9; 14.5]. The significant effects in verbal episodic memory, visual-spatial function and Tinetti mobility test remained after 6 months follow-up. Compared to the control group, the cognitive performance of the intervention group improved significantly in visual-spatial function: 〖ηp〗^2=0.15; p=0.04 [95% CI-0.47;1.38].
Conclusion: In patients with PD, a multimodal training program not only improves gait and stability but may also contribute to improvement of cognition.
Disclosure: Nothing to disclose

EPO-069

Musical Perception in Neurodegenerative Disorders, a Pilot Study

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Background and aims: According to recent studies, patients with Alzheimer's Disease (ADD) indicate attenuated melody processing and a reduced ability to perceive changes in amplitude and rhythm, while patients with Parkinson's Disease (PD), seem to have difficulties in rhythm perception and production. This study aimed to investigate whether patients with ADD and PD have deficits in the perception of melody, rhythm, and musical excerpt recognition as measured by the Montreal Battery of Evaluation of Amusia test (MBEA). Another objective was to explore the possible correlation of musical perception with other cognitive functions.
Methods: Musical perception was assessed to 10 patients with ADD, 10 patients with PD, and 10 healthy older adults. In addition, a neuropsychological assessment was performed including Addenbrooke's Cognitive Examination, Digit Span forward & backward, and Hopkin's Verbal Learning test – revised (HVLT-R).
Results: Patients with ADD performed worse than patients with PD and healthy individuals in the perception of melody and musical excerpt recognition but outperformed patients with PD in rhythm perception. The control group indicated higher scores in all musical perception scores than patients with ADD and PD. A strong positive correlation was found between the musical excerpt recognition and the total score of the verbal episodic memory test (HVLT-R) [rho (28) =.619], the short-term verbal memory (Digit Span Forward) [rho (28) =.481], and the verbal working memory test (Digit Span Backward) [rho (28) =.643].
Conclusion: Musical perception is affected differently in ADD and PD. Musical recognition is also strongly related to verbal episodic, short-term verbal, and verbal working memory tests.
Disclosure: Nothing to disclose.

EPO-070

Higher degree of cognitive impairment in late-onset compared to adult-onset MS patients with similar disease duration

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Background and aims: Cognitive impairment affects more than 70% of patients with multiple sclerosis (MS). This study aimed to investigate whether late-onset MS patients (LOMS, age at MS diagnosis >= 45 years) experience more cognitive impairment compared to adult-onset MS (AOMS) patients.
Methods: Participants were recruited from two Italian MS centers. Disease duration was capped at six years from MS diagnosis. All participants underwent an extensive neuropsychological test battery including the Symbol Digit Modalities Test (SDMT), Selective Reminding Test (SRT), Paced Auditory Serial Addition Test (PASAT), and Spatial Recall Test (SPART). Participants filled out questionnaires on fatigue (FSS) and depression (MADRS). To perform between-group comparisons, we used pairwise Wilcoxon tests with Holm-Bonferroni corrections. Patients with more than two abnormal tests were considered cognitively impaired.
Results: We included 139 AOMS, 39 LOMS and 169 healthy controls (HC). 20.5% of LOMS and 11.5% of AOMS were cognitively impaired (impairment in >= 2 cognitive domains). LOMS showed higher degree of cognitive impairment on the SDMT, SRT recall and SPART ($p < 0.01$ for all) compared to AOMS and HC ($p<0.01$ for all). No differences between AOMS and LOMS were found on the PASAT ($p>0.05$). Depression and fatigue did not differ between LOMS and AOMS ($p>0.05$ for all), but when compared to HCs ($p<0.01$).
Conclusion: LOMS were more frequently impaired on information processing speed, visuospatial memory and verbal learning and memory compared to AOMS with similar disease duration. Early cognitive intervention and rehabilitation are crucial in LOMS to prevent further cognitive decline.
Disclosure: AW received an ECTRIMS-MAGNIMS fellowship to pursue this research. All other authors report no conflicting interest regarding this abstract.

Headache 1

EPO-071

Relation of post-stroke headache to cerebrovascular pathology and hemodynamics

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Background and aims: Despite the high prevalence of cerebrovascular stroke, headache attributed to ischemic strokes is often undertreated and overlooked. The aim is to detect the relation of a post-stroke headache to cerebrovascular pathology and changes in hemodynamics through a high-resolution duplex ultrasound examination.

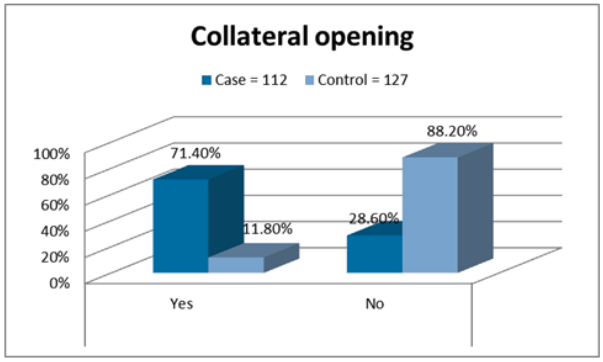
Methods: This is a case-control study that was conducted from January 2021 to August 2021.The study was conducted on 239 patients who presented with an acute ischemic stroke. Patients were subdivided into two groups; Group I included 112 patients with headache attributed to ischemic stroke (cases) and Group II included 127 headache-free stroke patients (controls). History included headache characteristics and risk factors. Clinical and radiological examination were preformed to detect the type of stroke. Ultrasound duplex examination of the extracranial and intracranial cerebrovascular system was carried for both groups.

Results: Post-stroke headache was more frequent in patients with posterior circulation infarction (58%). Post-stroke headache was reported within 7 days post-stroke in (61.6%) of patients. Pre-stroke headache was an independent predictor for post-stroke headache occurrence (OR=28.187, 95%CI; 6.612-120.158, P<0.001). Collateral opening and various degrees of intracranial vascular stenosis were strong predictors of headache occurrence (OR=25.071, 95% CI; 6.498-96.722, P<0.001).

Conclusion: Post-stroke-headache is a common phenomenon especially in patients with pre-stroke headache, history of old stroke, posterior circulation infarction, and large artery disease. The intracranial cerebrovascular pathological changes including opening of the collateral channels and variable degrees of stenosis of cerebrovascular systems were implicated in the production of that headache.

Disclosure: The authors declare that there was no conflict of interest.

Character, n (%)	Headache patients (n=112)
Pulsatile	30 (26.8%)
Stabbing	4 (3.6%)
Tighting	78 (69.6%)
Intensity, n (%)	
Moderate	82 (73.2%)
Severe	30 (26.8%)
Location, n (%)	
Anterior	57 (50.9%)
Posterior	35 (31.3%)
Diffuse	20 (17.9%)
Side, n (%)	
Ipsilateral to Infarction	65 (58%)
Contralateral to Infarction	15 (13.4%)
Unilateral alternating	7 (6.3%)
Bilateral	25 (22.3%)
Association, n (%)	
Nausea and Vomiting	46 (41.1%)
Photophobia	30 (26.8%)
Phonophobia	12 (10.7%)



Multivariate logistic regression to detect independent predictors of post-stroke headache				
Predictor variables	**OR**	**95% C.I.**		**P value**
		Lower	**Upper**	
Pre-stroke Headache	28.187	6.612	120.158	< 0.001
PCA stenosis <50%	84.657	10.418	687.947	< 0.001
VA4 stenosis <50%	842.472	50.262	14121.06	< 0.001
Intracranial cerebrovascular system pathological changes	25.071	6.498	96.722	< 0.001
Collateral opening	60.826	13.003	284.541	< 0.001

PCA, posterior cerebral artery; VA4, vertebral artery segment 4.
$p<0.05$ was considered statistically significant.

EPO-072

Neurophysiological and neuroimaging characteristics in migraine with visual aura

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Background and aims: Activation of the trigeminovascular system with trigeminal nuclei sensitization play a significant role in the migraine pathophysiology. The cortical spreading depression (CSD) underlying migraine aura may cause structural changes in the brain. We investigated the differences in the neurophysiological and MRI data between migraine patients with and without aura.

Methods: 48 migraine patients were examined during headache-free periods: 21 with visual aura (1st group) and 27 -without aura (2nd group). We used blink reflex (BR), sympathetic skin response (SSR) and MRI voxel-based morphometry (MRIvm).

Results: There were no differences between groups in male to female ratio, age and disease duration. However, in the 1st group, migraine attacks were observed more often, and they were shorter than in 2nd group. No differences were found between 1st and 2nd groups when comparing the all BR parameters. But compared to controls, migraine patients revealed an amplitude increase in the both BR components. Using SSR, sympathetic activity predominance was observed more often in the1st group(80,9%) compared to 2nd(62,9%) and control(50%). MRIvm demonstrated grey matter reduce in the pain processing areas in the both groups. Additionally, a volume increase in the structures responsible for visual information processing was observed in the 1st group (table).

Conclusion: The migraine patients have a sympathetic activity predominance, a supraspinal descending control deficiency on the brainstem and reduction in the structures volume involved in pain processing. Repetitive CSD with regional cortical hyperexcitability have long-term effects on the areas involved in the visual aura formation and leads to an increase in their volume.

Disclosure: Nothing to disclose.

Parameters	Control group n = 20	1st group (migraine patients with visual aura) n = 22	2nd group (migraine patients without visual aura) n = 26
	Median (IQR)		
Age, years	34 (20 – 44)	34 (22 – 43)	36 (21 – 44)
male to female ratio (M/F)	8/12	8 / 14	9/17
Disease duration, years		15 (7 - 19)	17 (8 – 20)
Migraine attacks duration, min		4 (2 – 7)	7 (4 – 11)*
Migraine attacks frequency, per month		2 (1 – 2)	1 (0,5 – 1,5)*
Headache intensity, visual analog scale		6 (5 – 8)	7 (5 – 8)
Values of the BR amplitudes			
A R1 ipsilat., mV	0,2 (0,1 – 0,3)	0,3 (0,2 – 0,4) Δ	0,4 (0,2 – 0,5)
A R2 ipsilat., mV	0,3 (0,2 – 0,4)	0,5 (0,3 – 0,8) Δ	0,6 (0,4 – 0,8)
A R2 contralat., mV	0,3 (0,2 – 0,4)	0,5 (0,3 – 0,7) Δ	0,5 (0,3 – 0,8)
Brain MRI measurements (mm3)			
Left amygdala	1485 (1358 - 1588)	1254 (1184 – 1368) Δ	1286 (1193 – 1373)
Right amygdala	1450 (1285 - 1583)	1307 (1174 – 1395) Δ	1275 (1188 – 1380)
Left postcentral gyrus	8378 (7591- 9737)	7579 (7253 – 85650) Δ	7680 (7174 - 8674)
Right postcentral gyrus	8300 (7633 - 9026)	7499 (7296 – 8648) Δ	7365 (6942 - 8894)
Left superior parietal lobule	13203 (10974 – 14958)	14210 (11274 -16649)	12868 (12065-13547) *
Right superior parietal lobule	13195 (10854 – 14839)	14306 (12857 - 16835)	13135 (11974-14783)
Left cuneus	3024 (2847-3212)	3514 (3368 – 3696)	3117 (2754 – 3372) *
Right cuneus	3118 (2893-3249)	3537 (3402 – 3692)	3164 (2929 -3243) *
Left lingual gyrus	6297 (5738 – 6398)	6997 (6237 – 7174)	6198 (5665 – 6468) *
Right lingual gyrus	6292 (5847 – 6458)	7097 (6347 – 7258)	6371 (5772 – 6542) *

IQR - interquartile range
* - Statistically significant difference ($p < 0.05$) between 1st and 2nd groups (Mann–Whitney test);
Δ - Statistically significant difference ($p < 0.05$) between control, 1st groups and 2nd groups (Kruskal–Wallis test)

Table. Comparative assessment of the patients with migraine and healthy controls

EPO-073

Frequency and impact of headache in transgender women patients: a pilot study.

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Background and aims: There are still uncertain data in the literature about the prevalence of headache in the transgender women population, as well as the impact of hormone replacement therapy. The objective of our study is to compare the prevalence, intensity, and impact of headaches in the transgender women population in comparison to cisgender women.

Methods: This study was a case-control observational pilot study. It was conducted at an outpatient endocrinology clinic, a reference in transgender patient care, in a tertiary university hospital in the northeast of Brazil. Samples were age-matched. Inclusion criteria were transgender with estrogen replacement. Exclusion criteria were cisgender pregnant women and cisgender women with amenorrhea. Headache impact was measured by the Headache Impact Test (HIT-6) scale and depression and anxiety were measured by The hospital Anxiety and Depression Scale (HADS).

Results: We analyzed 50 patients, 25 transgender women patients, and 25 cisgender women in the control group. The median age was 35 for each group. The intensity median in the transgender women group was 7,0(P25:7,0 -P75:9,0) and in the cisgender group was 6,0(P25:5,5 -P75:8,0). We found higher frequency rates of headache impact(52%vs40% - Pvalue:0,002), anxiety(52%vs36%- Pvalue:0,260), and depression (24%vs12%- Pvalue:0,274) in the transgender women sample.

Characteristics		Transgender women (n= 25)	Cisgender women (n= 25)	P value	OR (CI 95%)
Age (years)	Mean (P_{25}; P_{75})	35 (25; 39)	35 (28; 45)	0,155	
Headache in the last 12 months n (%)	Yes No	22 (88%) 3 (12%)	25 (100%) 0 (0%)	0,076	Undefined (0,60-undefined)
Episodes headache number (days/3 months)	Mean (P25; P75)	5 (2; 12)	8 (2,5; 12)	0,762	
Headache intensity (EVN[1])	Mean (P25; P75)	7 (7; 9)	6 (5,5; 8)	0,011	
Migraine n (%)	Yes No	11 (44%) 14 (56%)	14 (56%) 11 (44%)	0,400	1,60(0,51-5,06)
Tension type headache n (%)	Yes No	9 (36%) 16 (53%)	11 (44%) 14 (56%)	0,567	1,38 (0,43-4,46)
Headache impact (HIT-6[2]) n (%)	Impact	13(52%)	10 (40%)	0,002	0,62(0,195-1,92)
Ansiety (HAD-A[3]) n (%)	Yes No	13 (52%) 12 (48%)	9 (36%) 16 (64%)	0,260	0,52 (0,16-1,64)
Depression (HAD-D[3]) n (%)	Yes No	6 (24%) 19 (76%)	3(12%) 22 (88%)	0,274	0,43(0,08-2,01)

Table 1 - Characterization of the sample

Conclusion: We observed a higher rate of impact of headache and intensity in the transgender women group, and a higher rate of anxiety and depression in the transgender women group, without statistical significance difference. We conduced a pilot study and type II error is a possibility.
Disclosure: We do not have conflicts of interest to declare.

EPO-074

Primary headache in transgender men: a pilot study.

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Background and aims: The prevalence of headaches in transgender individuals on crossed hormone replacement therapy is not well established in the literature. The study's main objective is to analyze the prevalence and impact of headaches among transgender men on gender-affirming hormone therapy.
Methods: This study was a case-control observational pilot study. It was conducted at a reference outpatient endocrinology clinic in a tertiary university hospital. The sample was age-matched. Inclusion criteria were composed of transgender men patients on gender-affirming hormone therapy. Exclusion criteria were individuals with previous use of anabolic steroids and pregnant transgender men. The intensity was measured by the Visual Analogue Scale(VAS). Headache Impact Test(HIT-6) was used to estimate the headache impact. The hospital Anxiety and Depression Scale(HADS) was used to diagnose anxiety and depression.
Results: The total number of study participants was 50 men, and 25 of them were transgender. The median age of the sample was 30 years old(P25=25;P75=36) among transgender men and 32 years old(P25=26;P75=40) among cisgender men. We found a statistical difference of intensity between the two groups, with a median intensity in transgender men group of 7(P25=5;P75=8,5) and the median of cisgender men group was 5(P25=4;P75=6) Pvalue:0,005. Transgender men had a significantly higher rate of headache impact 52,0%vs12,0%(CI0.22-0.53;pvalue:0,002) and a higher frequency of anxiety 56,0%vs25,0%(CI=0.07-0.85–pvalue:0,028) and depression 36,0%vs 00,0% (CI=0.00-0.29 – p value:0,001).

Characteristics		Trangender women (n= 25)	Cisgender women (n= 25)	P value	OR (CI 95%)
Age (years)	Mean (P_{25}; P_{75})	30 (25; 36)	32 (25; 40)	0,491	
Headache in the last 12 months n (%)	Yes No	22 (88%) 3 (12%)	24 (96%) 1 (4%)	0,302	3,20 (0,32-89,49)
Episodes headache number (days/3 months)	Mean (P25; P75)	6 (1; 27)	3 (1; 6)	0,158	
Headache intensity (VAS[1])	Mean (P25; P75)	7 (5; 8,5)	5 (4; 6)	0,005	
Migraine n (%)	Yes No	14 (56%) 11 (44%)	8 (32%) 17 (68%)	0,091	0,37 (0,11-1,20)
Tension type headache n (%)	Yes No	8 (32%) 17 (68%)	16 (64%) 9 (36%)	0,025	3,67 (1,14-12,53)
Headache impact (HIT-6[2]) n (%)	Impact	13 (52%)	3 (12%)	0,002	0,13 (0,02-0,53)
Ansiety (HAD-A[3]) n (%)	Yes No	14 (56%) 11 (44%)	6 (25%) 19 (75%)	0,021	0,25 (0,07-0,85)
Depression (HAD-D[3]) n (%)	Yes No	9 (36%) 16 (64%)	0 25 (100%)	< 0,001	0,00 (0,00-0,29)

Table 1 - Characterization of the sample.

Conclusion: We found a higher prevalence of TTH among cisgender men and a higher rate of impact of headache among transgender men, as well as higher rates of anxiety and depression.
Disclosure: We do not have conflicts of interest to declare.

EPO-075

Real-world effectiveness of switching to fremanezumab from other CGRP pathway targeting mAbs: PEARL 3rd interim analysis

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Background and aims: Patients who do not benefit from or tolerate preventive migraine treatment with a monoclonal antibody (mAb) targeting the calcitonin gene-related peptide (CGRP) pathway may benefit from switching to another; however, effectiveness data on this are limited and granular.

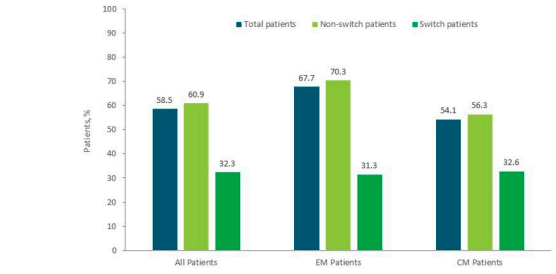
Methods: PEARL (EUPAS35111) is an observational, prospective, Phase IV study, evaluating the effectiveness of fremanezumab for migraine prevention in adults with episodic or chronic migraine (EM, CM). Patient data are recorded through daily headache diaries, including information on past-preventive treatment. This third interim analysis was conducted when all enrolled patients had completed >=6 months of treatment, and this sub-analysis explored the proportion of switch patients (previously treated with another mAb targeting the CGRP pathway) achieving >=50% (EM and CM) and >=30% (CM only) reduction in monthly migraine days (MMD) during the 6 months post-fremanezumab initiation.

Results: Of 732 patients with available data, 62 were switch patients (Table 1). One patient had been previously treated with galcanezumab, 59 with erenumab and two with galcanezumab and erenumab on separate occasions. During the first 6 months of fremanezumab treatment, 20 switch patients (32.3%) achieved >=50% MMD reduction, with similar proportions for EM and CM patients (Figure 1). Notably, 28 patients (60.9%) with CM achieved >=30% MMD reduction (Figure 2).

	Total patients (N=62)	EM patients (n=16)	CM patients (n=46)
Switch due to lack of efficacy, n (%)	26 (41.9)	6 (37.5)	20 (43.5)
Switch due to reasons other than 'lack of efficacy', n (%)	36 (58.1)	10 (62.5)	26 (56.5)

CGRP, calcitonin gene-related peptide; CM, chronic migraine; EM, episodic migraine; mAb, monoclonal antibody.

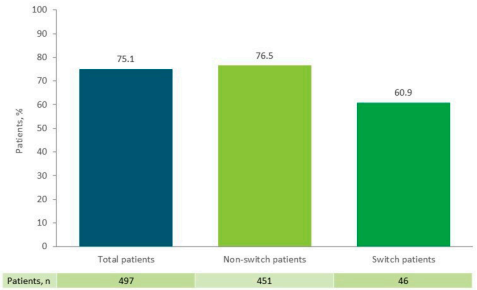
Table 1: Reasons for switching to fremanezumab from another mAb targeting the CGRP pathway according to patients at baseline visit, by migraine type.



Total patients, n	732	235	497
Non-switch patients, n	670	219	451
Switch patients, n	62	16	46

At cut-off, not all data for this endpoint were available and missing data have been excluded. The number of patients prematurely discontinuing the study and the number of patients that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers. CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.

Figure 1: Proportion of Total, Non-switch and Switch patients with >=50% reduction in MMD during the 6 months after fremanezumab initiation, by migraine type.



Patients, n	497	451	46

At cut-off, not all data for this endpoint were available and missing data have been excluded. The number of patients prematurely discontinuing the study and the number of patients that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers. CM, chronic migraine; MMD, monthly migraine days.

Figure 2: Proportion of Total, Non-switch and Switch patients with CM with >=30% reduction in MMD during the 6 months after fremanezumab initiation.

Conclusion: This analysis provides real-world evidence of fremanezumab effectiveness in over 30% of patients with EM and CM who had previously failed or not tolerated another mAb targeting the CGRP pathway. Switching to fremanezumab should be considered for these patients as it may offer a beneficial treatment option.
Disclosure: Funded by Teva Pharmaceuticals.

EPO-076

Long-term effectiveness of eptinezumab in patients with prior preventive migraine treatment failures

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Background and aims: DELIVER (NCT04418765) evaluated the efficacy and safety of eptinezumab for migraine prevention in patients with migraine and prior preventive treatment failures. Here, we report results of the 48-week dose-blinded extension period.
Methods: Eptinezumab 100mg and 300mg were evaluated vs placebo (infusions every 12 weeks) in adults with migraine and 2-4 documented preventive treatment failures. Patients randomized to placebo during the initial treatment period received eptinezumab 100mg or 300mg in the extension period; patients initially receiving eptinezumab continued their assigned dose. Efficacy measures included change from baseline in number of monthly migraine days (MMDs), >=50% and >=75% reduction from baseline in MMDs (ie, migraine responder rates [MRRs]), change from baseline in the 6-item Headache Impact Test (HIT-6), migraine severity, and acute headache medication use.
Results: 782/865 patients (90.4%) completed the extension period. Patients switching from placebo experienced an initial significant decrease in MMDs (Figure), migraine severity, acute headache medication use, and HIT-6 scores after the first eptinezumab dose (weeks 25¬-36); similar to what was initially observed (weeks 1-12). All treatment arms had sustained MMD reductions, with >=50% and >=75% MRRs of >60% and >30%, respectively, during weeks 61-72. No new safety or tolerability concerns were identified.

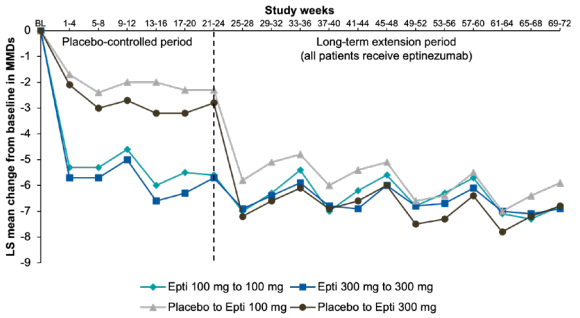

Figure. Change in MMDs with up to 18 months of eptinezumab treatment. Abbreviations: BL, baseline; Epti, eptinezumab; LS, least squares; MMDs, monthly migraine days.

Conclusion: The long-term effectiveness of eptinezumab is highlighted by the >90% completion rate of the DELIVER extension period. Marked and sustained reductions in MMDs, increases in MRRs, and reductions in migraine severity and burden experienced by those switching from placebo to active treatment indicate long-term effectiveness of eptinezumab for up to 18 months.
Disclosure: MA-Fees: AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, Teva. ST-Grants: Allergan/AbbVie, Amgen, Eli Lilly, Lundbeck, Neurolief, Novartis, Satsuma, Zosano. Fees: Aeon, Allergan/AbbVie, Alphasights, Amgen, Aruene, Axsome Thera, Becker Pharm. Consulting: BSI, Biohaven, CVHP, ClickThera, CoolTech, CRG, Decision Resource, Defined Health, DRG, Eli Lilly, ExpertConnect, FCB Health, Fenix, GLG, Guidepoint Global, Health Advances, HSC, HMP Comm, Impel, Initiator Pharma, InteractiveForums, Keyquest, Krog and Partners, Lundbeck, M3 Global Research, Magnolia Innovation, MJH Holdings, Miravo Healthcare, Neurofront Thera, Neurolief, Novartis, P Value Comm, Pain Insights Inc, Palion Medical, Pulmatrix, Putnam Associates, Rehaler, SAI Medical Partners, Satsuma, Slingshot Insights, SGI, Strategy Inc, SMC, System Analytic, Taylor and Francis, Teva, Theranica, Tremeau, Trinity Partners, Unity HA, Vial, XOC, Zosano. CME: AAN, AHS, ACHS, CME, DHC, Forefront Collaborative, HME, HMP Global, MAI, MMC, NACE, NAC for CME, OSU, PER, PlatformQ Education, Primed, VME, WebMD/Medscape. AG-Fees: Abbvie/Allergan, Amgen, Ärztekammer Nordrhein, Ärztekammer Westfalen Lippe, DGS, Esanum perfood, Grünenthal, Hexal, Hormosan, Lilly, Lundbeck, Medscape, Mundipharma, Novartis, Stada, Streamed Up, Teva. BJ, AE, MKJ-Employees of Lundbeck LLC. AJS-Fees: AbbVie, Allergan, Amgen, Axsome Therapeutics, Eli Lilly, Everyday Health, Impel, Lundbeck, Med-IQ, Medscape, Neurolief, Novartis, Satsuma, Teva, Theranica.

EPO-077

Patient-perceived improvements in migraine and most bothersome symptom among patients treated with eptinezumab

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Background and aims: This post hoc analysis of 24-week data from DELIVER (NCT04418765) evaluated the improvement in patient-identified most bothersome symptom (PI-MBS) and explored the relationship between PI-MBS and Patient Global Impression of Change (PGIC) among patients treated with eptinezumab.
Methods: Patients identified the PI-MBS at baseline and rated its change at week 12 and 24; patients also completed the PGIC assessment using an identical scale. The impact and maintenance of PI-MBS improvement between weeks 12 and 24 among eptinezumab-treated patients (i.e., pooling 100mg and 300mg in those who completed PI-MBS at both timepoints; N=563) was evaluated through a frequency table. The relationship between PI-MBS and PGIC was assessed in all patients (eptinezumab and placebo) who reported on both scales at both weeks (N=865) using Spearman's rank correlation test and a frequency table.
Results: At week 12, 52.4% eptinezumab-treated (versus 19.5% placebo; $p<0.001$) had much or very much improved PI-MBS. Of the 52.4%, 79.3% maintained or further improved PI-MBS by week 24. There was a strong relationship between improvement in PI-MBS and PGIC ($r=0.85$, $p<0.001$). The overlap of PGIC and PI-MBS scores was 68.2% (95%CI: 66.0, 70.4). 87.9% of patients with improved PGIC also improved in PI-MBS. 96.0% of patients had an PI-MBS change within +/-1 level of the PGIC score.
Conclusion: Patients treated with eptinezumab experienced sustained improvement in PI-MBS over 24 weeks. The strong relationship between PI-MBS and PGIC suggests that they are both important contributors to patients' perception and assessment tools for overall improvement in migraine.
Disclosure: SA-Employee of Lundbeck A/S AR-Employee of Lundbeck A/S XL-Employee of Lundbeck A/S LB-Employee of Lundbeck A/S SR-Employee of Lundbeck A/S. Stock/Options: Novartis AB

EPO-078

Responders and super-responders to anti-CGRP mAbs: the large, prospective, multicenter, real-life, I-NEED study

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Background and aims: In randomized clinical trials (RCTs), responders (>50% response) to monoclonal antibodies (mAbs) targeting calcitonin gene-related peptide (CGRP) range from 30% to 49%, while super-responder (>75% response) from 12% to 19%. We prospectively explored response and super-response to anti-CGRP mAbs in high-frequency episodic migraine (HFEM: 8-14 days/month) and chronic migraine (CM) in a large, real-life population.
Methods: Multicenter (n=29), prospective, cohort, real-life study, across 10 Italian regions. We enrolled all consecutive patients with HFEM or CM receiving >1 anti-CGRP mAbs dose from 01/02/2019 to 28/12/2022. All subjects had failed >3 preventive medications classes. Primary endpoint: responders at week 12. Secondary endpoints: super-responders at week 12, and responder and super-responder at weeks 4, 24 and 48.
Results: 1582 patients received >1 dose of mAbs (erenumab/fremanezumab/galcanezumab: 912/463/207). Responders/super-responders were monitored at weeks 12, 24 and 48 in all centers, conforming to Italian Medicines Agency regulations. Eight centers monitored treatment effects monthly, according to their routine practice. The table summarize results.

Table

		HFEM (n=473)		CM (n=1109)	
Week	Patients (n)	Responders	Super-responders	Responders	Super-responders
4	1582	48.9%	17.7%	49.5%	19.6%
12	1124	**58.3%**	**23.8%**	**63.4%**	**32.2%**
24	880	55.6%	25.8%	69.0%	37.2%
48	507	59.4%	30.0%	71.7%	44.2%

(Primary endpoint in **BOLD**)

Conclusion: Proportions of responders and super-responders to anti-CGRP mAbs in real-life are greater than in RCTs. Response and super-response occur very early (week 4), increase progressively (especially in CM patients) and are sustained over time (48 weeks).

Disclosure: P. Barbanti received grants and honoraria from Alder, Allergan, Angelini, Assosalute, Bayer, ElectroCore, Eli-Lilly, GSK, Lundbeck, Lusofarmaco, 1MED, MSD, New Penta, Noema Pharma, Novartis, Stx-Med, Teva, Visufarma, Zambon C. Aurilia received grants from FB-Health, Lusofarmaco, Almirall, Eli-Lilly Novartis and Teva G. Egeo received grants from Eli-Lilly, Novartis, New Penta and Ecupharma P. Torelli received grants and honoraria from Allergan, Teva, Eli-Lilly and Novartis C. Finocchi received grants and honoraria from Novartis, Eli Lilly, TEVA, AIM group F. d'Onofrio received grant and honoraria from Novartis, Teva, Neopharmed Gentili, Qbgroupsrl, K link srl and Eli-Lilly S. Messina has no disclosures to declare B. Colombohas received congress fee from Teva and Novartis. A. Carnevalehas no disclosures to declare M. Aguggia received grants from Novartis and Lilly M. Tasillo has no disclosures to declare M. Filippi is Editor-in-Chief of the Journal of Neurology; received compensation from Bayer, Biogen Idec, Merck-Serono, Novartis, Roche, Sanofi Genzyme, Takeda, Teva Pharmaceutical Industries; research support from Biogen Idec, Merck-Serono, Novartis, Roche, Teva Pharmaceutical Industries, Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, and ARiSLA G. Fiorentini has no disclosures to declare. B. Orlando has no disclosures to declare. S. Proietti has no disclosures to declare. S. Bonassi has no disclosures to declare.

EPO-079

Anti-CGRP monoclonal antibodies normalize peripheral sensitization in migraineurs

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Background and aims: Peripheral sensitization is abnormal in migraineurs as documented by Pressure Pain Threshold (PPT) which investigates nociceptive afferent fibres differently from laser or electrical stimulus. This study investigates changes of PPT as a neurophysiological effect of anti-CGRP monoclonal antibodies (mAbs) in migraineurs.
Methods: According to the Andersen's standardized guidelines, five muscles of the trigemino-cervical-complex and one far from this area were tested. PPT values of all above-mentioned muscles were measured at baseline (t0) and after 3 (t1) and 4 (t2) months after the first injection of an anti-CGRP mAb. Data were compared with PPT in healthy controls.
Results: 11 migraineurs and 11 healthy controls (mean age 43±15; F=63.6%) were enrolled. Patients were diagnosed as high-frequency episodic migraine (45.5%) or chronic migraine (54.5%) and treated with Erenumab (63.6%), Fremanezumab (27.3%) or Galcanezumab (9.1%). Migraine outcomes improved at t1 and t2 (migraine days/month: 18.2±6.9 t0 vs 8±4.7 t1 vs 6.1±3.8 t2; severe hours/month: 28.1±40.7 t0 vs 1.6±2.9 t1 vs 3.7±5.6 t2; MIDAS: 100±25 t0 vs 21±15.4 t1). At t0, migraineurs showed a significant lower PPT respect to controls in all muscles, except in the left temporalis and procerus. PPT increased in all migraineurs' muscles at t1 and t2 without significant differences between migraineurs and healthy controls.
Conclusion: PPT detects an abnormal peripheral sensitization in high-frequency episodic migraine and chronic migraine. Treatment with anti-CGRP mAb in migraineurs reduces the peripheral hypersensitivity detected by PPT, correlating with the improvement of the headache.
Disclosure: The authors have no conflicts of interest to declare.

EPO-080

Anti-CGRP antibodies effects on migraine psychiatric comorbidities

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Background and aims: We evaluated the effects of the treatment with monoclonal antibodies (mAbs) acting on the calcitonin gene-related peptide (CGRP) or its receptor (anti-CGRP/R mAbs) on depression, anxiety, and fatigue in migraine patients resistant to traditional prophylaxis.
Methods: 77 patients (77% females, median age 47 years old) with chronic resistant migraine, studied in an open-label longitudinal study, underwent anti-CGRP mAbs (57%) or its receptor treatment (43%). Clinical parameters including allodynia and psychiatric comorbid symptoms were evaluated with specific questionnaire and scales at baseline and at 3-month follow-up. Responders were defined as subjects with at least 50% reduction of headache frequency after three months treatment.
Results: Twenty-ninesubjects (38%) were non-responders and 48 subjects (62%) were responders. Comorbid psychiatric scoring and migraine burden did not differed between groups at baseline. In responders the reduction of disease severity in terms of frequency (median days/month 22 vs 4 $p < 0.001$) and allodynia (6.00 vs 1.50 $p < 0.001$) was associated with a significant decrease of migraine-related disability, fatigue and psychiatric comorbidities. Also in non-responders a significant reduction of the headache frequency (median 30.0 vs 20.0 p=0.003), was reported as well as reduced migraine-related disability, but no significant improvement was observed for psychiatric

symptoms.
Conclusion: Anti-CGRP/R mAbs treatment improves psychiatric symptoms as expressed by both depression and anxiety score values only in responder subjects indicating that they are likely related to chronic pain condition. Further studies comparing anti-CHRP/R with other prophylaxis may help understand its potential specific role in psychiatric comorbidities.
Disclosure: Nothing to disclose.

EPO-081

Migraine and COVID-19: Migraine headache developement after COVID-19 and SARS-CoV-2 vaccination in migraine patients

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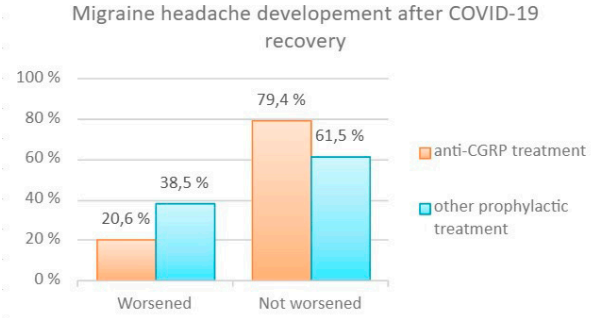
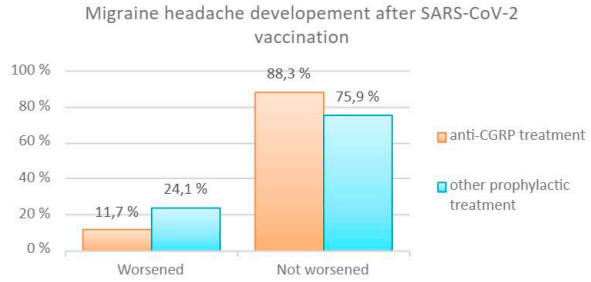
Background and aims: Migraine is a common primary headache with great impact on quality of life and socioeconomic status. It was demonstrated that COVID-19 infection can lead to headache in healthy population as well as in migraine patients. Our objective was to assess how migraine headache developed during one month following COVID-19 depending on prophylactic treatment in migraine patients. Furthermore, we analyzed the impact of SARS-CoV-2 vaccination on migraine headache as well.
Methods: We conducted an in-person survey with 388 patients diagnosed with migraine in 6 Headache Centers in Czech Rebublic. We recorded demographic data, migraine history, prophylactic treatment, COVID-19 history, SARS-CoV-2 vaccination history, subjective worsening of migraine headache during one month after COVID-19 recovery and worsening of headache after vaccination. Comparisons between groups of patients with and without anti-CGRP treatment were performed using Chi-square test. $P<0.05$ was considered statistically significant.
Results: 300 of our subjects had COVID-19 infection. There was no difference in frequence of headache during the infection between patients treated with and without anti-CGRP. However, patients with anti-CGRP treatment reported less frequently (20.6%) worsening of migraine headache in the following month after recovery from COVID-19 compared to patients with other prophylactis medication (38.5%). Similarly, worsening of migraine headache after vaccination was less frequent in group with anti-CGRP treatment (11.7%) in comparison to group with other prophylactics (24.1%).



Migraine headache developement after COVID-19 recovery



Migraine headache developement after SARS-CoV-2 vaccination

Conclusion: Our results showed that patients treated with anti-CGRP were less likely to experience worsening of their migraine after recovery from COVID-19 as well as after vaccination in comparison to patients with other prophylactic treatment.
Disclosure: Nothing to disclose.

EPO-082

Long-term effectiveness of eptinezumab in treatment of patients with chronic migraine and medication-overuse headache

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Background and aims: PREVAIL demonstrated long-term safety, tolerability, and meaningful reductions in migraine-related burden with repeated eptinezumab doses in patients with chronic migraine (CM). Medication-overuse headache (MOH), a secondary headache disorder caused by overuse of acute medication, exacerbates CM. This analysis evaluated eptinezumab in patients with CM and MOH.

Methods: PREVAIL (NCT02985398) was a single-arm, open-label trial in which adults with CM received eptinezumab 300mg every 12 weeks (wks) for up to 8 doses. MOH diagnosis at screening was based on International Classification of Headache Disorders criteria. Long-term effectiveness endpoints included: Migraine Disability Assessment (MIDAS), 6-item Headache Impact Test (HIT-6), patient-identified most bothersome symptom (PI-MBS), Patient Global Impression of Change (PGIC), EQ-5D-5L visual analog scale (VAS), and 36-item Short-Form Health Survey (SF-36).
Results: 49/128 (38.3%) patients with CM had a secondary MOH diagnosis. All patient-reported outcomes showed marked improvements at the first post-baseline assessments (Wk4 or Wk12) that was maintained or improved throughout the study. MIDAS total score decreased from 60.0 (baseline) to 8.6 (Wk84). MIDAS-derived headache days decreased from 47.5 (baseline) to 11.8 (Wk84). HIT-6 total score decreased from 65.2 (baseline) to 53.3 (Wk84). At Wk48, 67.4% and 76.1% of patients reported "much" or "very much" improved PI-MBS and PGIC, respectively. Mean EQ-5D-5L VAS total score improved from 79.9 (baseline) to 83.3 (Wk48). Patients reported improved health-related quality of life per the SF-36. No new safety signals were identified in patients with CM and MOH.
Conclusion: In patients with CM and MOH, long-term treatment with eptinezumab was associated with improvements in multiple patient-reported outcomes.
Disclosure: AB: Consulting fees-Alder, Allergan, Amgen, Biohaven, electroCore, Lilly, Lundbeck, Novartis, Promius, Supernus, Teva, and Theranica. DK: Personal compensation for serving on a Scientific Advisory or Data Safety Monitoring board for: Amgen, Novartis, Biohaven, Eli Lilly, Lundbeck. Speakers Bureau fees for: Amgen, Eli Lilly, Teva, Allergan, Lundbeck, Biohaven. RC-Employee at Lundbeck at time of study. PM: personal fees and research support: AbbVie, Amgen/Novartis, Biohaven, Eli Lilly, Lundbeck, and Teva; consulting fees: Aeon; Speakers Bureau fees: Lilly, Teva, AbbVie, Biohaven, Lundbeck and has received stock or an ownership interest from Precept. LB-Employee of Lundbeck. JH: personal fees and research support-Lundbeck. Consulting fees-Lundbeck, Impel NeuroPharma

EPO-083

Anti-CGRP Monoclonal Antibodies for the Treatment of Migraine with Aura: a prospective observational cohort study

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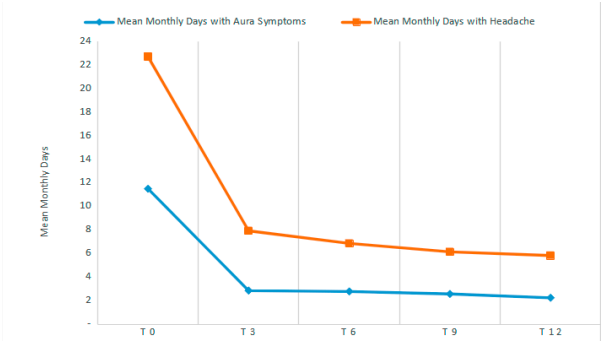
Background and aims: About 25% of migraineurs experience aura symptoms. Aura is a reversible focal neurological phenomenon involving visual, sensory, speech, and motor symptoms that usually precede migraine pain. Monoclonal antibodies against calcitonin-related peptide (anti-CGRP mAbs) are effective in preventing chronic and episodic migraine, but little is known about their effectiveness in specifically preventing migraine with aura. This study aims at evaluating the effectiveness of anti-CGRP mAbs in migraine with aura, and aura symptoms.
Methods: This is a prospective observational cohort study, aiming at evaluating the efficacy of Erenumab, Fremanezumab and Galcanezumab for the treatment of 14 patients suffering from migraine with aura. Duration of follow-up was 12 months. We assesed mean monthly days with aura symptoms, with or without subsequent headache, as well as mean monthly days with headache, by reviewing standardized headache diaries every three months.
Results: We observed a mean reduction of mean monthly days with aura symptoms of - 8.17 (- 5.76, - 10.57; CI 95%) and a mean reduction of mean monthly days with headache of - 15.92 (- 11.09, - 20.75; CI 95%). No significant differences were found bewteen mAbs.



Mean Monthly Days Reduction of Headaches and Aura Symptoms

Conclusion: Our findings show that anti-CGRP mAbs are highly effective in migraine with aura, both in reducing mean monthly headache days and mean monthly days with aura symptoms.
Disclosure: Simone Braca, Angelo Miele, Antornio Stornaiuolo and Mattia Sansone declare that there is no conflict of interest. Cinzia Valeria Russo received personal compensation from Sanofi Genzyme and Merck Serono. Roberto De Simone received personal compensation from Lilly for oral presentations (2020 – 2021).

EPO-084

Diagnosis and misdiagnosis of resistant and refractory migraine – Data from the REFINE study

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Background and aims: : Resistant and refractory migraine are burdensome conditions. Some patients may receive inaccurate diagnoses, leading to unnecessary diagnostic tests and treatments. We evaluated the history of misdiagnosis and use of neuroimaging in patients with resistant (RES) and refractory (REF) migraine compared to non-resistant, non-refractory (NRNR) patients.

Methods: The REFINE study is an observational, multicenter, international study including patients with migraine stratified as REF, RES, or NRNR. In this analysis we assessed patients' baseline characteristics.

Results: We included 612 patients: 340 (55.6%) with NRNR migraine, 228 (37.3%) with RES and 44 (7.2%) with REF. Overall, a misdiagnosis was made in the medical history of 184 (30.1%) cases, with a lower number of misdiagnoses in the REF group (15% vs. 33% of RES and vs. 30% of NRNR, p=0.020). The most frequent misdiagnoses included sinusitis (57, 31.0%), cervical spine disorders (68, 37.0%), hormonal headache (29, 15.7%), and temporomandibular disturbances (21, 11.4%). REF patients had also higher prevalence of accesses to the Emergency Department (27% vs. 16% of RES vs. 13.5% of NRNR, p=0.017). REF (88% and 43%) and RES (97% and 45%) patients underwent, at least once, brain and/or cervical magnetic resonance imaging (MRI) in higher proportion, compared to NRNR (74% and 29%, p<0.001 and p=0.005). Moreover REFs underwent brain MRI and computed tomography scan more frequently.

Conclusion: REF patients had lower rates of misdiagnosis, probably due to their difficult condition, resulting in higher use of neuroradiological exams and access to urgent medical care to exclude secondary diagnoses.

Disclosure: Nothing to declare.

EPO-085

COMPLICATION OF LUMBAR PUNCTURE: RETROSPECTIVE ANALYSIS OF A MONOCENTRIC SERIES.

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Background and aims: Describe the incidence and characteristics of the complications of the lumbar puncture (LP), analyzing possible risk factors in a monocentric series.

Methods: Retrospective study of the medical records of patients undergoing LP in the neurology department, in a period of fifteen years (January 2006-December 2020). The clinical characteristics of the patients are specifically collected (gender, age, weight, height, body mass index [BMI], history of headache, antiplatelet or anticoagulant treatment), and the indication (diagnostic, cerebrospinal fluid removal, [CSF] intrathecal treatment) of LP, and the characteristics of the registered complications.

Results: In the study period, 1,950 patients (950 women/1,000 men), with a mean age of 56.2 years (SD= 18) underwent a total of 2,331 LPs. The procedure was repeated at least 2 times in 218 (11.2%) patients. Indications were diagnostic, CSF drainage and therapeutic in 73.7%, 11.8% and 14.5%, respectively. Complications were recorded in 167 of the LPs (7.2%): headache (103 [4.4%]), low back pain (57 [2.5%]), chemical arachnoiditis (7 [0.3%]); vasovagal symptoms (5 [0.21%]), transient lumbar monoradiculopathy (7 [0.3%]), bacterial meningitis (1 [0.04%]), and spinal epidural hematoma (1 [0.04%]). A history of headache, female gender, a lower BMI, and younger age were significantly associated with a higher risk of post-puncture headache.

Conclusion: In our series, complications have been reported in 7.2% of LPs. The most common was headache (4.4%). A history of headache, female gender, low BMI, and young age are the factors that are associated with a higher risk of this last complication.

Disclosure: With respect to this communication, there are no relationships that could be perceived as potential conflicts of interest. The communication that I present has not been financed, in whole or in part, by any company with economic interests in the products, equipment or similar mentioned in it.

Neuroimmunology 1

EPO-086

Influence of FCGR3A-V158F polymorphism on the therapeutic response to Ocrelizumab in patients with Multiple Sclerosis

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Background and aims: Recent evidence demonstrated that the fragment c gamma receptor 3A (FCGR3A) 158F genotype is an independent predictor of peripheral B-cell depletion and clinical response to rituximab in patients with neuromyelitis optica, as it reduces the affinity of the receptor for human IgG. To evaluate the influence of FCGR3A genotypes on B cell kinetics and disease activity in Relapsing Multiple Sclerosis (RMS) patients on ocrelizumab.
Methods: Ocrelizumab-treated RMS patients were consecutively enrolled at the time of drug initiation and were prospectively followed-up for eighteen months. We collected clinical (EDSS and number of relapses) and immunological (B cell count) data every six months. Radiological data (presence of gadolinium lesion/s) were collected at six and eighteen months of follow-up. At enrollment, patients were genotyped for the FCGR3A-V158F polymorphisms. To explore the Influence of FCGR3A-V158F polymorphisms on the therapeutic response to Ocrelizumab we applied logistic and Poisson regression models, as appropriate.
Results: We enrolled 45 RMS patients. There was no statistically significant association of FCGR3A gene polymorphism (either according to recessive or dominant pattern) with the presence of disease activity or early B cell repopulation (at six-, twelve- and eighteen-month follow-ups). However, all the patients that experienced early B cell reappearance at 6 months (9 on 45) carried at least one F allele (p=0,153).
Conclusion: These results suggest further investigation of the possible relationship between B lymphocyte kinetics under ocrelizumab treatment and the FCGR3A polymorphism.
Disclosure: The authors declare no competing interests for this work.

EPO-087

Prevalence of HLA DQ2 and DQ8 in seronegative neuromyelitis optica spectrum disorders

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Background and aims: Neuromyelitis optica spectrum disorders is an entity not well understood whose pathophysiological substrate is unknown yet. Despite the discovery of the AQP-4 and MOG antibodies, there are still a high number of patients diagnosed with NMOSD who remaining seronegative. HLA-DQ2 and HLA-DQ8 are gene alleles that predispose to celiac disease, nevertheless their association to other autoimmune disorders is unclear so far.
Methods: We evaluate patients diagnosed with seronegative NMOSD at the unit of neuroimmunology and multiple sclerosis of Girona - University Hospital Dr. Josep of Girona, Spain, compared with seropositive NMOSD patients from February 2019 to December 2022. All patients met criteria to be diagnosed with NMOSD. All patients who were positive for AQP-4 and MOG were considered as seropositive. No patient had history of celiac disease.
Results: We collected a total of 18 patients who met NMOSD criteria, seropositive as well as seronegative. Of 18 patients, 12 were seronegative NMOSD (66.66%) Of 12 seronegative NMOSD patients, 75% were positive for either HLA-DQ2 or HLA-DQ8 92% patients had marked improvement after reduction of gluten consumption measured by EDSS. The prevalence of HLA-DQ2/DQ8 in seropositive NMOSD patients was 33.33% HLA-DQ2 was the allele more frequently associated to NMOSD seronegative as well seropositive.
Conclusion: Despite there are still lacking further studies which evaluate the pathogenic role HLA-DQ2/DQ8 in non-celiac patients, the positivity for these alleles could be a useful diagnostic biomarker for seronegative forms of NMOSD. In addition, this finding may bring therapeutic implications as the reduced gluten consumption could favor better outcomes in patients with NMOSD.
Disclosure: Nothing to disclose.

EPO-088

Estensive spinal hypertrophic pachymeningitis in IgG4-related disease.

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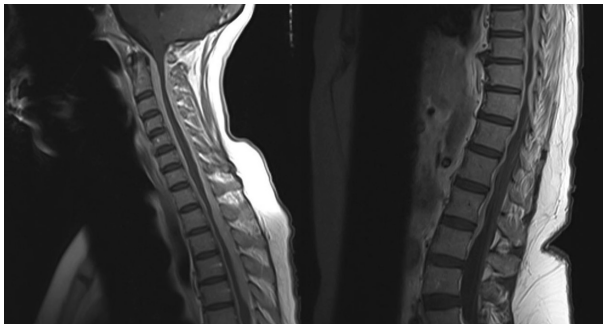
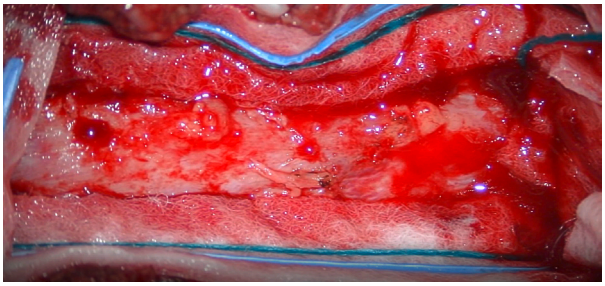
Background and aims: We describe a 66-year-old woman with a two-month history of neck stiffness, limbs dysesthesias and progressive weakness to inability to walk, diagnosed as an isolated extensive spinal hypertrophic pachymeningitis (HP) due to IgG4-related disease (IgG4-RD).
Methods: HP diagnosis due to IgG4-RD could be challenging because clinical features are non-specific. Medical assessment should include comprehensive evaluation to exclude differential diagnosis and histopathological exam represents the diagnostic gold standard.
Results: Cervicothoracic-MRI disclosed almost complete obliteration of cerebrospinal fluid signal in the entire spinal tract, with marked contrast enhancement of the meningeal envelopes, and with signal alteration in the cervical-thoracic spinal cord due to compressive myelopathy. A complete workup was performed, disclosing high serum concentration of IgG4, and total body CT scan and FDG-PET also showed signs of subclinical aortitis. Meningeal biopsy revealed lymphoplasmacytic infiltrate, with high-level-per-field plasma-cells and an IgG4+/IgG+ ratio >40%, confirming HP due to IgG4-RD diagnosis. Patient was treated with high-doses steroids, followed by rituximab (two-1g infusions 15 days apart), with clinical improvement.



Intraoperative tissue observation of spinal meningeal revealed pearly-colored dura mater, increased consistency, and tendency to hemorrhage. Two focal mamelon-like extroversions are also present.



Spinal MRI (T1-weighted post-contrast sequence) showing almost complete obliteration of cerebrospinal fluid (CSF) signal in the entire spinal tract, with meningeal Gadolinium enhancement around the entire spinal cord.

Conclusion: Despite IgG4-RD HP mainly affects brain meninges, clinicians should be aware that isolated cases of spinal HP could also occur. Such involvement might also warrant for an aggressive immunotherapy due to the risk of long-term neurological disability.
Disclosure: Nothing to disclose.

EPO-089

Determination of which factors are more effective on work difficulties in persons with multiple sclerosis

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Background and aims: Employment is known to significantly contribute to the quality of life in persons with MS (pwMS), and any workplace difficulties that arise directly from MS can play an important role in work life. This study aims to utilize magnetic resonance imaging (MRI) to calculate subcortical gray matter (scGM) volumes to examine the neurological underpinnings of work difficulties in pwMS. The secondary aim is to determine which factors are more effective on work difficulties.
Methods: Twenty-three pwMS employees were included. Physical disability was assessed with Expanded Disability Status Score (EDSS), Timed-25-Foot-Walk (T25FW) test, and Nine-Hole Peg test. Brief International Cognitive Assessment in MS (BICAMS) was used to evaluate cognitive functions. Facial Emotion Identification (FEI), Reading the Mind in the Eyes Test (RMET), and Empathy Quotient (EQ) was used to assess social cognition. ScGM volume calculated with freesurfer from 3T MRI.
Results: According to the linear regression model, cognition and physical disability were not effective factors in work difficulties ($p<0.05$). However, it was found that the decrease in the EQ score, scGM Volume, Total Gray Matter Volume, Left Thalamus, Left Putamen, Left Hippocampus, Right Thalamus, Right Caudate, and Right Hippocampus increased the severity of work difficulties ($p<0.05$).

Risk factors (physical disability) on severity of work difficulties			
Risk Factors	Beta Coefficient	95% CI	P value
EDSS	0.228	-3.586; 9.475	0.465
Timed 25 Foot Walk Test	0.009	-1.912; 1.981	0.557
Nine-Hole Peg Test	0.443	-0.002; 5.200	0.228

Risk factors (social cognition and brain volumes) on severity of work difficulties			
Risk Factors	Beta Coefficient	95% CI	P value
Reading the Mind in the Eyes Test	-0.411	-5.041; 0.203	0.068
Facial Emotion Identification	-0.192	-2.881; 1.068	0.346
Empathy Quotient	-0.530	-1.527; -0.148	**0.020**

Risk factors (cognition) on severity of work difficulties			
Risk Factors	Beta Coefficient	95% CI	P value
Symbol Digit Modalities Test	-0.300	-1.126; 0.338	0.273
California Verbal Learning Test	0.071	-2.097; 2.675	0.398
Brief Visuospatial Memory Test-Revised	-0.266	-1.664; 0.691	0.803

Risk factors (scGM) on severity of work difficulties			
Risk Factors	Beta Coefficient	95% CI	P value
Subcortical Gray Matter Volume	-0.057		**0.011**
Total Gray Matter Volume	-0.001		**0.008**
Left Thalamus	-0.084		**0.007**
Left Caudate	-0.004		0.936
Left Putamen	-0.069		**0.041**
Left Hippocampus	-1.141		**0.017**
Left Amygdala	0.035		0.249
Right Thalamus	-0.067		**0.024**
Right Caudate	-0.120		**0.027**
Right Putamen	-0.043		0.244
Right Hippocampus	-0.080		**0.020**
Right Amygdala	-0.038		0.238

Results

Conclusion: This study shows which factor could be more effective on work difficulties in pwMS. There is a highly complex relationship between ScGM, work difficulties, and social cognitive impairment. It is still debatable how the thalamus, hippocampus, putamen, and caudate volumes affect work difficulties and needs to be studied with other employment-related factors in larger groups.
Disclosure: Nothing to disclose

EPO-090

Predictive and diagnostic significance of markers in the progression of HIV encephalopathy in children

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Background and aims: The study included 260 children 153 boys and 107 girls, 59% and 41%, respectively, diagnostic markers in the development of HIV encephalopathy with varying severity were assessed. Diagnostic markers were interpreted by the concentration of IL-6, IL-10, TNF-alpha, C-reactive protein and C3, C4 complement components.
Methods: PCR study, Student's t-test.
Results: The study of indicators in children with HIV found that the concentration of TNF-alpha and IL-6 were increased compared to the reference values (12.67±0.25pg/ml and 23.04±0.64pg/ml, respectively, at the reference, values less than 8.1pg/ml and 7pg/ml, respectively), and the concentration of IL-10 is reduced (5.93±0.10pg/ml with a reference value of more than 9.1pg/ml). The concentration of complement components 3 and 4 as a whole in the entire cohort of children included in the study remained within the normal range and amounted to 1.07 ± 0.05 g/l for C3 and 0.38 ± 0.04 g/l for C4 (reference values are 0.9-2.07g/l and 0.174-0.522g/l, respectively).
Conclusion: An increase in the concentration of IL-6 above 19.6pg/ml is associated with an increase in the risk of developing symptomatic HIVE by 9.14 times, an increase in the concentration of TNF-alpha above 12.5pg/ml – 4.07 times ($P<0.001$ for both factors).
Disclosure: A comparative analysis of the concentration of markers in patients with AND was carried out in comparison with the group of MAD + HAD, and the frequency of occurrence of symptomatic HIVE was determined depending on the diagnostic concentration of markers.

EPO-091

Neural organoids to model neuroinflammation: a systematic review focused on microglia's integration

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Background and aims: Neural organoids are in vitro models, made from human pluripotent stem cells, grown in three-dimensional conditions, which can complement and accelerate neurological research. Neuroinflammation is a common condition to several neurological diseases, in which inflammatory pathways involving nervous system cells lead to neuronal loss and disability. Microglia is thought to play a main role in cell's interaction. Therefore, microglia's integration into neural organoids is crucial to the study of neuroinflammation.

Methods: A comprehensive search was conducted using Embase and PubMed to identify relevant studies. The inclusion criteria were original studies using neural organoids to study neuroinflammation pathways and/or microglia integration. After duplicates and reports excluded (figure 1), 31 articles were included in the review. PRISMA recommendations were followed.

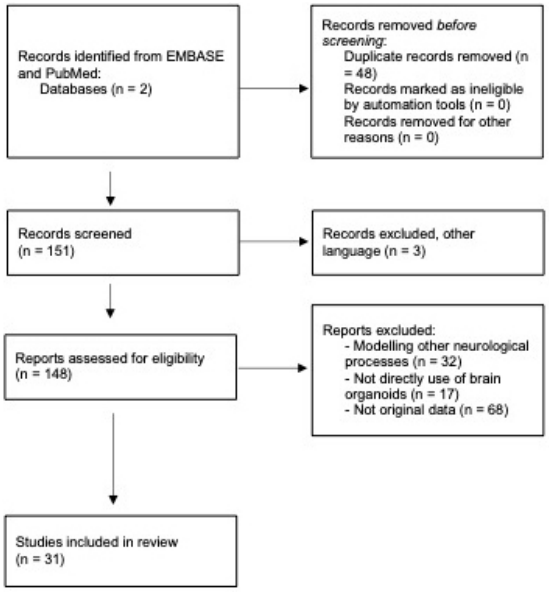

Figure 1. Flow diagram of study selection

Results: Microglia's integration into neural organoids is a bioengineering challenge. This has been achieved through various experimental models that have studied neuroinflammation's pathways in models of different neurological diseases (table 1). The use of cocultures, grafting of organoids into mice and the use of on-a-chip technologies have enabled this integration (figure 2). Different molecular techniques have been used to test the identity and functionality of microglia. There are important limitations regarding the use of neural organoid technology for the study of neurological diseases, notably the lack of standardisation.

Reference	Microglia's integration	Disease	Triggering factor	Main findings
Ormel *et al* (2018), Sun *et al* (2022), Bodnar *et al* (2021)	Innately developed	-	-	Microglia innately develops in neural organoids and assembloids. It mimics the transcriptome and inflammatory response.
Samudyata *et al* (2021)	Innately developed	COVID-19	SARS-CoV-2	Innately developed microglia causes extensive cell death and loss of synapses
Kim *et al* (2022)	Innately developed	AD	SARS-CoV-2	SARS-CoV-2 infection facilitates AD pathology
Winkler *et al* (2019)	Innately developed	La Crosse encephalitis	LACV	Neural maturation increases the susceptibility of neurons to LACV. IFN signaling is protective.
Speicher *et al* (2022), Sabate-Soler *et al* (2022), Popova *et al* (2022), Fagerlund *et al* (2022), Song *et al* (2019), Bejoy *et al* (2019), Gao *et al* (2022), Carroll *et al* (2021)*, Abreu *et al* (2018), Schwartz *et al* (2015), Barry *et al* (2017)	Coculture at different times into guided and unguided neural organoids.	-	Different inflammatory triggers	Integrated microglia demonstrate in vivo-like phenotype
Mansour *et al* (2018)	Grafting	-	-	Grafted organoids showed integration of microglia and growth of axons of the host brain
Zhang *et al* (2020)	Exposition to activated microglia	Glioblastoma	LPS	dPGS-treated microglia reduce invasion of the tumor in a neural organoid
Cakir *et al* (2022)	Coculture with overexpression of transcription factor and grafting	AD	Aβ protein	Integrated microglia demonstrate in vivo-like phenotype and protects against Aβ
Wenzel *et al* (2022)	Coculture	AD	Aβ protein	Aβ augments the release of cardiolipin from microglia into the extracellular space, where it can enhance the astrocytes and microglia's endocytosis of Aβ
Marotta *et al* (2022)	Coculture of patient-specific cells	PPMS and PD	Microgravity	Dysregulation of cell division, DNA repair, packaging and post-translational modifications.
Xu *et al* (2021)	Coculture	Zika disease	Zika	Integrated microglia demonstrate in vivo-like phenotype and respond to Zika virus infection
Muffat *et al* (2018)	Coculture of infected and uninfected microglia	Zika and Dengue	Zika and Dengue viruses	Microglia may act as a viral reservoir of Zika virus. Zika and Dengue viruses affect the integrity of BBB allowing infection of the brain.
Jin *et al* (2022)	Coculture of patient-specific cells	DS and AD	Tau protein	DS microglia undergo senescence and exhibit elevated type-I-interferon signaling
Dos Reis *et al* (2020), Gumbs *et al*. (2022)	Coculture of infected and uninfected microglia	HAND	HIV infection	Infected organoids exhibited increased inflammatory response
Nzou *et al* (2020)	Coculture	BBB dysfunction	Hypoxia	Anti-inflammatory agents in neural organoids showed reduced damage to hypoxic condition
Ao *et al* (2021)	On-a-chip	Substance use disorder	Opioid receptor agonist	Microglia responds after exposure to opioid receptor agonist

Table 1. Approaches of microglia's integration into neural organoids and different neuroinflammatory pathways and diseases studied.
Abbreviations: AD: Alzheimer's disease, Aβ: Amyloid-beta, BBB: blood-brain-barrier, dPGS: dendritic polyglycerol sulfate, DNA: deoxyribonucleic acid, DS: Down's syndrome, HAND: HIV-associated neurocognitive disorder, HIV: human immunodeficiency virus, IFN: interferon, LACV: La Crosse virus, LPS: lipopolysaccharide, PD: Parkinson's disease, PPMS: primary progressive multiple sclerosis. *Murine cells.

Table 1. Approaches of microglia's integration into neural organoids and different neuroinflammatory pathways and diseases studied.

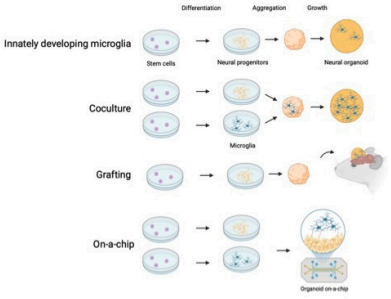

Figure 2. Microglia's integration into neural organoids

Conclusion: The use of neural organoids with integrated microglia is a novel and promising tool for the study of neuroinflammation. It can be used as disease models for the study of neurological disease's pathophysiology, the discovery of new therapeutic targets and the development of new treatments.

Disclosure: The authors present no disclosures or conflict of interest.

EPO-092

Prognostic value of quantitative and longitudinal CASPR2/LGI1 antibody testing in patients with autoimmune encephalitis

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Background and aims: Autoantibodies against Leucine-rich glioma-inactivated 1 (LGI1) and anti-contactin-associated protein-like 2 (CASPR2) are diagnostic and pathogenic markers of of autoimmune encephalitis (AE). We aimed to study the relevance of longitudinal anti-LGI1/CASPR2 titres.
Methods: Retrospective cohort study including patients with anti-LGI1/CASPR2 definite AE, and at least one available longitudinal sample > 60 days from onset. Titers were measured with endpoint dilution using a live cell-based assay. Sixteen/99 samples (16%) were classified as from "acute phase", 15 (15%) as "postacute" and 68 (69%) as "remission". Outcome was measured with modified Rankin Scale (mRS) and with Clinical Assessment Scale in Autoimmune Encephalitis (CASE).
Results: We enrolled 18 patients (anti-CASPR2=7; LGI1=11). Median age at diagnosis was 63 (range:46-83), and 7 were females. Manifestations at onset included seizures (18/18), psychiatric symptoms (10/18) and cognitive dysfunction (9/18). Median follow-up was 31 months (range 3-57). Seven/18 patients had relapses. Acute phase samples had higher median titres (1:10400, range 400-102400) compared to post-acute (1:3200) and remission (1:200) samples ($p<0.001$), even analyzing separately anti-LGI1 ($p<0.001$) and CASPR2 ($p=0,0197$) sera. Titres did not correlate with disease severity at onset/follow-up. Relapses always occurred with a positive sample (n=7), and in 3 patients with pre-relapse samples available titres increased at relapse. Seven patients became seronegative (2 with anti-CASPR2, 4 after rituximab) after a median time from diagnosis of 12 months (range 5–58), and none experienced post-seroconversion relapses.
Conclusion: Anti-CASPR2/LGI1 titres correlate with disease phase. Seroconversion-to-negative might associate with treatment and relapse risk. warranting further studied on antibody-titres as a biomarker in AE.
Disclosure: Nothing to disclose.

EPO-093

A case of treatment-refractory anti nuclear-rim necrotizing autoimmune myositis

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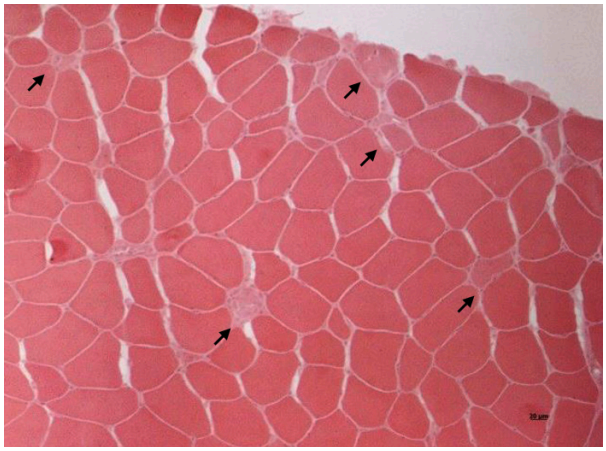
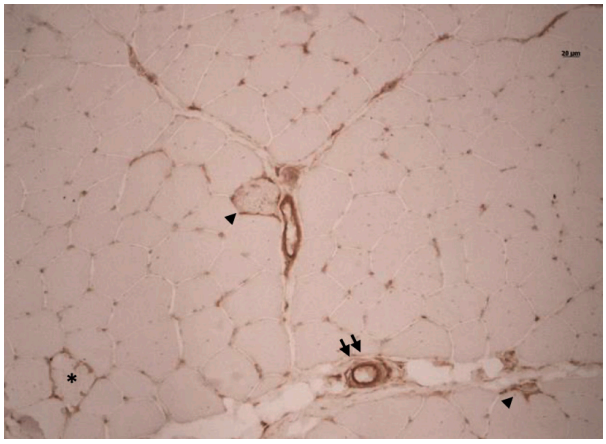
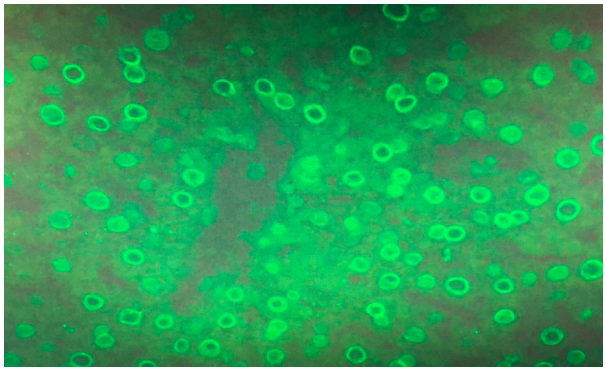
Background and aims: We describe the case of a 30-year-old patient affected by necrotizing autoimmune myositis with predominantly bulbar symptoms and positivity for anti-nuclear-rim antibodies.
Methods: We report this case detailing medical and clinical history together with histological, genetic and autoimmune tests.
Results: A 30-year-old male was referred to our department due to onset of dysphagia and dysarthria. High CPK levels and electromyographic test were consistent with acute autoimmune myositis. Despite the presence of an anti-nuclear-rim pattern of antinuclear antibodies, myositis-specific autoantibodies panel tested negative. Muscular biopsy was then performed and showed a necrotizing autoimmune myositis. Patient was then treated with high-dose steroids, with a rapid, but incomplete, response. Due to persistent clinical and biochemical abnormalities, intravenous immunoglobulins (2g/kg over 5 days) and cyclophosphamide (1 g/m^2) were administered. Due to a clinical and biochemical relapse patient was re-treated with high-dose steroids followed by rituximab (two 1 g infusions 15-day apart). A complete and long-lasting response was then achieved. Genetic analysis tested positive for HLA DQA1 (02:01, 03:01) and DQB1 (02:01, 03:02) haplotypes, described in some cases of autoimmune myositis associated with antibodies anti-nuclear pore complex.
Conclusion: In this report we show a case of anti-nuclear-rim autoimmune myositis showing that, albeit rare, this autoimmune pattern reflects the presence of a necrotizing myositis that could be refractory to conventional treatment and might need rituximab administration to induce a long-lasting remission.



Haematoxylin-Eosin staining (magnification 20x). Several necrotic or degenerating fibres are evident (arrows).



Immunoperoxidase with antibody against MHC class 1 (magnification 20x). The reaction is focal in some fibres both at the sarcolemma (asterisk) or at the sarcoplasm level (arrow heads). Vessels are also positive (double arrows).



Anti-nuclear-rim pattern of antinuclear antibodies.

Disclosure: Conflict of Interest Disclosures: None reported.

EPO-094

Carpe protocol: chronic ambulatory treatment with rituximab and plasma exchangefor immune-mediated neurologic disorders

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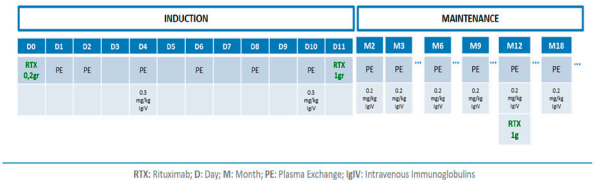
Background and aims: In acute or subacute immune-mediated disorders such as autoimmune encephalitis, treatment with steroids, plasma exchange (PE), or intravenous immunoglobulins (IVIg), and rituximab or cyclophosphamide is widely used. In contrast, for chronic presentations the long-term use of PE has not been explored, and therapeutic options are very limited.

Methods: CARPE protocol (Fig.1) comprises: 1) an induction phase (days 0 to 11), with rituximab combined with 6 PE and 2 IVIg sessions; and 2) a maintenance phase (monthly sessions), in which one PE is followed by IVIg on the same day.



Carpe Protocol Schedule

Results: Nine patients (5 males); median age 45 years (range 31-72) were included. Four had polyneuropathy (2 chronic idiopathic demyelinating polyneuropathy, 1 with anti-disialosyl IgM antibodies, and 1 anti-Hu); 3 drug-resistant epilepsy (2 with anti-GAD65, and 1 anti-Ma2); and 2 other anti-GAD65 associated syndromes (1 stiff-person syndrome; 1 cerebellar ataxia). Seven patients previously received diverse therapies (5 IVIg, 4 rituximab, 3 steroids, 2 azathioprine or mycophenolate, 1 cyclophosphamide, 1 hematopoietic stem-cell transplantation), and 2 patients received CARPE as initial therapy. After a median follow-up of 8 months (range 6-31), including a median of 7 maintenance PE (range 5-18), all patients remained in the protocol. We observed clinical stability or mild improvement in all. Anti-GAD65 titers decreased in 3 of 4 patients. Adverse events were mild: headache (7 patients), presyncope (2), hypoglycemia (1) and compressive radial nerve neurapraxia (1)

Conclusion: CARPE is a safe and well tolerated therapeutic option for patients with established immune-mediated neurologic disorders.

Disclosure: Nothing to disclose.

EPO-095

Neuropsychiatric symptoms and sleep disorders in autoimmune encephalitis: from the acute stage to the long term

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Background and aims: Autoimmune encephalitis (AE) involves neuropsychiatric changes during the acute stage, which vary from mild mood disorders to overt psychosis. Sleep disruption is also increasingly identified, being a prominent feature of certain types of AE. However, how both these issues evolve in the long-term is not well defined. We aim to characterize sleep and mood disorders in this setting.
Methods: Observational cross-sectional study, including ≥18-yo patients diagnosed with AE followed at a Portuguese tertiary centre (January 2007-December 2021). Sociodemographic and clinical data were obtained from electronic records. Questionnaires to evaluate sleep quality and anxiety and mood disorders were applied (Satisfaction, Alertness, Timing, Efficiency and Duration Questionnaire for Sleep Health Measurement [SATED-RU]; Pittsburgh Sleep Quality Index [PSQI-PT], Hospital Anxiety and Depression Scale [HADS]).
Results: We enrolled thirteen patients (median follow-up 62 months [29-97.5]). The median age on evaluation was 44-yo; 5(38.5%) were female. Five patients (38.5%) had anti-NMDAR, 3(23.1%) anti-LGI1, 1(7.7%) anti-neurexin, 1(7.7%) anti-Gluk2, 1(7.7%) anti-Yo, and 2(15.4%) had seronegative AE. During the acute stage most patients had neuropsychiatric and behavioral changes (n=11, 85.4%); sleep was inconsistently recorded, but insomnia was reported in 7 (53.8%). During follow-up 3 subjects presented mild depression (23.1%); anxiety frequency was 38.5%. No patient experienced mania or psychosis. Five patients (38.5%) reported bad sleep quality, scoring higher with greater admission delay (r=0.574, p=0.040).
Conclusion: We found subtle but frequent disturbances in mood, anxiety and sleep quality in this sample. If not systematically evaluated, these changes might go unrecognized and if left untreated can significantly impair patients' quality of life.
Disclosure: The authors have nothing to declare.

EPO-096

Clinical characteristics and predictors of relapse in anti-LGI1 encephalitis

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Background and aims: Autoimmune encephalitis (AE) with antibodies against leucine-rich glioma-inactivated 1 (LGI1) is usually monophasic, but approximately 15% of patients experience a relapse. Herein, we aim to clinically characterize the relapses and identify factors predicting their appearance.
Methods: Retrospective chart review of patients with isolated LGI1-antibody positivity in serum and/or cerebrospinal fluid (CSF). Relapse was defined as a worsening of previous symptoms or appearance of new symptoms after clinical stabilization.
Results: Among 216 patients with enough clinical data, we identified 30 (14%) that experienced a total of 33 relapses (table 1, figure 1). The median time to first relapse was 23.9 months (range 4.9-110.1). During relapses, clinical manifestations included memory impairment (70%), psychiatric/behavioral symptoms, facio-brachial dystonic and temporal lobe seizures (30% each). Brain imaging was abnormal in 16/26 (62%), while CSF was inflammatory in 13/25 (52%). LGI1-antibody testing was positive in 16/23 in serum (70%) and in 9/21 (43%) in CSF. At last follow-up 14 patients (47%) had a poor outcome. Patients that relapsed did not differ in their initial clinical and paraclinical features from a group of 85 patients that did not relapse and had similar length of follow-up (table 2). However, residual cognitive dysfunction after the initial episode was significantly associated with an increased risk of relapse (hazard ratio = 9.5, 95% confidence interval 1.7-182.0, p=0.038).

Table 1: Summary of main clinical and paraclinical features during the relapses.

	Relapses (n=33)
Median age at relapse, years (range, IQR)	68 (30-90; 14)
Median delay onset-first relapse, months (range, IQR)	23.9 (4.9-110.1, 17.8)
Median delay stabilization-relapse, months (range, IQR)	10.2 (2.5-85; 11.2)
Relapse occurring under immunotherapy	8 (24)
Median follow-up after relapse, months (range, IQR)	15.7 (0.3-65.6, 20.8)
Relapse onset	
Acute	6 (18)
Subacute	27 (82)
Clinical features	
Memory impairment	23 (70)
FBDS	10 (30)
TLS	10 (30)
Other seizures	8 (24)
Psychiatric	10 (30)
Other symptoms[a]	11 (33)
Hyponatremia	4/28 (14)
mRS score	3 (2-5; 1)
CASE score	3 (0-8; 2)
Paraclinical findings	
T2/FLAIR hyperintensity of limbic structures on brain MRI[b]	14/26 (54)
EEG documenting ictal activity	3/25 (12)
Inflammatory CSF	13/25 (52)
Mean CSF protein content (n=20)	0.58 ± 0.48
Mean CSF leukocyte count (n=20)	14.9 ± 48.2
Oligoclonal bands	0/16 (0)
LGI1-Ab positivity in serum	16/23 (70)
LGI1-Ab positivity in CSF	9/21 (43)
Altered metabolism in brain FDG-PET	2/5 (40)
Treatment	
IVIG	9 (27)
CS	15 (45)
RTX	19 (58)
Cyclophosphamide	10 (30)
Outcome (n=30 patients)	
Median mRS (range, IQR) after encephalitis and relapse	2 (0-6, 2)
Poor outcome (mRS ≥3)	14 (47)
Cognitive dysfunction	23 (77)

[a] sleep disturbances, 4; repeated falls and gait instability, 2; mood disorders, 2; abnormal limb movements, 1; buccal dyskinesia, 1; aphasia, 1.

[b] 2/26 patients developed T2/FLAIR hyperintensity of other areas (1 basal ganglia, 1 cerebellar peduncles and mesencephalon).

Abbreviations: IQR, interquartile range; FBDS, faciobrachial dystonic seizures; TLS, temporal lobe seizures; mRS, modified Rankin Scale; CASE, Clinical Assessment Scale in Autoimmune Encephalitis; MRI, magnetic resonance imaging; EEG, eletroencephalogram; CSF, cerebrospinal fluid; LGI1, leuchine-rich glioma-inactivated protein 1; Ab, antibody; FDG-PET,

Table 2: Characteristics of the initial encephalitis episode in relapsing patients compared to the control group.

	Relapsing patients (n=30)	**Control group (n=85)**	**p**
Median age at onset, years (range, IQR)	66 (29-86, 17)	64 (21-83, 14)	0.30
Male sex	23 (77)	51 (60)	0.10
Median diagnostic delay, days (range, IQR)	73 (18-3339, 130)	136 (2-1530, 161.5)	0.09
Median follow-up, months (range, IQR)[a]	23.9 (4.9-110.1, 17.8)	36.2 (24.4-156.7, 26)	< 0.001
Clinical features			
FBDS	14 (47)	45 (53)	0.55
TLS	14 (47)	48 (56)	0.35
SE	2 (7)	7 (8)	1
Other seizures	21 (70)	54 (64)	0.52
Psychiatric/behavioural	26 (87)	62 (73)	0.13
Memory impairment	29 (97)	83 (98)	1
Maximal mRS	3 (2-5, 1)	3 (1-5, 1)	0.13
Paraclinical findings			
Inflammatory CSF	20 (67)	40/82 (49)	0.09
Pleocytosis (>=5 cells/mm^3)	4/29 (14)	15/84 (18)	0.78
LGI1-Ab positivity in CSF	24 (80)	62/79 (78)	0.86
ICU admission	4 (13)	10/80 (13)	0.91
Hyperintensity of limbic structures on MRI	20/29 (69)	62/84 (74)	0.61
First-line treatment			
IVIG only	4 (12)	15 (18)	0.78
CS only	2 (7)	8 (9)	1
Combination IVIG+CS	23 (77)	59 (69)	0.45
Median delay onset-start of any first-line therapy, days (range, IQR)	81 (17-360, 118)	145 (6-750, 156.5)	0.013
Second-line treatment	18 (60)	48 (56)	0.74
RTX only	6 (20)	15 (18)	0.77
Cyclophosphamide only	3 (10)	8 (9)	1
RTX + cyclophosphamide	9 (30)	26 (31)	0.95
Median delay onset-start of any second-line therapy, days (range, IQR)	167.5 (43-960, 105)	230 (55-1516, 214.5)	0.09
Chronic oral immunosuppression	5 (17)	16 (19)	0.79
Outcome			
Median mRS (range, IQR)[b]	1 (0-4; 1)	1 (0-5, 2)	0.75
Poor outcome (mRS ≥3)	6 (20)	14 (16)	0.66
Cognitive dysfunction	23 (77)	51 (60)	0.1

[a] time to relapse in the relapsing group

[b] after encephalitis resolution and clinical stabilization in the relapsing group, and at last follow-up in the control group

Abbreviations: IQR, interquartile range; FBDS, faciobrachial dystonic seizures; TLS, temporal lobe seizures; SE, status epilepticus; mRS, modified Rankin Scale; CSF, cerebrospinal fluid; LGI1, leuchine-rich glioma-inactivated protein 1; Ab, antibody; ICU, intensive care unit; MRI, magnetic resonance imaging; IVIG, intravenous immunoglobulins; CS, corticosteroids; RTX, rituximab.

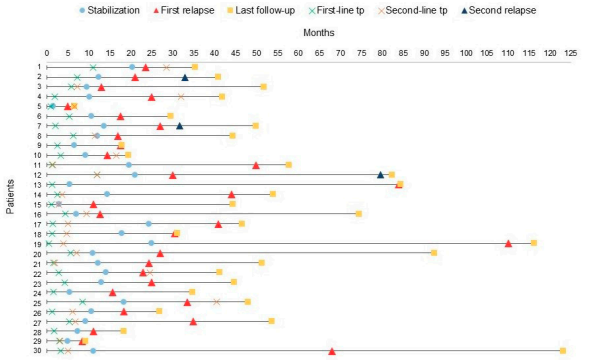

Figure 1: Swimmer plot illustrating the disease course and treatment of the relapsing patients.

Conclusion: Relapses can occur years after the initial episode of LGI11-encephalitis and should be suspected even without paraclinical signs of inflammation. Residual cognitive dysfunction after initial encephalitis increases the risk of future relapses.

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EPO-097

Fixed cell-based assay vs live cell-based assay for MOGAD diagnosis: a comparative study

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Background and aims: Myelin Oligodendrocytes Glycoprotein-Antibodies (MOG-Abs)-associated disease (MOGAD) is an inflammatory disorder in which the diagnosis relies on MOG-Abs presence in patients with a compatible phenotype. The gold-standard for MOG-Abs

detection is live cell-based assay (LCBA), but commercial fixed cell-based assays (FCBA) are often used. Previous studies comparing LCBA vs FCBA reported a lower specificity in FCBA and similar sensitivity. Aim of the study was to characterize patients tested negative on LCBA but positive on FCBA in a prospective French cohort.
Methods: Serum samples referred for MOG-Abs testing were analyzed using both techniques (Euroimmun FCBA, in-house LCBA). Clinical information were collected by the referring physicians. Two neurologists reviewed the clinical records and classified the cases into 3 groups: MOGAD, Multiple Sclerosis (MS), other neurological disorders (OND).
Results: Overall, 222/1166 prospective samples tested positive for MOG-Abs, 151/222 were positive with both techniques, 11 were positive only on LCBA, 71 were positive only on FCBA. Clinical information was available for 40/71 patients. Of these 40 patients, median age at onset was 36.5 [IQR 24.5-49.4], 60% were female. Clinical presentation at onset were optic neuritis (37.5%), myelitis (37.5%), brainstem syndrome (20%), cerebral focal syndrome (10%), cortical syndrome (7.5%) and ADEM (2.5%). Final diagnosis was MOGAD in 17/40 (42.5%), MS in 14/40 (35%), OND in 9/40 (22.5%). Two patients fulfilled diagnostic criteria both for MOGAD and NMOSD.
Conclusion: Though FCBA is associated to a risk of false positive results, testing with both LCBA and FCBA could increase diagnostic accuracy for MOGAD.
Disclosure: Nothing to disclose.

EPO-098

A non-invasive approach to demonstrate the underlying neuroinflammatory responses to severe TBI

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Background and aims: Neuroinflammation is a secondary injury mechanism that contributes to significant mortality and morbidity with severe traumatic brain injury (sTBI). Therefore, the application of non-invasive methods for detecting the neuroinflammatory response is of great interest. This study assessed the temporal profile of ionised calcium-binding adaptor molecule 1 (Iba1) and transmembrane Protein 119 (TMEM119) microglia marker proteins in the urine of sTBI patients for 7 days post-injury as a method of conceptualising the underlying neuroinflammatory response.
Methods: Urine samples were acquired from fifteen patients with sTBI upon hospital admission and the subsequent 7 days post-injury. Western blot analysis was used to quantify the urinary levels of Iba-1 and TMEM119 expression in each sample. The patients were stratified by functional outcomes (group 1, death- vegetative state; group 2, moderate-to- severe disability; group 3, good outcomes).
Results: Iba1 was detected in all (100%) whilst TMEM119 was detected in 65% of urine samples. The mean total normalised Iba1 expression increased for group 2 whilst the opposite response was observed for groups 1 and 3. The mean total normalised TMEM119 expression decreased for group 3 whilst the opposite response was observed for groups 1 and 2. However, these findings were not statistically significant. No significant differences were found in Iba1 or TMEM119 expression between favourable and unfavourable outcome groups.
Conclusion: Overall, this study cannot associate urinary Iba1 or TMEM119 expression with functional outcomes. However, the presence and temporal patterns of the urinary microglia markers suggest it may be reflective of the underlying neuroinflammatory process and merits further studies.
Disclosure: Nothing to disclose.

EPO-099

Autoimmune encephalitis during pregnancy: a diagnostic and therapeutic challenge

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Background and aims: Autoimmune encephalitis (AE) is one of the most common causes of noninfectious encephalitis in youth. In this systematic review, we summarize and analyze the available data on the diagnostic and therapeutic approach to AE during pregnancy, highlighting the associated maternal and fetal clinical outcomes.
Methods: A systematic search of the literature to identify the diagnostic and therapeutic management of AE during pregnancy and the associated maternal and fetal clinical outcomes was performed.

Results: Data from 49 patients were extrapolated. AE onset was mainly observed during the first trimester of pregnancy. Psychiatric manifestations and seizures were the first clinical symptoms. Cerebrospinal fluid (CSF) analysis was reported in 39 cases. Cellular pleocytosis was found in 30 and AE-specific autoantibody positivity in 33 patients. The most frequent autoantibodies detected were against the anti-NMDA receptor. EEG was performed in all patients, with 21 showing normal findings. Thirteen patients presented hyperintense signal changes on T2-FLAIR sequences, mostly in the temporal region. Tumor screening was reported in 45 cases, with positive findings in 14. Forty-four patients were treated with single or combination first-line immunosuppressants. Most of the women had an excellent early outcome after delivery. In long-term follow-up, 22 women showed persistent neurological deficits. Twelve cases of fetal death were reported. Newborn outcome was normal in 33 cases.
Conclusion: The diagnosis and treatment of AE during pregnancy are challenging. Caution should be paid to the potential teratogenic effects of several medical and diagnostic interventions. Maternal and fetal outcomes are mostly positive, although mothers may show long-term neurological deficits.
Disclosure: Nothing to disclose.

EPO-100

Proximal myopathy as a prominent feature of anti-IgLON5 disease

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Background and aims: Anti-IgLON5 disease is a novel entity, and recognizing all clinical symptoms and clues for diagnosis is therefore important. We specifically investigate the neuromuscular symptoms, and provide a link between IgLON5 and biopsy-proven myopathy. Moreover, response to immunotherapy is assessed.
Methods: All patients diagnosed in the Netherlands between 2016 and 2021 were included. National coverage was ascertained.
Results: Fifteen patients with anti-IgLON5 disease were included. Seven patients (47%) were male, the median age at symptom onset was 62 years (range 45-85). The median time from symptom onset to diagnosis was six years (range 0.6-23). Most striking were the neuromuscular symptoms, present in 7/15 patients (47%), including proximal muscle weakness (n=7), atrophy (n=5), and fasciculations (n=3). Muscle biopsy in six of them confirmed myopathy, with myopathic alterations in all, neurogenic lesion in one and immune cell infiltration in another patient. Other symptoms were sleep disorders (n=12), gait abnormalities (n=13), movement disorders (n=12), bulbar symptoms (n=10), dysautonomic symptoms (8/14), behavioural changes (n=8) and cognitive disorders (n=6). The median follow-up time since symptom onset was 90 months (range 12-297). Eleven patients (73%) were treated with first-line immunotherapy, showing a partial or temporary response in ten of them (91%). Eight of them were treated with second-line therapy (rituximab), showing some response in 4/7 patients and stabilization in 1/7 of the patients in which the effect could be assessed.
Conclusion: We found proximal myopathy as a new clinical feature in anti-IgLON5 disease. This finding extends the clinical phenotype and can be an important clue for diagnosis.
Disclosure: Nothing to disclose.

COVID-19; Infectious diseases 1

EPO-101

MRI findings in viral meningo-encephalitis – a study of 129 patients

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Background and aims: In workup of acute encephalitis (E) and meningoencephalitis (ME) brain magnetic resonance imaging (MRI) is essential to confirm and rule out alternative diagnoses, but is not an established prognostic tool. We aimed to 1) systematically describe MRI findings in patients (p) with viral E/ME 2) identify eventual MR related factors predicting clinical outcomes.
Methods: We conducted a retrospective analysis of p with E who underwent MRI scan and were treated in Inselspital 2016 - 2018.
Results: From a total of 258 p included in the original study (1), 129 made part of our analysis. Of 129 p, 28 were classified as E and 101 as ME. Most frequent causes were tick borne encephalitis in 54 (TBE, 42%), varicella zoster virus in 9 (VZV, 7%) and herpes simplex virus I in 7 (HSVI, 5%). In 52 (40%) p, disease cause remained unclear. First MRI were performed 7 days (median, IQR: 10) after symptom onset. Overall, abnormal diffusion-weighted imaging (DWI) and/or fluid attenuated inversion recovery (FLAIR) was found in 17 and 30%. All HSVE p had abnormal FLAIR and DWI scans, 27% of TBE and 31% of unknown E cases had abnormal MRI findings, most importantly FLAIR sequences showed signal abnormalities.
Conclusion: Rates and localization of MRI changes in different infectious causes of E vary significantly. Most important MRI changes are found in FLAIR sequences. Whether localization and lesion load correlates with clinical outcome is currently analysed. Results will be presented at the congress.
Disclosure: Nothing to disclose.

EPO-102

The return of spread of meningitis?: The drop in child vaccinations after the COVID-19 pandemic

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Background and aims: In Brazil, that drop of vaccination in children made the meningitis rate increase from 2021 to 2022, approximately 1000 cases were registered in some states, and this alarmed WHO and other world institutions. The principals risk factors of meningitis are extremes of age, undervaccination, exposures and chronic medical disorders. Among these risk factors, the current drop in vaccination has been prevalent in the world after the COVID-19 pandemic period. Related to the low demand for health services and the concentration of efforts on caring for patients affected by coronavirus, there was a large wave of anti-vaccination. Furthermore, international studies showed that the global vaccination coverage continued to decline in 2021.
Methods: Ecological study, based on interrupted time series, carried out with data collected through the European Health for All database (HFA-DB).
Results: According to the HFA-DB, the WHO European region has a vaccination rate of Tdap vaccine from 95,8% in 2013 to 94,3% in 2020, Measles 95,1% in 2013 to 94,2% in 2020, HBV in 2018 94,1% to 93% in 2020 and Hib in 2013 with 93,1% to 94% in 2019 to drop to 93,3% in 2020.
Conclusion: The covid-19 pandemic has fueled an ongoing backlash in vaccinations, which has been achieved through decades of advertising and studies. Mainly, in European countries, it is necessary to observe and disseminate more news and research that influence the immunization of children from birth. Thus, reversing the decline in vaccination and increasing prevention against meningitis.
Disclosure: No potential conflict of interest was reported by the author.

EPO-103

Immune Response Following COVID-19 Vaccination (mRNA or Non-mRNA) in Evobrutinib-treated Patients with RMS: An Update

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Background and aims: Evobrutinib is a highly selective, CNS-penetrant, covalent Bruton's tyrosine kinase inhibitor currently under clinical investigation for the treatment of relapsing multiple sclerosis (RMS). Building on our previous findings, we investigated the humoral response of evobrutinib-treated patients with RMS (PwRMS) to mRNA and non-mRNA COVID-19 vaccination during the open-label extension (OLE) of a Phase II clinical trial (NCT02975349).

Methods: A post hoc analysis was performed among PwRMS who received both evobrutinib 75mg twice-daily and COVID-19 vaccines during the OLE period (n=45; mRNA n=37, non-mRNA n=8; booster n=14). Immunoglobulin G (lgG) anti-S1/S2 (SARS CoV-2 spike protein domains) specific COVID-19-antibodies were measured using an indirect chemiluminescence immunoassay (DiaSorin Molecular LLC, USA; lower limit of quantification, 3.8AU/ml; seronegative<15.0 AU/ml, seropositive≥15.0 AU/ml).
Results: Baseline mean(±SD) age of patients was 46.0±9.6 years, 68.9% were female and mean/minimum evobrutinib exposure pre-vaccination was 105.2/88.7 weeks. Of 45 evobrutinib-treated patients, 43 developed or increased S1/S2 lgG antibody levels post-vaccination (Table1). Patients who were either S1/S2 lgG seronegative or seropositive pre-vaccination demonstrated an antibody response post-vaccination. Most patients (n=36/45), whether seronegative or seropositive, demonstrated a 10–100-fold increase of S1/S2 lgG antibody levels from pre- to post-vaccination (Table2). S1/S2 lgG levels post-booster were higher versus post-vaccination.

	mRNA Covid vaccinated patients n=37	Non-mRNA Covid vaccinated patients n=8
Pre-vaccination	8.5±4.3	12.1±3.2
Post-vaccination	247.7±4.5	197.1±6.2

Data are represented as geometric mean ± SD, AU/mL

Table 1: S1/S2 lgG antibody levels at pre- and post-vaccination time-points (by vaccine type)

S1/S2 lgG antibody levels	Seronegative patients n=32	Seropositive patients n=13	All patients N=45
Pre-vaccination	4.3 ± 1.3	55.5 ± 4.0	9.0 ± 4.0
Post-Vaccination	133.6 ± 3.7	984.4 ± 2.9	237.8 ± 4.7
Fold change from pre- to post-vaccination	31.0 ± 3.4	17.7 ± 3.3	26.4 ± 3.4

Data are represented as geometric mean ± SD, AU/mL
Fold change are ratio between the post-dose and pre-dose IgG antibody levels

Table 2: S1/S2 lgG antibody levels at pre- and post-vaccination time-points (by serostatus at pre-vaccination)

Conclusion: This analysis supports our prior data showing that evobrutinib-treated PwRMS can mount an antibody response to mRNA COVID-19 vaccination. These results provide additional evidence that evobrutinib-treated PwRMS can mount a humoral response to COVID-19 vaccinations and that, with boosters, antibody levels increase further than after the first vaccination cycle.
Disclosure: Study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945) and EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755), Detailed author disclosures will be included in the presentation.

EPO-104

Does serum and CSF cytokine dosage differ between post- and para-infectious SARS-CoV-2-related Guillain-Barré Syndrome?

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Background and aims: Guillain–Barré syndrome (GBS) is a postinfectious immune-mediated polyneuropathy, which pathogenic hypothesis comprises virus-related neuropathogenic mechanisms and hyperacute immune response. We explored the hypothesis of a hyperacute immune response by dosing cytokines on CSF and serum of patients with SARS-CoV-2-related GBS.
Methods: Twenty-six patients with SARS-CoV-2-related GBS were divided in two groups: 1) "classic onset", 2) "parainfectious onset, according to whether they developed GBS after 7 days or before 7 days from COVID-19 onset. We dosed cytokines (IL-1b, IL-6, IL-8, TNF-alpha) on CSF and serum, compared the dosages in both groups and correlated the dosage of each cytokine with the severity of both infection and GBS, both at onset and at last follow-up.
Results: Fifteen patients were listed in the "classic onset" group (F = 6, mean age 62) and 11 in the "parainfectious onset" group (F = 4, mean age 62). Sixteen patients developed COVID-19 pneumonia, 9 developed upper respiratory tract infection and 1 developed gastrointestinal symptoms; 7 were admitted in ICU, 8 were not hospitalized. The mean GBS disability scale (GBS-DS) was 4 at onset and 2 at follow-up. We found no difference in the total amount of cytokines in serum and CSF between the two groups. No correlation was found between the dosage of each cytokine and severity of COVID-19 and GBS-DS both at onset and follow-up.
Conclusion: Since our observations showed no differences in the amount of cytokines between the two groups, we can conclude that the cause of a parainfectious onset must be other than hyperacute immune response.
Disclosure: The authors declare that they have no competing financial interests.

EPO-105

FATIGUE IN POST-COVID SYNDROME: A POSSIBLE CENTRAL ETIOLOGY?

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Background and aims: Post-COVID syndrome consists in symptoms persistence for more than 12 weeks after acute infection begins. Fatigue is a frequent and long-lasting symptom, its pathophysiology is still unclear. We assessed fatigue presence with a validated questionnaire (short modified fatigue impact scales sMFIS5) and investigated possible correlations between perceived fatigue and brain metabolism in patients with post-COVID syndrome.
Methods: We considered two patients populations visited in our clinic for post-COVID syndrome: P1 (69 subjects affected by neurological symptoms other than fatigue; 35 females; mean age: 59 +/- 12 years) and P2 (260 subjects not affected by any neurological symptom; 97 females; mean age: 64 +/- 11 years). 18 P1 pts (P3; mean age: 67 +/- 8 years; 10 females) performed brain FDG-PET at least six months after COVID resolution. PET images were processed using SPM12 to assess correlation between sMFIS scores and regional metabolism, considering inter-individual sex and age differences. P value of 0.001 uncorrected at voxel level and of 0.05 FWE corrected at voxel level were considered significant.
Results: Fatigue (sMFIS greater than or equal to 5) was prevalent in P1 (76%) than in P2 (47%). In P3 sMFIS scores were 9.1 +/- 3.2. Voxel-wise correlation of sMFIS scores with brain metabolism revealed a left temporal pole significant cluster, with lower relative metabolism linked to higher levels of perceived fatigue.
Conclusion: Our data suggest a possible fatigue central etiology since observed fatigue higher levels in P1 and an association between long-term fatigue and temporal dysfunction after Sars-Cov2 infection.
Disclosure: Nothing to disclose.

EPO-106

Not myopathic, but autonomic changes in patients with Long-COVID Syndrome (PASC).

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Background and aims: Neurological sequelae following SARS-CoV-2 infection still represent a serious concern both for neurologists and neuroscientists. In our paper, we investigated myalgia and fatigue as symptoms in Long-COVID patients with an electrophysiological approach, comprising the evaluation of sympathetic skin responses (SSRs) and quantitative Electromyography (qEMG).
Methods: 12 patients were enrolled, referred to our attention because of myalgia, pain or muscle cramps, which persisted about six months after the diagnosis of SARS-CoV-2 infection. They underwent conventional Electroneurography (ENG), needle electromyography (EMG) and SSRs; moreover, qEMG was performed by sampling at least 20 Motor Unit Potentials (20-30 MUPs), during weak voluntary contraction, in deltoid and tibialis anterior muscles. The mean duration, amplitude, and percentage of polyphasic potentials were assessed and compared with healthy and age-matched volunteers.
Results: ENG did not disclose significant changes compared to healthy subjects; qEMG showed MUPs similar to those recorded in healthy volunteers, in terms of polyphasia (deltoid: p=0.24; TA: p=0.35), MUP area (deltoid: p=0.45; TA: p=0.44), mean duration (deltoid: p=0.06; TA: p=0.45) and amplitude (deltoid: p=0.27; TA: p=0.63). SSRs were not recordable from lower limbs in seven patients (58%), and from the upper ones in three of them (25%). In remaining cases, SSR latencies are significantly longer compared to healthy volunteers when recorded from lower limbs (p=0.0019).

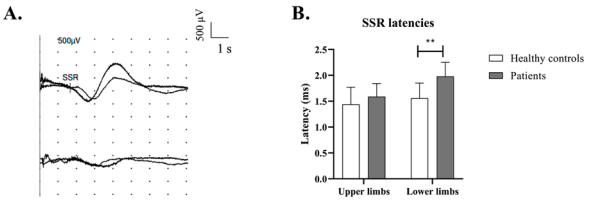

Figure 1 – Neurophysiological evidence of a small-fibers neuropathy (SFN).

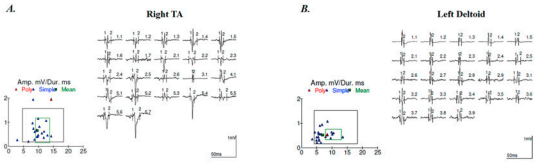

Figure 2 – Quantitative EMG in a representative long-COVID patient.

Conclusion: Our data suggest an involvement of the autonomic system, with a focus on cholinergic efferent sympathetic activity, without any evidence of myopathic changes.
Disclosure: Nothing to disclose.

EPO-107

DNA of herpesviridae is not detectable in cerebrospinal fluid of patients with neurological symptoms in Post-COVID-19

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Background and aims: Underlying pathophysiological mechanisms of Post-COVID-19 syndrome (PCS) are yet to be determined, but one of the possible mechanisms contributing to PCS is the reactivation of latent herpesviruses. In this study, we analyzed cerebrospinal fluid (CSF) and blood for viral DNA via PCR in PCS patients with neurological symptoms.
Methods: Patients fulfilling WHO PCS criteria and with a positive SARS-CoV-2 PCR result at least three months before presentation were included. Preexisting neurological and psychiatric diseases led to exclusion. DNAs of HSV1, HSV2, VZV, CMV, EBV and HHV6 were analyzed in CSF and blood via PCR.
Results: Sixty patients were included. No DNAs of HSV1, VZV, EBV, CMV and HHV6 were detectable in patients' CSF. One patient had a borderline positive result of HSV2 DNA in CSF with no signs of HSV-2 encephalitis in standard CSF analysis. There was one borderline positive PCR result for HSV1 and HHV6 in blood analysis. For EBV, four patients had a borderline positive PCR result in blood with a detection of less than 1000 copies per milliliter in quantitative analysis.
Conclusion: We found no evidence of replication of herpesviridae in the central nervous system of PCS patients with neurological manifestations. We detected a small number of borderline positive EBV results in blood of patients, so further investigation of the role of EBV including serological studies and analysis of EBV-specific T-cells in PCS patients is needed.
Disclosure: This study was partially funded by the Deutsche Forschungsgesellschaft (DFG; grant number FR 4479/1-1 | PR 1274/8-1 | WA 4101/2-1).

EPO-108

Presenting the Post-Corona-Virus Immune Treatment trial (PoCoVIT) – a study outline

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Background and aims: The Post COVID-19 syndrome (PCS) is a severely debilitating condition in which cognitive impairment is reported frequently. Recent research underlines the relevance of (auto-) immunological hyperreactivity in the central nervous system. However, there is little evidence for treatment strategies. Here, we present the Post-Corona-Virus Immune Treatment trial (PoCoVIT), a randomized controlled trial starting in 2023 that will investigate the effects of immunosuppression on cognitive deficits in PCS.
Methods: Patients ≥18y, matching the WHO criteria of PCS and reporting cognitive impairment as leading deficit are eligible. 418 participants will be allocated 1:1 to 4 weeks of 1mg/kg bodyweight oral methylprednisolone (followed by 14d tapering) or placebo. After a washout period, all participants will receive unblinded methylprednisolone over 6 weeks. All participants will undergo structural MRI at baseline. Participants found to have anti-neuronal autoantibodies in cerebrospinal fluid will be subjected to functional MRI. Primary outcome is an increase ≥ 15 points in the memory satisfaction subdomain on the Multifactorial Memory Questionnaire (MMQ) that will be assessed at baseline, follow-up 1 (two weeks after blinded treatment phase) and 2 (two weeks after unblinded treatment).
Results: The primary study aim is to investigate the effects of methylprednisolone versus placebo on cognitive deficits in PCS. Among others, secondary study objectives include the changes in neuropsychological functions and quality of life.
Conclusion: These findings will provide information on treatment strategies for PCS and potentially enable greater insights into the underlying pathophysiological mechanisms of the syndrome.
Disclosure: This study will be conducted within the Nationale Klinische Studiengruppe (NKSG) for the investigation of PCS and ME/CFS and has been supported by a Bundesministerium für Bildung und Forschung (BMBF) grant.

EPO-109

Comparison of the HFNC and NIMV Usage on COVID-19 Severity Scales With Neuroinflammatory and Neurocognitive Aspects

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Background and aims: Coronavirus disease (COVID-19) is a fatal disease that affects all systems, especially the pulmonary system and can affect pulmonary-cerebral interaction. This study compares the effects of High-Flow Nasal Cannula Oxygen (HFNC) and Non-Invasive Mechanical Ventilator (NIMV) use on COVID-19 severity scales and neuroinflammatory parameters determine its relevance on the cognitive system.
Methods: We conducted this study on 50 patients using HFNC (n:25) or NIMV (n:25), who were followed up with COVID-19 pneumonia in the Neurology Intensive Care Unit (ICU). Demographic data, COVID-19 severity scales (Brescia-COVID Respiratory Severity Scale (BCRSS), Rapid COVID-19 Severity Index (QCSI), H-Index), serum neuroinflammatory parameters, Coronavirus Anxiety Scale (CAS) and Montreal Cognitive Assessment Scale were evaluated and compared on the first and seventh days in both groups. In addition, thorax computed tomography (CT) findings, Total Lung Severity Score (TLSS) were determined.
Results: Both groups were homogeneous in terms of age, gender, and education level. Each participant had at least one RT-PCR test of positivity. At the end of the 7th day, QCSI and H-Index were higher in the NIMV group; MOCA was lower in the NIMV group(Table-1); CAS scores were higher in the NIMV group(Table-2); ESR, NLO, pro-calcitonin and troponin values from neuroinflammatory parameters were higher in the NIMV group($p<0.05$).

	HFNC(mean±2)	NIMV(mean±2)	p
MONTREAL COGNITIVE ASSESSMENT (MOCA) (1. Day Measurement)	19,2	18,84	0,117€
MONTREAL COGNITIVE ASSESSMENT (MOCA) (7. Day Measurement)	19,48	15,84	**0,044€***

*p<0,01 *p<0,05
n: Number; %: Percentage,:
€ Mann Whitney-U test ¥ Student's t test

Table-1. Comparison of MoCA (Day 1-7) in NIMV and HFNC group

				Groups		Critical Value	p
				HFNC	NIMV		
Coronavirus Anxiety Scale (CAS)	1.Day Measurement	Negative	n	3	1	1,087	0,297
			%	75,0%	25,0%		
		Positive	n	22	24		
			%	47,8%	52,2%		
	7. Day Measurement	Negative	n	13	1	**14,286**	**0,001****
			%	92,9%	7,1%		
		Positive	n	12	24		
			%	33,3%	66,7%		

*p<0,01 *p<0,05
n: Number; %: Percentage,:
ç Chi-Square Test

Table-2. Comparison of CAS (Day 1-7) in NIMV and HFNC group

Conclusion: We concluded that the noninvasive oxygen module to be selected for patients to be monitored in intensive care conditions may affect COVID-19 severity, neuroinflammatory levels, and neurological, cognitive processes. In this aspect, the use of HFNC should be given priority in patients considered for noninvasive ventilation.
Disclosure: No affiliations with or involvement in any organization or entity with any financial interest exist.

EPO-110

Small fibre neuropathy in long-COVID-19 syndrome: a prospective case series.

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Background and aims: Peripheral nervous system disorders are part of the spectrum of neurological complications that may follow the SARS-CoV-2 infection, known as "long COVID-19" syndrome. Recent evidence suggest that small fibre neuropathy (SFN) could be responsible of some long-COVID-19 manifestations, such as acral paraesthesia and pain, but the role of small fibre damage in this population and its clinical impact remains unclear. In this prospective observational study, we aimed to assess small fibre damage in patients complaining of new-onset sensory symptoms and pain after SARS-CoV-2 infection.
Methods: We collected clinical data, standardized questionnaires assessing pain severity and autonomic symptoms, and investigated quantitative sensory testing (QST) and skin biopsy in 26 prospectively enrolled patients with new-onset paraesthesia and pain after SARS-Cov-2 infection. Inclusion criteria were age > 18 years, symptoms persisting from at least six months, and normal nerve conduction study.
Results: All patients developed new- onset paraesthesia, burning or electric shock-like pain, and autonomic symptoms within 2 months following infection, with acute onset in 9 patients. Skin biopsy confirmed intraepidermal nerve fibre reduction at calf in 6 patients, while 9 had thermal detection abnormalities at QST. Overall, 11 patients met diagnostic criteria for SFN. Of the remaining 15 patients, with diffuse pain and paraesthesia, 9 met diagnostic criteria for fibromyalgia.
Conclusion: Our study suggests that Sars-Cov-2 infection can trigger SFN, manifesting both acutely or short after COVID-19 with a variety of painful and autonomic symptoms. Fibromyalgia can underlie painful and autonomic symptoms in a considerable proportion of patients who don't fulfil SFN criteria.
Disclosure: Nothing to disclose.

EPO-111

Central Nervous System Tuberculosis: Clinical Manifestations And Neuroradiological Features

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Background and aims: Tuberculosis is a global health problem and remains the first cause of death by infectious disease in the world. Central nervous system tuberculosis (CNST) represents a severe presentation of the disease and is known for its clinical and radiological polymorphism. We aim to describe the clinical and radiological characteristics of CNST in a Tunisian cohort.
Methods: We conducted a retrospective study of 25 patients with CNST from the neurology department between 2004 and 2022. All patients underwent a cerebral +/- spinal MRI and a bacteriological study of cerebrospinal fluid (CSF).
Results: In this cohort, sex ratio was 1.08 and the mean age at onset was 47.7 years (20-83 years). At onset, patients' complaints were motor deficit (23.5%); headaches (17.6%); behavioral problems (11.7%); and altered consciousness (11.7%). On examination, clinical symptoms were: cerebellar ataxia (25%); hemiparesis (25%); paraparesis (16.7%); posterior cord syndrome (12.5%); confusion (12.5%) and cranial nerve impairment (8.3%). Among them, 29.2% had meningoencephalitis; 12.5% had radiculo-myelitis and 4.7% had meningo-encephalo-radiculo-myelitis. CSF analysis showed predominantly lymphocytic meningitis with hypoglycorrhachia in 37.5%, while CSF BK research was positive in only 4.7%. On neuroimaging, cerebral tuberculomas (66.7%); myelitis (16.7%); pachymeningitis (12.5%) and hydrocephalus (8.3%) were the most common features. At follow-up, 62.5% had a favorable disease course, while 16.6% had complications and 8.3% died.
Conclusion: CSNT is a serious health problem. However, clinical polymorphism and diagnostic difficulties should not delay therapeutic management.
Disclosure: Nothing to disclose.

EPO-112

Neuroimmune disorders after SARS-CoV2 vaccination

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Background and aims: Several neuroimmune syndromes have been reported after exposure to SARS-CoV2 vaccine. The aim of this study was to know the frequency and characteristics of these syndromes.
Methods: Observational retrospective cohort study, including patients who were hospitalized in the Neurology department of La Paz University Hospital from January 2021 to May 2022 with a probable neuroimmune disorder. Demographic, clinical and outcome data were collected, comparing recently exposed to SARS-CoV2 vaccine cases to those who weren't.
Results: From a total of 108 patients, 30 were excluded because of a final diagnosis other than immune mediated. Thirty-six patients (46.2%) had received one dose of COVID-19 vaccine in the 3 months prior (21.8% during the previous month). 63.9% were women and the median age was 51.2 years (SD 22.6), without significative difference with the non-recently vaccinated (Mann-Whitney U p=0.256). The Biontech-Pfizer vaccine was the most frequent (63.9%). The neurological syndromes found (vaccinated/total) were: polyradiculoneuropathy (8/16), encephalitis (5/11), multiple sclerosis relapse (5/16), optic neuritis (1/4), myelitis (3/6), cranial nerve neuropathy (6/10), aseptic meningitis (1/3) and others (7/11). 22.2% of the recently vaccinated patients had suffered a previous SARS-CoV2 infection (vs 21.4% of non-recently vaccinated). 61.1% of the recently vaccinated cases received acute immunomodulatory treatment and 47.2% presented complete clinical improvement, without significant differences with non-recently vaccinated cases (Chi-squared p=0.643; p=0.570).
Conclusion: The most frequent neuroimmune disorders after the recent vaccination against SARS-CoV2 were polyradiculoneuropathies and cranial neuropathies. The neuroimmune syndromes that appear after the administration of the Covid-19 vaccine don't seem to present specific differences.
Disclosure: Nothing to disclose.

Movement disorders 1

EPO-113

Cervical Vestibular-Evoked Myogenic Potentials in Patients with Parkinson's disease

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Background and aims: The role of vestibular otolith function and its central connections is still obscure and overlooked. We aimed to investigate brain stem function and to understand the abnormalities of cVEMPs and their differential clinical correlations with symptoms related to brainstem involvement in Parkinson's disease (PD) patients using a validated, comprehensive, neurophysiologic tool; Cervical vestibular-evoked myogenic potentials (cVEMPs).
Methods: This study is an observational prospective case-control study that was conducted from January 2022 to November 2022. The study was conducted on 62 subjects, and they were equally subdivided into two groups; Group I (Cases) included patients diagnosed with idiopathic PD and Group II (Controls) included age and gender healthy matched subjects. Cervical Vestibular-Evoked Myogenic Potentials (cVEMP) testing was carried out for all subjects to assess the saccular function and inferior branch of the vestibular nerve.
Results: However, the prolonged latencies of P13 and N23 were positively correlated with UPDRS-III and H&Y Scale; the P13-N23 amplitude didn't show significant correlation. Having the identification of cVEMP, the response was present in about two-third of the case group with a statistically significant difference between the two groups (P<0.001). Among the case group, the mean P13 latency and N23 latency was significantly prolonged, while the mean P13-N23 amplitude was significantly reduced with a statistically significant difference between the two groups (P<0.001).
Conclusion: We demonstrated the pathophysiological dynamics of saccular part of otolith and its central connection involvement in patients with PD using a cVEMP can be considered an electrophysiological marker to explore brainstem dysfunction.
Disclosure: The authors declare that there was no conflict of interest.

Table 1. Clinical characteristics among the case group.

Variable	Case group (n=31)
Age (years)*	63.10 ± 9.44
Gender (males), n (%)	19 (61.3%)
Disease duration (years)*	7.10 ± 4.02
Most affected side, n (%)	
Right side of the body	12 (38.7%)
Left side of the body	19 (61.3%)
History of falls, n (%)	
None	20 (64.5%)
Rare falling	6 (19.4%)
Occasionally falls	3 (9.7%)
Falls on average once daily	2 (6.5%)
Falls more than once daily	0 (0%)
The Pull test, n (%)	
Normal	25 (80.6%)
Retropulsion but recovers unaided	3 (9.7%)
Absence of postural response	2 (6.5%)
Very unstable; *tends to lose balance spontaneously*	1 (3.2%)
Unable to stand without assistance	0 (0%)
H&Y Scale*	1.77 ± 0.62
UPDRS-III*	14.10 ± 8.42

*Data presented as mean ± standard deviation (SD).
UPDRS-III; Unified Parkinson's Disease Rating Scale section III, **H&Y Scale;** Hoehn and Yahr scale

Table 2. Characteristics of cVEMP in patients with Parkinson's disease.

	Case group (n=31)
Present VEMP Response, n (%)	22 (70.9%)
Gender (males)	13 (59.1%)
History of fall	4 (18.2%)
Postural instability	2 (9.1%)
Absent VEMP Response, n (%)	9 (29%)
Gender (males)	6 (66.7%)
History of fall	7 (77.8%)
Postural instability	3 (33.3%)
cVEMP Response (P13 latency), r*	
UPDRS-III	0.391
H&Y Scale	0.552
cVEMP Response (N23 latency), r*	
UPDRS-III	0.566
H&Y Scale	0.623
cVEMP Response (P13-N23 Amplitude), r*	
UPDRS-III	- 0.266
H&Y Scale	- 0.277

*The Pearson correlation coefficient **(r)** was used to describe the degree of relationship between two variables. The sign of correlation coefficient (+ , −) defines the direction of the relationship, either positive or negative
UPDRS-III; Unified Parkinson's Disease Rating Scale section III, **H&Y Scale**; Hoehn and Yahr scale, **cVEMP;** Cervical vestibular-evoked myogenic potential.

Table 3. Identification of cVEMP among the included subjects.

Variable	Case group (n=31)	Control group (n=31)	P value^{x}
cVEMP, n (%)			
Present response	22 (70.9%)	31 (100%)	< 0.001
Absent response	9 (29%)	0 (0%)	< 0.001
P13 latency (ms)	15.57 ± 2.82	12.23 ± 2.02	0.001
N23 latency (ms)	24.68 ± 2.78	21.13 ± 1.98	0.001
P13-N23 Amplitude (μv)	37.85 ± 4.35	49.31 ± 2.77	0.001

*Data presented as mean ± standard deviation (SD)
^{x}***P*<0.05** was considered statistically significant
cVEMP; Cervical vestibular-evoked myogenic potential

EPO-114

A new variant for autosomal recessive complicated hereditary spastic paraplegia (SPG26) - a case report

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Background and aims: The term hereditary spastic paraplegia (HSP) describes a group of inherited heterogeneous disorders characterized by progressive spasticity and weakness of the lower limbs. One of the less common variants is spastic paraplegia-26 (SPG26), an autosomal recessive form that begins in the first 2 decades of life with gait disturbance. Some patients have upper limb involvement and additional features such as intellectual disability, peripheral neuropathy, dysarthria and cerebellar signs. The SPG26 is caused by mutation in the B4GALNT1 gene on chromosome 12q13.
Methods: We present a clinical case compatible with SPG-26.
Results: A 55-year-old woman consulted for progressive gait impairment since she was 6 years old and intellectual disability. Family history shows similar clinical features in paternal cousins and brothers. All of them made their clinical debut in their childhood. The neurological examination revealed scanned dysarthria, hypometric saccades, skew deviation, mild spastic tetraparesis, cerebellar dysmetria, hyperreflexia, extensor plantar responses and pes equinovarus. The genetic study identified our patient as a homozygous carrier of the change of uncertain significance c.1399G>A (p.G467R) in the B4GALNT1 gene. Biallelic variants in this gene are responsible for an autosomal recessive form of complicated spastic paraparesis. Other disease-related missense variants affecting the same domain have been described. Family segregation is in progress.

Cambios de interés clinico detectados

Teniendo en cuenta la información clínica referida, destacamos las siguientes variantes asociadas al fenotipo del paciente:

Gen	HGVSc	HGVSp	dbSNP	MAF	Genotipo	Herencia	Clasificación
B4GALNT1	NM_001478.4: c.1399G>A	NP_001469.1: p.G467R	.	0.000004019 (gnomAD)	homocigosis	AR	Significado clínico incierto

Conclusion: We present an undescribed variant of the B4GALNT1 gene and a family history compatible with SPG-26. The descriptions of new variants by new genetic advances are important as they provide information for research and genetic advice.
Disclosure: The authors do not have conflicts of interest.

EPO-115

Bilateral and bi-hemispheric deep brain stimulation (DBS) in Lesch-Nyhan Disease: shifting the treatment paradigm

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Background and aims: Lesch-Nyhan Disease (LND) is a rare debilitating genetic x-linked disorder caused by a mutation affecting the HPRTI gene, encoding the purine salvage enzyme. When the enzymatic activity is under 2% patients present with severe intellectual disability, behavioral and extrapyramidal symptoms, classically characterized by self-injury behavior (SIB), dystonia and opisthotonus, and currently there is no specific and effective medical treatment for these deficits. Very few cases of LND have been submitted to DBS, in different cerebral targets with variable results.
Methods: A 5-year-old male diagnosed with LND at 11 months, Xq26.3 deletion, presented with severe generalized dystonia, opisthotonus, and SIB with severe bite injuries. DBS was done with the implantation of 4 electrodes, targeting nucleus accubens (NA) and motor internal globus pallidus (GPi) bilaterally.
Results: In the immediate post-surgical assessment, the patient was globally calmer, revealed less SIB and improvement in dyskinetic movements. Fourteen days after surgery, according to the parents, he was calmer and there were no self-mutilating behaviors during this period, and additionally presented with less dystonia and without opisthotonus.
Conclusion: DBS may present as a promising treatment of refractory SIB and dystonia in LND. There are still many open questions, particularly concerning ideal time frame for surgery, with some reports pointing towards the benefit of early treatment of SIB during critical windows of development; and optimal targets, with growing evidence supporting the benefits of GPi and NA bilateral and bi-hemispheric stimulation. Additional studies and longer follow up is needed to better inform the effectiveness and safety of DBS in LND.
Disclosure: Nothing to disclose.

EPO-116

Asymmetry and side concordance of rest tremor and bradykinesia in patients with essential tremor

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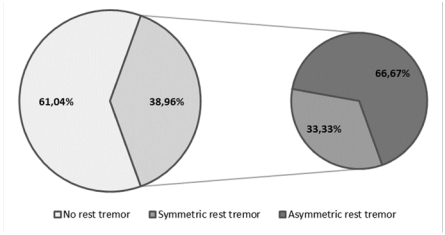
Background and aims: Subtle parkinsonian signs, i.e., rest tremor and bradykinesia, can occur in patients with essential tremor (ET) and can be considered soft signs for the definition of ET-plus. In the present study, we aimed to investigate the clinical and kinematic features of rest tremor and bradykinesia in ET, with a focus on body distribution and side concordance.

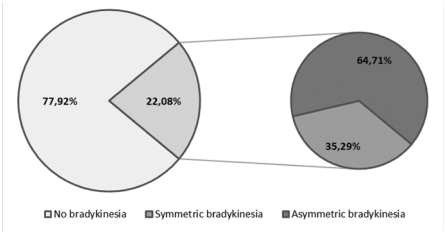
Methods: Standardized clinical scales and a kinematic system for movement analysis were used to assess tremor and movement velocity during repetitive finger movements in a sample of 77 ET patients. We then investigated tremor asymmetry, side concordance and possible correlations between motor symptoms in our sample.

Results: Rest tremor and bradykinesia were clinically detectable in 30 (38.96%) and 17 (22.08%) out of 77 patients, and clearly asymmetric in 66.67% and 64.71% of cases, respectively. In patients with asymmetric rest tremor, asymmetry of the movement velocity was observed in 15 cases (75%). However, in the majority of patients (9 out of 15, 60%), there was no side concordance between rest tremor and bradykinesia. Conversely, we observed a side concordance between asymmetric postural tremor and bradykinesia in a high percentage of cases (13 out of 17 patients, 76.47%: p=0.02). No correlation was observed between action tremor amplitude and movement velocity.



	ET patients with rest tremor	ET patients without rest tremor	p
Sex	14F/16M (46.67%/53.33%)	17F/30M(36.17%/63.83%)	0.36
Age (years)	71.93 ± 7.73	66.47 ± 14.74	0.06
Age of onset (years)	53.03 ± 19.51	54.46 ± 18.25	0.75
Tremor duration (years)	18.9 ± 16.34	12.01 ± 11.64	**0.03**
Family history	14Y/16N (46.67%/53.33%)	27Y/20N(57.45%/42.55%)	0.36
FTM-TRS total score	31.47 ± 13.69	16.38 ± 11.20	**<0.01**

Characteristics of ET patients with and without rest tremor. The pie charts show the prevalence of rest tremor in our sample and the percentage of patients in which it is asymmetrical. Significant p-values are in bold.



	ET patients with bradykinesia	ET patients without bradykinesia	p
Sex	7F/10M (41.18%/58.82%)	24F/36M(40%/60%)	0.93
Age (years)	70.76 ± 12.43	67.98 ± 12.83	0.43
Age of onset (years)	54.53 ± 18.9	53.73 ± 18.72	0.88
Tremor duration (years)	16.24 ± 11.23	14.26 ± 14.71	0.61
Family history	30Y/30N (50%/50%)	11Y/6N(64.71%/35.29%)	**0.02**
FTM-TRS total score	27.71 ± 13.49	20.72 ± 14.15	0.07

Characteristics of ET patients with and without bradykinesia. Pie charts show the prevalence of clinically detectable bradykinesia in our sample and the percentage of patients in whom it is asymmetric. Significant p-values are in bold.

	N° of patients with both soft signs asymmetric	Concordant	Discordant	p
Rest tremor - Bradykinesia	15	6 (40%)	9 (60%)	0.4
Rest tremor - Action tremor	12	7 (58.3%)	5 (41.7%)	0.41
Bradykinesia - Action tremor	17	13 (76.47%)	4 (23.53%)	**0.02**

Data regarding the side concordance of the different motor symptoms in ET patients. Significant p-values are in bold in the table and marked with an asterisk in the graphs.

Conclusion: Rest tremor and bradykinesia are relatively frequent in ET and often asymmetric. Our findings suggest that these parkinsonian soft signs in ET possibly reflect different pathophysiological mechanisms. In contrast, postural tremor and bradykinesia may share a common pathophysiological basis, possibly reflecting the prominent cerebellar involvement in ET.

Disclosure: Nothing to disclose.

EPO-117

Wilson's disease and dangerous of copper deficiency phenomenon – the systematic review

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Background and aims: Wilson's disease (WD) is a genetic disorder with copper accumulation in tissues leading to clinical symptoms (mainly hepatic, neuropsychiatric). The

copper metabolism results in WD patients show increased serum "free copper" with its normalization during WD treatment. As WD treatment is lifelong, the possibility of copper deficiency (CD) during WD long treatment may occur. Aim of our study was to systematically assess data according to CD in WD, its frequency, association with anti-copper drug as its clinical symptoms and outcome.
Methods: This systematic literature review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies were identified by searching the PubMed database (up to 23 December 2022).
Results: Among the 19 articles, 21 cases of CD were described, most commonly in patients treated with zinc salts(16/21; 76%). The symptoms of CD occur insidiously during long WD treatment, including: sideroblastic anemia, neutropenia, axonal-sensory-neuropathy, posterior cord myelopathy or increased ratio of epileptic seizures(or epilepsy). The diagnosis of CD is based on clinical symptoms and severe decrease of urinary copper excretion(<20 μg/24 hours in patients treated with zinc or<100 μg/24 hours on chelators) with low serum copper and ceruloplasmin in WD patients.
Conclusion: Physicians should be aware of CD possibility during WD treatment. The transient discontinuation of anti-copper treatment usually reverses the CD in the serum, as well as pancytopenia, however the clinical symptoms, mainly neuropathy and myelopathy caused by CD, may persist. The regular control of copper metabolism during WD treatment is needed to avoid CD.
Disclosure: The authors have no potential conflict of interest to report.

EPO-118

Is there horizontal transmission of Creutzfeldt-Jakob disease?

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Background and aims: Sporadic Creutzfeldt-Jakob disease (s-CJD) is a rare, fatal neurodegenerative disorder. Familial cases of Creutzfeldt-Jakob disease (f-CJD) due to mutations in the PRNP gene are even rarer around the world; however, in Israel there is a focus of f-CJD patients carrying the E200K mutation. As the number of CJD E200K carriers in Israel is high and increasing, transmission of CJD to normal people was suspected. If such transmission occurs, the incidence of s-CJD would be expected to increase.
Methods: Using data from the national CJD registry and official statistics on the Israeli population, we studied incidence rates of f-CJD and s-CJD for the period from 1985 to 2018 applying the SEER statistical packet developed in the US National Cancer Institute.
Results: In total, 621 CJD patients (405 f-CJD and 216 s-CJD) cases are included in the registry. In the cohort of f-CJD patients the mean age-adjusted annual incidence rate over the above-mentioned period was 1.88±0.09 (95% CI: 1.7–2.08) per 1,000,000. In the cohort of s-CJD patents, the mean age-adjusted incidence rate over the same period was 0.93±0.06 (95% CI: 0.81–1.06) per 1,000,000 people. No significant time trends were found over the observation period in either s-CJD or f-CJD.
Conclusion: Israel has a high predominance of f-CJD compared to s-CJD. Between 1985 and 2018, the annual age adjusted incidence rates for both forms of CJD remained stable. Thus, there is no evidence that CJD is transmitted from affected individuals to others.
Disclosure: Nothing to disclose.

EPO-119

Action myoclonus (Lance-Adams syndrome). 3 different causes of 3 unique cases

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Background and aims: Lance-Adams syndrome (LAS) is a disease that may appear after a period of cerebral hypoxia usually after cardio-respiratory arrest of different etiology.
Methods: Diagnosis is clinical. LAS has no correlation with EEG or neuroimaging abnormalities.
Results: Case 1. Cardiac arrest caused by poisoning with belladonna tincture. The patient had been resuscitated, consciousness was recovered with the consequent onset of myoclonic hyperkinesis, provoked by ideation of movement or any movement itself, aggravated by unexpected sounds and disappeared in rest and sleep. Cerebellar gait ataxia affected independent standing. Case 2. The patient was admitted with acutely onset myoclonic jerks. Patient's history is specific for severe heart failure (LVEF 40%), respiratory insufficiency, severe obesity (BMI 35,8). Most of the time patient takes sitting position (with head droop forward on chest), because of severe dyspnea. Case 3. A 71 years old man was admitted to the hospital on the 12th-day of COVID-19 with severe cerebellar ataxia, myoclonus and cognitive impairment. The day before admission generalized tonic-clonic seizures occured and repeated on the day of admission.

Case 1. Action myoclonus (Lance-Adams syndrome) as a consequence of cardiorespiratory arrest caused by accidental poisoning with belladonna tincture.

Case 2. Action myoclonus (Lance-Adams syndrome) as a consequence of chronic brain hypoperfusion.

Case 3. Action myoclonus (Lance-Adams syndrome) secondary to generalized tonic-clonic seizures during COVID-19.

Conclusion: Lance-Adams syndrome, as a manifestation of posthypoxic encephalopathy after cardiorespiratory arrest and successful resuscitation with restoration of consciousness, intellectual-mnestic functions, but with preservation of subcortical myoclonus, grievously violating self-service. In the abstract we are describing 3 different causes of the same symptom, occurred in 3 different patients: as a consequence of cardiorespiratory arrest caused by poisoning with belladonna tincture, as a consequence of chronic brain hypoperfusion and secondary to generalized tonic-clonic seizures during COVID-19.

Disclosure: Prof., MD, T. Slobodin., Department of Neurology No l. Shupyk National Healthcare University of Ukraine. Kyiv Ukraine - management of the patients, descriptive part of the abstract. PhD Student, MD, S. Bandrivska - Department of Neurology No l. Shupyk National Healthcare University of Ukraine. Kyiv Ukraine - assistance in management of the patients, video recording of patients.

EPO-120

Pantothenate kinase-associated neurodegeneration: clinical, radiological and genetic study of six Tunisian families

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Background and aims: Pantothenate kinase-associated neurodegeneration (PKAN) is a rare neurodegenerative disorder caused by mutations in the PANK2 gene. It is characterized by progressive extrapyramidal dysfunction due to excessive iron deposition in the basal ganglia. Herein, we describe the genetic, clinical, radiological and therapeutical aspects of PANK2 mutations in pediatric patients.
Methods: We conducted a retrospective study over a 15-year-period including children diagnosed with PKAN. Genetic confirmation was performed by Sanger sequencing of the coding regions of the PKAN2 gene (NM_153638.3). Epidemiological, clinical, radiological and therapeutical aspects were analyzed.
Results: Four girls and two boys have been included. The mean age of onset was 4.4 years [1,13]. Sex-ratio(F/M) was 2/1. Four children had developmental delay. Oromandibular dystonia was the main clinical feature found in all patients. Other symptoms were dysarthria(n=1), parkinsonism(n=3) and behavioral changes(n=1). In all cases, Brain MRI showed the "eye-of-the-tiger" sign. CT scan showed calcifications in the basal ganglia in two cases. Genomic studies revealed five different PANK2 mutations. Molecular analysis showed the mutation in a homozygous state in five patients.
Conclusion: Study of this pediatric series highlights the particularity of the classical forms of PKAN compared to the late-onset forms. Dystonia is the major sign in the classical forms. The evolution is rapidly unfavorable. No curative treatment has proven to be effective. Genetic counselling is therefore essential in affected families.
Disclosure: I declare that there are no conflicts of interests.

EPO-121

Differential diagnostic and therapeutic challenges in atypical Parkinsonian disorders

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Background and aims: Heterogenous clinical presentation of atypical Parkinsonian disorders pose major challenges to accurately diagnose patients suffering from these conditions. In past decades, significant advancements in genomic technologies have provided us with increasing insight into the molecular pathogenesis of disorders, fueling new hopes to incorporate molecular knowledge into diagnostic and therapeutic approaches towards managing these conditions.
Methods: To facilitate the diagnostic succes of patients with atypical Parkinsonian disorders, we performed whole exome sequencing to better understand the genetic background and optimize therapy.
Results: WES identified the genetic background of atypical Parkinsonian symptoms in three pateints. Patient #1 presented with right sided rigidity, severe bradykinesia, followed by dystonia, atypical tremor and complex psychiatric symptoms, including anxiety, mood swings, panic attacks. WES detected a rare, heterozygous variant of unidentified significance (VUS) (c.1991G>A) in PDE10A gene, associated with striatal degenaration, limb and orofacial dyskinesia. DATSCAN supported the diagnosis. #2 patient's symptoms started after physical trauma. Acute left arm dystonia occured, followed by ipsilateral rigidity, bradykinesia and mental confusion. Atypical symtoms improved spontaneously after several weeks. WES revealed pathogenic mutation (c.18877C>T) in ATP1A3 gene, linked to rapid-onset dystonia-parkinsonism. His father had milder, but similar symptoms. Patient #3 showed symptoms of ataxia and muscle weakness, later parkinsonism, tetrapyramidal signs and severe orthostasis appeared. WES discovered a rare CHCHD2 gene VUS (c.179C>T), which was prevoiusly associated with Parkinson's disease and MSA.
Conclusion: In conclusion, genetic testing is an important differential diagnostic tool in rare neurodegenerative disorders. Understanding the molecular background may help choose the right therapeutic approaches in atypical Parkinsonian disorders.
Disclosure: Nothing to disclose.

EPO-122

CLINICAL AND IMAGING CHARACTERIZATION OF A COHORT OF SEVENTY-ONE MULTIPLE SYSTEM ATROPHY PATIENTS

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Background and aims: MSA is a rare neurodegenerative disease, classified into two subtypes, MSA-P and MSA-C. Beyond the core symptoms, many non-motor features can be part of the clinical picture. The diagnosis in the early stages can be challenging. This study aimed to review the characteristics of large cohort of MSA patients diagnosis in our center.
Methods: We examined a cohort of 71 patients with probable MSA, according to the Gilman criteria [1], assessed at the Movement Disorders clinic of Ospedale Maggiore Policlinico in Milan between 2012 and 2022.

Results: All patients are European. 37 patients had MSA-P and 34 MSA-C. The two sexes were equally distributed. Age at onset was slightly lower in MSA-C (58 years) than in MSA-P (62 years). In MSA-P the symptoms at onset were equally distributed among motor (54%) and non-motor (46%), whereas in MSA-C there was a prevalence in the motor onset (80%). All patients experienced autonomic dysfunction, with 90% of MSA-P and 80% of MSA-C presenting orthostatic hypotension, and all patients having genitourinary disturbances; constipation was more common in MSA-C (96%) than in MSA-P (73%). A small subset of patients presented hyposmia. The most common MRI findings were: atrophy of putamen (P 28%, C 9%), middle cerebellar peduncle (P 4%, C 21%), pons (P 4%, C 24%), cerebellum (P 16%, C 65%), and hot cross bun sign (P 8%, C 35%). Study outcomes confirmed previous clinical and imaging data from the literature [2].
Conclusion: MSA is still insidious, but some clinical and imaging features can help the diagnostic process.
Disclosure: Nothing to disclose.

EPO-123

Neurophysiological changes of primary motor cortex in patients with essential tremor-plus

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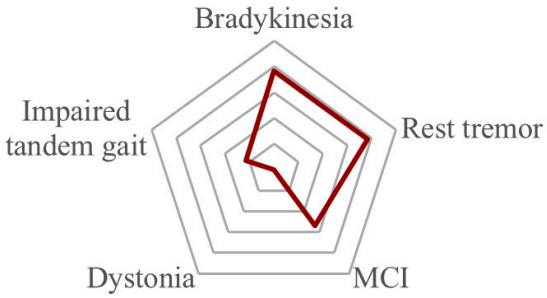
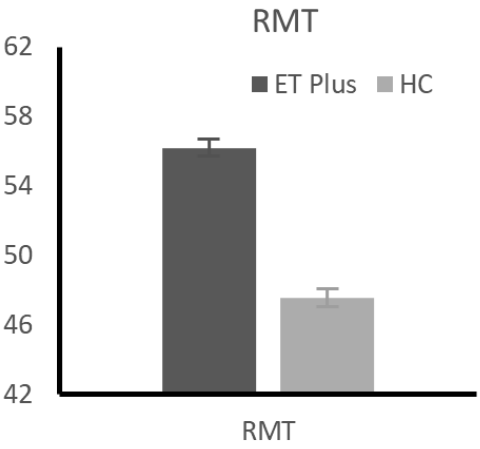
Background and aims: Essential tremor-plus (ET-plus) represents a recently introduced entity indicating ET patients with additional neurological signs of uncertain significance. The aims of our study was to investigate possible neurophysiological changes of the primary motor cortex (M1) and their relationship with soft signs in patients with ET-plus.
Methods: Thirteen ET-plus patients were enrolled (5 females, 70±7.97 years). Most patients had rest tremor, subtle bradykinesia, MCI and only 3 of them had impaired tandem gait. Patients were evaluated by standardized clinical scales. Objective measurements of rest tremor and bradykinesia were obtained by kinematic analysis. M1 excitability was assessed by the recordings of resting motor thresholds (RMTs), input/output curve of the motor-evoked potentials (MEPs), short-interval intracortical inhibition (SICI) and short-latency afferent inhibition (SAI). Plasticity-like mechanisms were indexed according to MEPs amplitude changes after intermittent theta-burst stimulation (iTBS). Data were compared to those from 16 healthy controls (HCs).

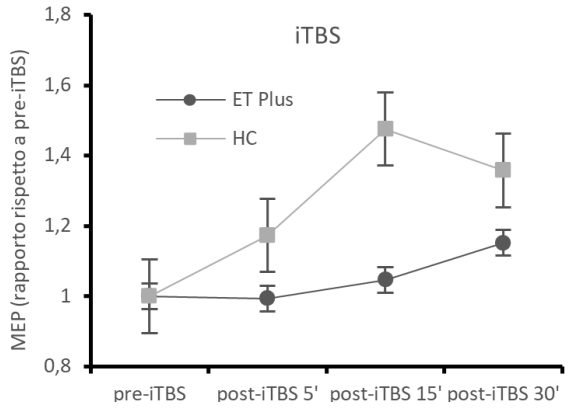


Distribution of the different soft sign in patients with Essential tremor plus (ET-Plus)

Results: Compared to HCs, ET-plus patients had higher RMTs (P=0.019), indicating a lower corticospinal excitability and a lower MEPs facilitation after iTBS (P=0.032), reflecting a lower cortical plasticity. ET patients were slower than HCs during finger tapping (P=0.03). No correlations were found between neurophysiological, clinical and kinematic data, nor relationships between neurophysiological changes of M1 and the type or severity of soft signs in ET plus patients.



Motor evoked potential (MEP) amplitude of the resting motor threshold (RMT) in the 2 groups. Essential tremor plus (ET-Plus) (black indicator) and healthy controls (HC) (grey indicator)



Motor evoked potential (MEP) amplitude changes (Y-axis) induced by the intermittent theta burst stimulation (iTBS) protocol in the 2 groups. Essential tremor plus (ET-Plus) (black indicator) and healthy controls (HC) (grey indicator)

Conclusion: We here provided novel information on excitability and plasticity abnormalities of M1 in patients with ET-plus. Our results suggest that neurophysiological changes of M1 underline common pathophysiological mechanisms in the different forms of ET plus patients
Disclosure: No conflict of interest.

EPO-124

Novel insights into the origin of subthalamic (STN) beta oscillations in Parkinson's Disease

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Background and aims: Neuronal subthalamic (STN) activity in Parkinson's Disease (PD) is characterized by an excessive rhythm in beta band frequency range (12-35 Hz), which is normalized by levodopa. The aim of our study was to explore the origin of beta oscillations, by assessing possible changes of subthalamic LFPs in different moments during Deep Brain Stimulation (DBS) surgery. That is of key importance because the beta rhythm is now considered the most reliable electrophysiological marker for guiding novel adaptive DBS approaches.
Methods: STN signals were recorded in four patients in three different moments during DBS implantation: before sedation, during Propofol alone and under the effect of both Propofol and Rocuronium. LFPs were analyzed in terms of both linear and non-linear analyses (e.g. power spectral density, sample entropy and multi-scale entropy), as well as burst analysis.
Results: Although other analyses, either linear or non-linear, did not disclose any statistical difference among the three experimental conditions, burst analysis revealed significant changes in terms of mean amplitude and beta burst duration during curarization when compared to other experimental conditions.
Conclusion: Whether there is an involvement of the peripheral system, or gamma-motoneurons, in the modulation of the hyper-synchronized β power is still a matter of debate, our work could highlight novel insights into the origin of the beta rhythm, possibly suggesting that these oscillations arise away from the basal ganglia network.
Disclosure: I have no conflicts of interest to declare.

EPO-125

Phase-amplitude coupling between beta power and high frequency oscillations as a biomarker for deep brain stimulation.

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Background and aims: The aim of this work was to study the potential clinical usefulness of the beta power phase-amplitude coupling (PAC) with high frequency oscillations (HFO´s). Beta hypersynchrony has been introduced into clinical practice recently in Parkinson´s disease (PD) to identify the best stimulation contact and for adaptive deep brain stimulation (aDBS) sensing. However, many other oscillopathies accompany the disease and beta power sensing is not optimal for all patients.
Methods: Subthalamic nucleus (STN) local field potentials (LFP´s) from externalized DBS electrodes were recorded and analyzed in PD patients (n=19). Beta power and HFO´s were evaluated in resting state condition, then the phase-amplitude coupling (PAC) was studied and correlated with the electrode contact positions and structural connectivity.
Results: Beta- HFO´s PAC (mainly in 200-400Hz range) was observed in all subjects. PAC was significantly stronger during high beta power episodes and in more affected sides. Moreover, this PAC was detectable also in contacts located within the STN, where beta power was non-conclusive.
Conclusion: Coupling between beta power and HFO´s increases with the beta power synchronization, which is known to be a correlate of PD off state. Beta- HFO´s PAC seems to be more sensitive than beta power fluctuations itself and could be more helpful in the best stimulation contact clinical selection and probably also as potential future input signal for aDBS.
Disclosure: This research has been financially supported by Czech science foundation GAČR 21-25953S

EPO-126

GPi-DBS in a patient with pathology-confirmed Corticobasal Degeneration

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Background and aims: Deep brain stimulation (DBS) may be very effective for focal dystonia1. There have been no case reports of DBS for corticobasal syndrome (CBS), except one patient initially diagnosed with Parkinson's disease and referred to as a 'DBS failure'2.
Methods: We describe a male patient presenting at 70 years old with weakness in the left hand which progressed to dystonic hand posturing. Superimposed, there were painful, action-induced spasms. CBS was suspected but the very focal presentation and absence of cortical involvement (both clinically as on MRI brain) was atypical. EMG ruled out neuromuscular disorders and CSF was negative for paraneoplastic disorders (including stiff person syndrome).
Results: Multiple pharmacological agents were tried to address the dystonia and spasms including levodopa, baclofen, trihexyphenidyl, levetiracetam, valproic acid without success. Clonazepam initially provided some benefit. Botulinum toxin injections only had a partial and transient effect. Right GPi-DBS was undertaken four years after symptom onset. Despite multiple programming attempts the patient obtained only modest alleviation of symptoms. Six years after symptom onset, the patient underwent medical-assistance in dying. Prior to death, dystonic features were also present in the other limbs and graphesthesia had become apparent as well as some cognitive decline. Autopsy revealed pathognomonic features of the 4R tauopathy, corticobasal degeneration. Tau pathology predominated in motor and parietal cortices but affected basal ganglia and brainstem as well.
Conclusion: Lack of benefit of DBS highlights the complex pathophysiology of dystonic posturing in CBS that might be influenced by severe upper motor neuron involvement as exemplified in this case.
Disclosure: • Dr. Boogers – nothing relevant to this abstract • Dr. Candeias da Silva – nothing relevant to this abrasct • Dr. Marras – nothing relevant to this abstract • Dr. Kovacs - nothing relevant to this abstract • Dr. Lang – nothing relevant to this abstract • Dr. Fasano – nothing relevant to this abstract References 1. Vidailhet M, Jutras MF, Grabli D, Roze E. Deep brain stimulation for dystonia. J Neurol Neurosurg Psychiatry. 2013;84(9):1029-1042. doi:10.1136/jnnp-2011-301714 2. Okun MS, Tagliati M, Pourfar M, et al. Management of Referred Deep Brain Stimulation Failures. Arch Neurol. 2005;62(8):1250. doi:10.1001/archneur.62.8.noc40425

EPO-127

A simple machine learning algorithm to classifying atypical parkinsonian syndromes

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Background and aims: In the big data era, artificial intelligence techniques have been proposed to treat classification problems especially among neurodegenerative diseases. Aim of this study is to develop a machine learning (ML) algorithm based on clinical variables in order to correctly classify atypical parkinsonian syndromes (APS), such as Multiple system atrophy (MSA), Progressive supranuclear palsy (PSP) and Corticobasal syndrome (CBS).
Methods: This is a cross- sectional study of 22MSA-C, 13MCA-P, 15PSP and 10CBS patients. We used predictors such as clinico-demographics (age, gender, education, disease duration, MDS-UPDRSIII, LEDD, UMSARScore, PSPScore, Hoyen&Yahr, Schwab&England, SCOPA-AUT) five neuropsychological tests (MOCA, FAB, Goldenberg Scale, Digit Span total, Geriatric depression Scale). The "Pearson product moment correlation coefficient" (PPMCC) was obtained by the ratio of the covariance of two variables, normalized to the square root of their variances. Then, the values were normalized between 0-100%(100 the most important variable). Afterwards, the data was inserted into a KNN classifier model with feature scaling and k=4.
Results: SCOPA, MDS-UPDRS III, MOCA and FAB scores were the variables that mostly influence the APS type (100%, 78%, 72%, 66% respectively). Regarding the KNN classifier model, the accuracy was 71.11%, the precision values 66.67%, 52%, 66.67% ,100% for each class, the recall values 85.71%, 66.67%, 43.33% and 50% for each class, and 75%, 50%, 44.44% and 66.67% for each class MSA-C, MCA-P, PSP and CBS respectively.
Conclusion: Despite the small sample, the data was adequate to fit in a KNN-ML model and determine in a quite satisfying degree from which APS does a patient suffer.
Disclosure: Nothing to disclose.

Epilepsy 1

EPO-128

Neuroimaging findings after a first seizure – interim report from the Swiss First study

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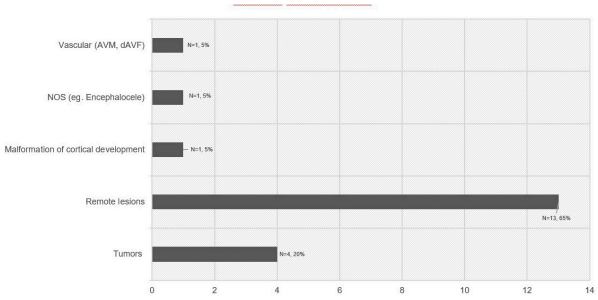
Background and aims: MRI can depict potentially structural epileptogenic lesions as well as incidental, potentially non-epileptogenic lesions after a first seizure. The SWISS FIRST study was closed in December 2022. Here, we report the interim results about incidence of structural and peri-ictal image abnormalities in first seizure patients.
Methods: All patients underwent MRI with a dedicated epilepsy imaging protocol (incl. SWI, DWI and perfusion imaging). Diagnostic criteria for established epilepsy follow the ILAE practical guidelines and were determined after 2 years of follow-up. MRI lesions were classified as either structural epileptogenic lesions (SEL), potentially nonepiletogenic lesions (pNEL) or normal MRI.
Results: Overall, 615 patients were investigated with MRI after a first suspected epileptic seizure. Up to now, 83 received a final diagnosis. Fifty-nine were diagnosed with established epilepsy based (71%, mean age 51.0 ± 19.2, M: 34, F: 25). In patients with established epilepsy, SEL were present in 34% and pNEL in 49%. Main findings were remote lesions (65%), brain tumors (20%), vascular lesions (5%) and malformations of cortical development (5%) (Image). Transient peri-ictal MR signal abnormalities (TPMA) were present in 15% of patient with SEL, 10% in patients with pNEL and none in nonlesional MRI (χ^2-test; n.s.).



Lesion distribution in the structural epileptogenic group cohort.

Conclusion: Both SEL and pNEL are common findings in patients who undergo immediate imaging after a first seizure, with similar distribution of WML in both cohorts. TPMA are rarely observed after a first seizure in comparison to established epilepsy or status epilepticus and do not differ significantly between SEL and pNEL patients.
Disclosure: The authors report these preliminary results on behalf of the SWISS FIRST investigators. The study was funded by the SWISS National Foundation (SINERGIA) project 180365: The SWISS FIRST Study

EPO-129

Investigation of Prognostic Characteristics of Medically-Refractory Epilepsy Based on Invasive Monitorization

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Background and aims: : In selected cases of medically-refractory epilepsy, pre-surgical invasive monitorization is critical for the precise lateralization and localization of the epileptogenic zone. This study was designed to determine the parameters which affect the post-surgical prognosis.
Methods: Patients who underwent epilepsy surgery between 2002-2022, with prior invasive monitorization were retrospectively analyzed. Clinical, electroencephalographical, neuropsychological and structural/functional neuroimaging findings and prognostic features of all patients were evaluated.
Results: Of 162 patients who met inclusion criteria, 111 with complete records were included (female/male: 54/57). The mean age at seizure onset was 9.26±7.74, at epilepsy surgery was 24.95±11.72, and the mean duration between the first seizure and surgery was 15.42±9.27 years. 45 patients were applied with the stereotactic-electroencephalography, 47 with subdural and 17 with subdural+depth electrodes. Fifty-three were temporal lobe and the others were extra-temporal epilepsy; thirty-five were with normal MRI. The most common pathologies in patients who underwent surgery were focal cortical dysplasia (n=67), hippocampal sclerosis (n=16) and gliosis (n=11). The statistical analysis demonstrated that high pre-surgical seizure frequency and high number of anti-seizure medications used, as well as the inability to discontinue anti-seizure medications post-surgically were associated with poor prognosis (Fig-1). The presence of neuropsychological findings compatible with the invasively-detected epileptogenic zone was found to be significantly correlated with Engel-1 outcome (Fig-2).

	All Patients	Engel Classification				Test Statistics	Test Name	P-value
		Engel 1	Engel 2	Engel 3	Engel 4			
First seizure age (year)	7 (0.1 - 41)	8 (1 - 41)	4 (1 - 29)	7 (1 - 20)	7 (0.5 - 17)	4.864	Kruskal-Wallis	0.182
Duration between invasive monitorisation and first seizure (year)	15 (0.9 - 42)	12 (1 - 37)	15 (9 - 42)	18 (6.9 - 39)	12.5 (8 - 30)	6.130	Kruskal-Wallis	0.105
Gender (n)	111	55	27	17	12	1.850	Chi-square	0.607
Male	57	26	15	8	8			
Female	54	29	12	9	4			
Seizure frequency (n)	105	50	26	17	12	4.747	Chi-square	**0.029***
1-11/year	3	1a	1a	0a	1a			
1-3/month	27	13a	9a	3a	2a			
1-6/week	46	25a	12a	6a	3a			
≥1/day	23	11a	3a	6a	3a			
Uncountless times	6	0a	1ab	2ab	3b			
Seizure chronotype (n)	105	50	26	17	12	2.097	Chi-square	0.148
Non-nocturnal	22	12	6	2	2			
Nocturnal	6	5	1	0	0			
Diurnal	77	33	19	15	10			
Anti-seizure medication count before surgery (numeric)	3 (1 - 7)	3 (1 - 5)	3 (2 - 5)	3 (2 - 5)	3 (2 - 7)	5.110	Kruskal-Wallis	0.164
Invasive monitorisation electrode count (numeric)	7 (4 - 17)	8 (4 - 12)	6 (4 - 17)	7 (4 - 9)	8.5 (7 - 11)	4.072	Kruskal-Wallis	0.254
Invasive monitorisation electrode type (n)	111	55	27	17	12	11.903	Chi-square	0.064
Depth electrode	45	24	13	2	6			
Subdural electrode	47	19	12	12	4			
Depth+Subdural electrode	19	12	2	3	2			
Invasive monitorisation electrode lateralisation (n)	111	55	27	17	12	8.556	Chi-square	0.200
Left	34	12	12	8	2			
Right	44	26	7	5	6			
Bilateral	33	17	8	4	4			
Invasive monitorisation electrode localisation (n)								
Temporal lobe	84	43	21	12	8	1.236	Chi-square	0.744
Insular lobe	26	16	5	2	3	2.99	Chi-square	0.393
Frontal lobe	76	34	19	13	10	2.674	Chi-square	0.445
Parietal lobe	70	30	20	12	8	3.238	Chi-square	0.356
Occipital lobe	22	9	6	5	2	1.413	Chi-square	0.702
Epilepsy surgery type (n)	111	55	27	17	12	2.690	Chi-square	0.101
Lesionectomy	24	11	3	6	4			
Tailored lesionectomy	39	16	11	6	6			
Lobectomy	44	27	13	5	0			
Hemispherectomy / Hemispherotomy	3	1	2	0	0			
Callosotomy	0	0	0	0	1			
Anti-seizure medication count after surgery (numeric)	2 (0 - 5)	1 (0 - 3)a	2 (1 - 3)b	2 (1 - 5)b	3 (2 - 5)c	41.556	Kruskal-Wallis	**<0.001*** **
Anti-seizure medication count difference before and after surgery (numeric)	1 (-2 - 5)	2 (0 - 5)a	1 (-1 - 3)ab	1 (-2 -2)b	0 (-1 - 5)bc	17.876	Kruskal-Wallis	**<0.001*** **
Pathology type (n)	106	52	25	17	12	0.109	Chi-square	0.741
Focal cortical dysplasia 1a	11	6	3	0	2			
Focal cortical dysplasia 1b	14	4	7	2	1			
Focal cortical dysplasia 1c	1	0	1	0	0			
Focal cortical dysplasia 2a	24	9	6	7	2			
Focal cortical dysplasia 2b	5	3	0	2	0			
Focal cortical dysplasia 3a	12	8	3	1	0			
Hypocampal sclerosis	16	9	4	2	1			
Glioma	3	3	0	0	0			
Hamartoma	2	1	0	0	1			
DNET	1	1	0	0	0			
Gliosis	11	5	1	2	3			
Others	6	3	0	1	2			

a,b,c: There is no statistical significance between variables with the same letter
Continuous data was presented as "median (minimum-maximum)"; categorical data was presented as "n" values

Non-invasive investigations and their consistent with invasive monitorisation results	All Patients	Engel I (+)	Engel I (-)	Test Statistics	P-value
Is epilepsy type consistent with invasive monitorisation results?	105	50	55	0.040	0.842
No	24	11	13		
Yes	81	39	42		
Is scalp EEG consistent with invasive monitorisation results?	105	50	55	0.064	0.801
No	5	3	2		
Yes	42	20	22		
Not applicable/Normal	1	0	1		
Partial (More extended)	57	27	30		
Partial (More limited)	0	0	0		
No test	0	0	0		
Is MRI consistent with invasive monitorisation results?	110	54	56	0.527	0.468
No	3	0	3		
Yes	50	25	25		
Not applicable/Normal	35	18	17		
Partial (More extended)	21	10	11		
Partial (More limited)	1	1	0		
No test	0	0	0		
Is NPT (Neuropsyhological assesment) consistent with invasive monitorisation results?	105	50	55	3.843	**0.050***
No	7	4a	3a		
Yes	19	14b	5a		
Not applicable/Normal	4	1a	3a		
Partial (More extended)	36	15a	21a		
Partial (More limited)	3	2a	1a		
No test	36	14a	22a		
Is PET/SPECT consistent with invasive monitorisation results?	108	53	55	0.650	0.420
No	5	1	4		
Yes	48	23	25		
Not applicable/Normal	12	7	5		
Partial (More extended)	21	10	11		
Partial (More limited)	0	0	0		
No test	22	12	10		

a,b,: There is no statistical significance between variables with the same letter
Categorical data was presented as "n" values

Conclusion: The extent to which the data obtained from the non-invasive assessment can predict the invasively-detected epileptogenic zone is critical, and this study has shown that clinical and neuropsychological findings were prominent in this regard.

Disclosure: The authors have no conflict of interest to declare.

EPO-130

Physical activity and sedentary behaviour in people with epilepsy

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Background and aims: There is accumulating evidence that physical activity (PA) is essential to promote health and well-being in people with epilepsy (PWE). However, detailed information on PA and sedentary behaviour in PWE is currently unclear. We aimed to contrast the activity behaviour between PWE and healthy controls.

Methods: The SenseWear activity monitor was used to measure PA behaviour in daily life. It was attached to the dominant upper side of participant for 7 consecutive days. Mental, emotional, and psychological health status were assessed with the Montreal Cognitive Assessment (MoCA, cognitive function), Generalized Anxiety Disorders scale 7-item (GAD-7, anxiety symptoms), Beck Depression Inventory (BDI, depression symptoms), Fatigue Severity Scale (the severity and impact of fatigue), Pittsburg Sleep Quality Index (self-perceived sleep quality). Health-related physical fitness was evaluated with the Activities-spesific Balance Confidence scale (balance confidence), Biodex Balance System- Fall Risk Index, 30-second Chair Stand test (lower-limb strength), Timed Up and Go test (functional mobility), Six-minute Walk test (functional exercise capacity).

Results: Sixty-three PWE and 65 healthy controls participated. PWE took on average less steps per day and engaged on average in less sleep duration and spent more time in sedentary compared with healthy individuals. The MoCA, GAD-7, BDI and physical fitness outcome measures of PWE were worse than healthy individuals ($p<0.05$, Table 1).

Table 1. Comparison of activity behaviour, mental, emotional, and psychological health status, and health-related physical fitness between the groups

	People with epilepsy group Median (IQR) (n=63)	Healthy controls group Median (IQR) (n=65)	p
SenseWear activity monitoring			
Daily steps (*steps/day*)	7765.2 (5090.2)	9764.7 (4126.7)	0.007*
Sedentary behaviour (*min/day*)	530.4 (133.1)	453.5 (99.7)	<0.001*
Sleep duration (*min/day*)	445.2 (118.5)	376.8 (91.1)	<0.001*
Mental, emotional, and psychological health status			
Montreal Cognitive Assessment (*0-30*)	24.0 (6.0)	28.0 (3.0)	<0.001*
Generalized Anxiety Disorders scale 7-item (*0-21*)	7.0 (9.0)	4.0 (7.0)	0.019*
Beck Depression Inventory (*0-63*)	12.0 (17.0)	5.0 (8.5)	<0.001*
Fatigue Severity Scale (*7-63*)	33.0 (19.0)	30.0 (22.5)	0.087
Pittsburg Sleep Quality Index *(0-21)*	4.5 (4.0)	4.0 (3.0)	0.481
Health-related physical fitness			
Activities-spesific Balance Confidence scale (*0-100*)	84.0 (16.3)	96.2 (6.8)	<0.001*
Biodex Balance System- Fall Risk Index	1.0 (0.6)	0.8 (0.4)	0.003*
30-second Chair Stand test (*times/30sec*)	18.0 (5.0)	20.0 (5.0)	0.001*
Timed Up and Go test (*sec*)	6.1 (0.9)	5.7 (0.7)	<0.001*
Six-minute Walk test (*meter*)	543.9 (71.7)	612.9 (59.7)	<0.001*

*p<0.05, Mann-Whitney U test.
IQR: Interquartile range.

Comparison of activity behaviour, mental, emotional, and psychological health status, and health-related physical fitness between the groups

Conclusion: PWE were engaged in excessive sedentary time compared to healthy individuals and suffered from mental, emotional, and psychological comorbid conditions and impairment in physical fitness. Future intervention strategies should include behaviour change techniques to promote PA participation in PWE.

Disclosure: The authors report there are no competing interests to declare. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

EPO-131

An iEEG investigation of sex-specific differences in seizure duration

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Background and aims: Male patients with epilepsy are at higher risk for bilateral tonic-clonic seizures (BTCS) as well as sudden death compared to female patients. Despite its tremendous clinical and personal implications, little is still known about sex specific differences in seizure propagation and termination. Aims: To investigate the seizure duration in male versus female epilepsy patients.
Methods: Adult patients with unifocal epilepsy and available intracranial EEG (iEEG) recordings (09/2006-03/2022) were identified retrospectively. Up to 20 clinical seizures were analyzed per patient, excluding patients with status epilepticus or periodic lateralized discharges. The seizure duration was determined based on the iEEG recordings. In case of a focal to BTCS (FBTCS), the duration of the focal and the generalized seizure phase were determined via EEG and seizure semiology. A multiple linear regression model was used for the sex-specific evaluation of the seizure duration, including age, epileptic hemispheric, frontal onset, lateralizing signs, onset during sleep, and aura as independent variables.
Results: A total of 100 patients (m/f=50/50; age: 33.6±12.2 years) and 758 seizures (120 FBTCS) was analyzed. While women had significantly longer focal seizures (p=0.021) than men, male patients revealed significantly longer FBTCS (p=0.001), including longer focal seizure phases (p=0.003). No significant difference was observed for the BTCS phase.
Conclusion: For the first time, sex-differences in seizure duration were described. Our findings may contribute to a better pathophysiological understanding of the sex-specific differences in seizure manifestation and associated risks and underline the yet unmet need of a sex-specific approach in epilepsy research and patient management.
Disclosure: Nothing to disclose.

EPO-132

Sustained ≥90% response and seizure freedom in patients with focal-onset seizures treated with cenobamate

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Background and aims: The maintenance of clinical response over time is a main concern in patients with epilepsy, thus, sustained seizure freedom is the ultimate goal of epilepsy treatment. Unfortunately, many studies failed to show sustained seizure freedom. Here, we analyze sustained seizure control in patients treated with cenobamate.
Methods: Adults with focal seizures despite treatment with 1-3 concomitant ASMs completed the double-blind treatment and entered the open label extension (OLE). 354 were included in the C017 OLE modified intent-to-treat population (mITT), 265 originally randomized to CNB, 90 to placebo. All patients underwent a 2-week double-blind conversion to a target dose of cenobamate 300 mg/d. This post-hoc analysis examined sustained seizure response >= 90% and sustained seizure freedom.
Results: During the OLE, >= 90% sustained response for at least one year was achieved by an estimated 38.5% of the patients, and an estimated 23.6% showed sustained seizure freedom. Among these patients, half of them achieved >= 90% sustained response from day 1 and time to achieved sustained seizure freedom,12 months. An estimated 28.4% of the patients achieved >= 90% sustained response for at least 2 years, and 14.3% of being seizure free. Sustained >= 90% response for at least 3-years was achieved by an estimated 23.9% of the patients and 7.5% were seizure-free.
Conclusion: These results suggest that adjunctive cenobamate is a promising drug and may be a suitable long-term treatment for patients with focal-onset seizures to achieve and maintain a high-level of clinical response, including seizure freedom.
Disclosure: The original study (NCT01866111) was supported by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Angelini S.p.a. (Rome, Italy).

EPO-133

Association of seizure frequency and suicidal tendencies in adults with epilepsy

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Background and aims: Adults with epilepsy (AWE) sometimes present suicidal tendencies (ST). In this study we aimed to understand whether seizure frequency was associated with ST in AWE.
Methods: AWE were assessed in epilepsy center: clinical interview covered the duration, seizure frequency during last month and last year, current medication. ST were assessed based on the respective Hamilton Depression Rating Scale (HAMD) item. Mann-Whitney U and Chi-square tests were used.
Results: Overall, 168 AE were divided into two groups: ST group (SG, n=24, mean age - 37±12.6, females – 41.7%) and no ST group (NSG, n=144, mean age – 34.5±13.6, females – 47.2%). AWE with ST were more in focal epilepsy, however not statistically significant (SG/NSG – 91.7%/74.3%, p=0.06). Epilepsy duration was similar

between groups (11.8 vs 10.8 yrs, p>0.05). Seizure frequency during the past year was significantly higher in SG (SG/NSG – 57.4/33.3, p<0.05). A similar tendency was seen for seizure frequency during the last month albeit not statistically significant (SG/NSG – 4.3/3.8, p>0.05). Interestingly, there was no difference between SG and NSG groups in regard to the presence of generalized tonic-clonic seizures (87.5% vs 89.5%, p>0.05).

Conclusion: Our results show that seizure frequency during the last year is higher in adults with epilepsy who have suicidal tendencies. This was not seen for seizure numbers in the preceding month. We found that patients with epilepsy are more likely to have suicidal tendencies. The presence of generalized tonic-clonic seizures and the duration of epilepsy were not associated with suicidal tendencies.

Disclosure: Nothing to disclose.

EPO-134

Cenobamate as treatment of "super-refractory" focal epilepsy: Results from a cohort of the Spanish expanded access

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Background and aims: Objective: To assess the effectiveness and tolerability of cenobamate (CNB) in patients with uncontrolled focal-onset seizures despite treatment with at least two anti-seizures medication (ASM) through a name-patient program (NPP) in Spain.

Methods: We performed an unicenter, retrospective, observational study aimed to determine the efficacy and safety of CNB in patients with a 3-month minimum follow-up. Inclusion criteria were 1) >=18 years; 2) focal seizures; 3) NPP-expanded access authorization. Data were obtained from medical records at baseline, 3- and 6-month visits.

Results: 39 patients with a mean(SD) age of 42,6(13,6) years and median(IQR) number of trialed ASM of 9(5-13) were included. At 3 months, the mean(SD) and median dose were 153,3mg(68,5) and 200mg, respectively. 50% and 90% seizure frequency reduction occurred in 64,8% and 16,2% of patients, respectively. 12% of patients become seizure-free. At 6 months, 72,7% of patients had 50% seizure reduction, 4,7% had 90% reduction and 4,7% become seizure-free with a mean and median dose of 213,6mg(53,8) and 200mg, respectively. 75,6% and 36,3% of patients reported adverse effects (AEs) at 3 and 6 months, including somnolence, dizziness, cognitive, fatigue, ataxia and diplopia. The number of concomitant ASM was reduced from a mean of 3,1 to 2,8 and 2,4 at 3- and 6-month visits, respectively. One patient discontinued treatment because of inefficacy and three due to AEs.

Conclusion: CNB is effective in "super-refractory" focal epilepsy and allowed for reducing drug load. Also, is a well-tolerated ASM with mild-moderate AEs that can be resolved by adjusting concomitant ASMs without leading to discontinuation.

Disclosure: P C-G and PJ S-C received (speaking) fees from Angellini.

EPO-135

Intraoperative electrocorticography in epilepsy surgery: data from the Epilepsy Center of Modena

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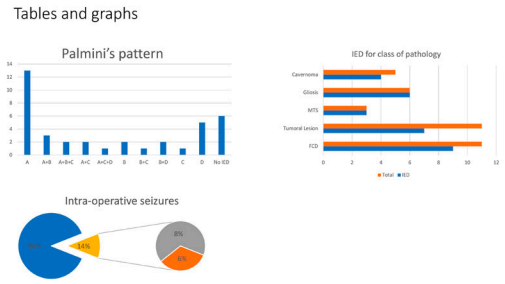
Background and aims: Intraoperative electrocorticography (ECoG) is used in epilepsy surgery to identify the presence of epileptiform activity related to the epileptogenic lesion. We present data regarding ECoG recordings collected from 2019 to 2022 at the Epilepsy Center of Modena.

Methods: All patients addressed to epilepsy surgery underwent serial iECoG recordings with 1 x 4 strip with platinum-iridium electrodes placed over and along the lesional cortex before resection and along the surgical neocortical margin of the resection. Bipolar and referential electrode montages were reviewed to identify epileptiform abnormalities. ECoG patterns were subdivided according to Palmini et al. classification.

Results: 49 patients underwent to surgical procedure. In 37 patients (26M, 11F, mean age 37.2Â±14.1) we could obtain at least one ECoG recording. Among the 35 pre-resection recordings, the following patterns were found: A (13/35), A+B (3/35), A+B+C (2/35), A+C (2/35), A+C+D (1/35), B (2/35), B+C (1/35) B+D (1/35), C (1/35), absence of epileptiform abnormalities (6/35). In 5/35 patients with tumoral lesions (3) and focal cortical dysplasia (FCD) (2/25), intraoperative electrographic seizures were recorded (D pattern). Abnormal ECoG patterns were found in 9/11 patients with FCD (type Ia, IIb, IIIa), in 7/11 patients with a tumoral lesion, 3/3 with hippocampal sclerosis, in 6/6 with gliosis and in 4/5 with a cavernoma.



Results of the frequency of Palmini classification Pattern, the IED related to different disease pathology and the Number of intra operative seizures

Conclusion: These findings demonstrated that there is a good concordance between the histopathological data and the ECoG patterns. ECoG could be a valuable operative instrument to identify epileptiform abnormalities during the surgical procedure with the potential to help in guiding the surgical resection extent.
Disclosure: Nothing to disclose.

EPO-136

Chemogenetic activation of the locus coeruleus increases noradrenaline levels and modulates hippocampal excitability

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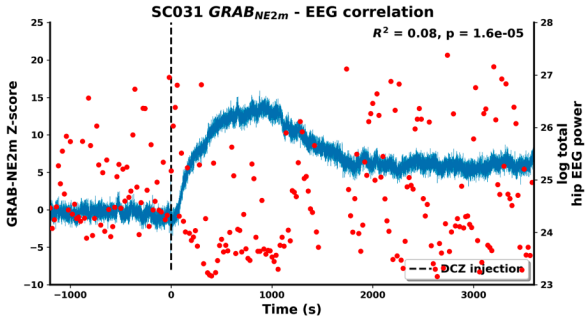
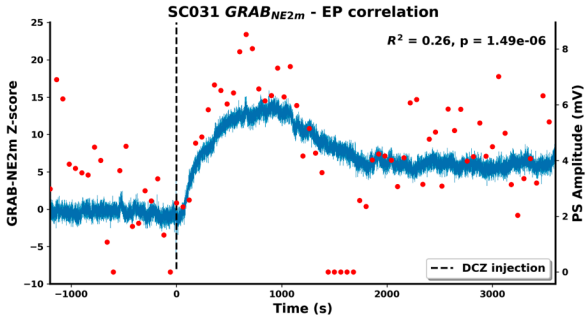
Background and aims: The brainstem locus coeruleus (LC) is the sole source of noradrenaline in the neocortex, hippocampus and cerebellum. Noradrenaline is a neuromodulator involved in the regulation of excitability of brain networks. Recent development of tools for precision modulation of the LC, including Designer Receptors Exclusively Activated by Designer Drugs, allow the study of LC physiology with unprecedented detail. In this study, we assessed the influence of activating the LC on noradrenergic signaling and excitability in the hippocampus.
Methods: Male Sprague Dawley rats (n=5) were injected with the viral vectors CAV2-PRSx8-hM3Dq-HA hSyn-mCherry in the LC and AAV9-hSyn-NE2m-mRuby3 in the hippocampus to induce expression of hM3Dq in LC neurons and the GRABNE2m biosensor in the hippocampus. All rats were implanted with a stimulation electrode in the perforant path and a recording optrode in the dentate gyrus. Rats were injected with deschloroclozapine (DCZ) to activate the LC and to assess the effects on noradrenaline signaling and dentate gyrus electrophysiology.
Results: Injection of DCZ resulted in an increase in GRABNE2m fluorescence, a decrease in EEG power and an increase in the amplitude of the population spike of the dentate gyrus evoked potential. Changes in population spike amplitude and EEG power were significantly correlated to the observed changes in GRABNE2m fluorescence.



Injection of DCZ, activating the LC, results in a pronounced increase in GRABne fluorescence, which is significantly correlated to a decrease in EEG power.



Injection of DCZ, activating the LC, leads to an increase in the amplitude of the population spike of the dentate gyrus evoked potential. This change is significantly correlated to changes in GRABne fluorescence.

Conclusion: This study is the first to assess the effect of chemogenetic activation of the LC on noradrenaline signaling in the hippocampus with GRAB-sensor technology, providing unprecedented temporal resolution. This research is able to confirm previous findings of pharmacological studies with superior precision and specificity.
Disclosure: Nothing to disclose.

EPO-137

Antiseizure medication monitoring: patient-self-collected versus nurse-collected volumetric absorptive microsampling

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Background and aims: Volumetric absorptive microsampling (VAMS - Mitra®, Neoteryx) is increasingly proposed as a clinically reliable sampling methodology for therapeutic drug monitoring (TDM). The study's aim was to establish the feasibility of patient self-collected VAMS as a practical tool for TDM of antiseizure medications (ASM).

Patient self-collected and nurse-collected-VAMS were compared. Plasma ASMs concentrations from venous blood were used as a reference standard to compare blood concentrations found in VAMS.
Methods: Persons with epilepsy (PWE) were enrolled in this study. Morning venous and capillary blood by VAMS were collected by nurses. Afterward, patients performed VAMS collection by themselves. Blood and plasma analyses were analyzed by ultra-high liquid chromatography-mass spectrometry. ASMs blood concentrations from nurse-collected-VAMS were compared to plasma concentrations. A cross-validation study was performed comparing ASMs concentrations obtained by nurse-collected versus patient-self-collected VAMS samples.
Results: 301 PWE (173 females, mean age: 44.33±16.10 years) were enrolled providing a total of 456 ASMs concentration measurements. Linear correlation analyses between ASMs plasma and blood nurse-collected-VAMS concentrations showed heterogeneous results depending on the analyte (R2 ranging from 0.4 to 0.9; $p<0.001$). Cross-validation analysis between nurse-collected vs patient self-collected VAMS showed a bias within ±20% for more than 78% of intrasubject ASMs determinations.
Conclusion: To our knowledge, this is the first study considering the real-world application of patient self-collected VAMS for ASMs-TDM. Furthermore, concentration from self-collected-VAMS has proved comparable with those from nurse-collected, demonstrating that patients' self-sampling can be feasible after minimal training. Results give a promising basis for at-home VAMS applications.
Disclosure: All authors declare no conflicts of interest.

EPO-138

Imaging neuronal currents for the delineation of the seizure onset zone in epilepsy: initial clinical experiences

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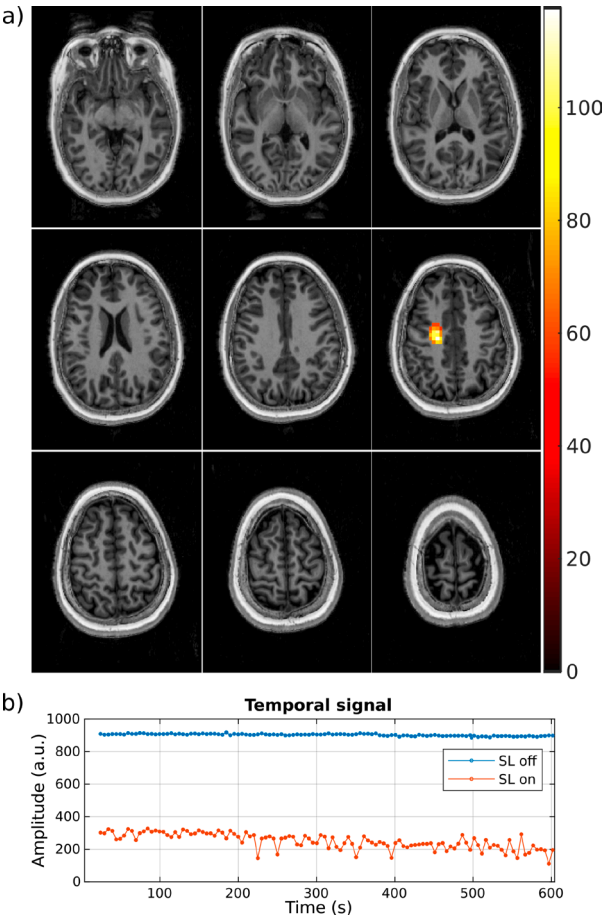
Background and aims: Non-invasive delineation of the seizure onset zone (SOZ) remains challenging for neurophysiological methods such as EEG or MEG, due to spatial accuracy. Neuronal current imaging (NCI) with magnetic resonance imaging is a novel functional neuroimaging method that simultaneously encodes functional and spatial information. As this method is frequency selective, we targeted high-frequency oscillations (~120Hz) as SOZ markers. In this work, we report on the initial experience in epilepsy patients, challenges and limitations of the method.
Methods: Eleven epilepsy patients (with negative MRI) and 24 healthy volunteers were imaged with NCI at pre adjusted spin-lock frequencies to target high-frequency oscillations. In the patients, results were compared with interictal EEG. A post-processing pipeline is presented and used to identify key features of the contrast.
Results: We used mean signal contrast and standard deviation to compare NCI signal intensity of epilepsy patients vs. healthy volunteers. Using the data from healthy volunteers, we determined the significant NCI threshold levels. Activations above threshold were identified in 8 out of 11 patients with negative MRI. Hemispheric concordance with the presumed seizure onset zone was depicted in 7 and lobar concordance in 4 patients. False-positive results were observed in 1 and false-negative results in 5 patients.



a) Exemplary case of NCI activation hemispheric concordant with EEG finding.

b) Signal temporal response of ROI within detected area for baseline and NCI contrast acquisition.

Conclusion: NCI is a novel imaging contrast that highlighted activated areas in 8 out of 11 patients with negative MRI. The method is currently under prospective evaluation in the SWISS FIRST study in first seizure patients.
Disclosure: This study was funded by the Swiss National Science Foundation via the SINERGIA project 180365: The SWISS FIRST study

EPO-139

Effects of hormonal replacement therapy on seizures' frequency of postmenopausal women with epilepsy:A systematic review

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Background and aims: Hormonal replacement therapy (HRT) is used for symptomatic treatment of menopause. Some evidence suggests a proconvulsant effect of estrogen and an anti-convulsant role of progesterone. Thus, the use of exogenous sex steroid hormones might influence the course of epilepsy in peri- and postmenopausal women with epilepsy (WWE). We conducted a systematic review on the impact of HRT on the frequency of seizures in WWE.
Methods: PubMed and Scopus were searched for articles published from inception until August 2022. Abstracts from the last five years from the European Academy of Neurology and European Epilepsy Congresses were also reviewed. Article reference lists were screened, and relevant articles were retrieved for consultation. Interventional and observational studies on WWE and mice models of estrogen deficiency were included. Critical appraisal was performed using the Revised Cochrane risk-of-bias tool for randomized trials (ROB2) and ROBINS-E tools.
Results: Of 497 manuscripts screened, twelve studies were included, including three human studies. One cross-sectional study showed a decrease in seizures' frequency in WWE using combined HRT (estrogen and progesterone), a case-control study showed an increase in comparison with controls and a randomized clinical trial found a dose-dependent increase in seizures' frequency in women with focal epilepsy taking combined HRT. Nine studies addressing the impact of HRT in rat models were also included, which showed conflicting results.
Conclusion: There is scarce evidence of the impact of HRT in WWE. Further studies should evaluate the harmful potential and prospective registries are needed for monitoring in this population
Disclosure: The authors do not have any conflict of interest to declare in relation to this project.

EPO-140

STEPPER (Status Epilepticus in Emilia Romagna): therapeutic interventions and quality of care in Emilia-Romagna Region

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Background and aims: SE (status epilepticus) is one of the primary neurological emergencies. Several studies conducted in Emilia Romagna Region (ERR), in the previous two decades have shown that mortality is still high and variable in different areas. STEPPER (STatus EPilePticus in ER) aimed at studying clinical characteristics, management and prognostic factors of SE in the adult population of ERR, focusing on refractory SE (RSE) and non-convulsive SE (NCSE).
Methods: We conducted a multicenter prospective observational study on SE in 17 neurological and intensive care units in ERR between 2019 and 2021. Follow-up was performed thirty days after SE onset.
Results: 610 cases were recruited: 56% female; mean age 70 years; 54% with prominent motor symptoms; 43% had in-hospital onset, 30% were NCSE in coma. Etiology was known in 87% of SE (acute 49%, remote 27%, progressive 20%, definite epileptic syndrome 3%). The mean pre-SE Rankin score was 2; mean STESS and EMSE were 3 and 71. 34% of cases were RSE. Benzodiazepines were used well beyond the first line of treatment, while only 47% of RSE cases received a third-line therapy with anesthetic drugs. Thirty-day mortality was 24% in the whole population, 24% in NCSE, and 38% in RSE. The mean Rankin score at follow-up was 3.
Conclusion: We confirmed high 30-day mortality of SE and worsening of functional outcome in survivors. High EMSE scores are in line with a poor prognosis in our cohort. Poor adherence to SE treatment guidelines might have influenced the prognosis in some cases
Disclosure: This study was funded by the Italian Ministry of Health (RF-2016- 02361365)

EPO-141

EEG Reactivity Predicts Individual Response to Vagal Nerve Stimulation (VNS) in Children with Drug-resistant Epilepsy

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Background and aims: Vagal nerve stimulation (VNS) represents a therapeutic option in patients with drug-resistant epilepsy. This type of treatment leads to significant seizure reduction in 50-60% patients (VNS responders). The resting 50 % patients do not profit from VNS therapy (VNS non-responders). We developed a statistic classifier - Pre-X-Stim - predicting VNS efficacy based on analysis of pre-implantation EEG (Brazdil et al., 2019). This classifier was developed in adult population (> 18 years). In this project, we tried to extrapolate our results on children population (< 18 years).

Methods: We retrospectively identified a group of children treated with VNS. In each child, EEG with photic stimulation and hyperventilation was found. EEG was filtered into four common frequency bands and segmented into 8 time-intervals based on their relation to photic stimulation and hyperventilation. Relative mean power was calculated for each time-interval in each frequency band. Then after, existing classifier post-processed relative mean powers in every child to determine the predicted response (predicted responder vs. predicted non-responder). As the last step, we compared the predicted and the real-life response to determine accuracy, sensitivity, and specificity.

Results: There were 6 children (median age 9 years, minimum 8 years, maximum 18 years). Two (33 %) children non-responders, the resting four (67 %) were responders to VNS therapy. We were able to predict correctly the response to VNS in 5 out of 6 children (accuracy 0,83, sensitivity 0,75, specificity 1).

Conclusion: Our statistic classifier – Pre-X-Stim – can predict VNS efficacy in both adult and children population.

Disclosure: This project is supported by the Ministry of Health of the Czech Republic, gran nr. NV19-04-00343.

EPO-142

Angiotensin receptor blocker (ARBs) drugs in post-stroke epilepsy (PSE) prevention: a retrospective observational study

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Background and aims: Among the risk factors for epilepsy and stroke, hypertension is a prominent one. Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blocker (ARBs) seem to promote a protective effect in the development of seizures in the general population. However, no data are available about their possible preventive role in post-stroke epilepsy (PSE). In this study, we evaluate the effectiveness of anti-hypertensive treatment in preventing PSE.

Methods: In this retrospective, observational study, patients with hypertension and diagnosis of ischemic stroke confirmed by clinical and neuroimaging evaluation were retrospectively selected between January 2016 and December 2022. Diagnosis of PSE was made according to ILAE criteria. The details of the anti-hypertensive treatment as well as demographics, and clinical and neuroradiological data were reviewed.

Results: 361 patients (mean age 70.2 ± 13.5 , 200 men, 58%) were enrolled. Twenty-seven (7.5%) patients developed PSE. Large vessel occlusion (p=0.031), atrial fibrillation (p=0.033), and cortico-sottocortical lesions (p=0.003) were related to a higher risk of PSE development. A lower risk of PSE was observed in patients treated with ARBs (p=0.027). No differences were observed according to ACEi, Calcium Channel Blocker, and Beta-blockers.

Conclusion: ARBs show a potential protective role in epilepsy development in patients with hypertension and stroke. If confirmed by larger studies, these findings suggest ARBs could be used as a novel approach for preventing epilepsy in patients with stroke.

Disclosure: Nothing to disclose.

MS and related disorders 1

EPO-143

Factors associated with decision to switch SPMS patients to siponimod versus staying on fingolimod

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Background and aims: To explore factors associated with switching to siponimod versus staying on fingolimod in SPMS patients treated with fingolimod.
Methods: Multicentric cross-sectional study. SPMS patients treated with fingolimod and switching from fingolimod to siponimod were enrolled. Patients in both groups were treated with fingolimod for at least 2 years until the time of enrollment. We collected demographics (age and sex) and clinical data (age at onset, treatment duration with fingolimod until the enrollment, EDSS at the time of enrollment, number of previous DMTs, relapses in the previous 12 months). Univariable and multivariable models were applied to explore factors associated with switching to siponimod versus staying on fingolimod.
Results: 100 SPMS patients were enrolled (demographics and clinicals are displayed in table 1). 40% of SPMS patients treated with fingolimod switched to siponimod. The multivariate regression analysis showed EDSS at baseline and number of previous DMTs as the only independent variables associated with the outcome (respectively OR: 0.60; 95%CI: 0.41 – 0.89; p = 0.011 and OR: 1.53; 95%CI: 1.02 – 2.31; p = 0.042; table 2). Furthermore, although not statistically significant, higher number of relapses in the previous year occurred in switched patients compared to patients on fingolimod (OR: 2.92; 95%CI: 0.67 – 12.78; p = 0.16; table 2).

Table 1 - Baseline characteristics and MS history

		Total	Switch group (from fingolimod to siponimod)	Comparator group (remaining on fingolimod)
Sex	Female, n (%)	65 (65.0%)	26 (65.0%)	39 (65.0%)
	Male, n (%)	35 (35.0%)	14 (35.0%)	21 (35.0%)
Age at enrolment (years), mean ± SD		51.7 ± 8.16	49.9 ± 8.05	52.8 ± 8.09
Age at onset (years), mean ± SD		29.0 ± 9.57	28.9 ± 9.22	29.1 ± 9.86
Age at diagnosis (years), mean ± SD		34.5 ± 9.76	33.5 ± 9.08	35.2 ± 10.24
Disease duration (years)		16.6 ± 7.88	15.9 ± 7.64	17.0 ± 8.08
Months of treatment with Fingolimod, mean ± SD and range		73.40 ± 31.63 (5.0 - 140.0)	70.89 ± 30.56 (5.0 - 127.0)	75.20 ± 32.77 (9.0 - 140.0)
Reason for switch	Ineffectiveness (activity), n (%)	6 (15.0%)	6 (15.0%)	
	Ineffectiveness (progression), n (%)	32 (80.0%)	32 (80.0%)	
	Safety reason or intolerance, n (%)	0 (0.0%)	0 (0.0%)	
	Other, n (%)	1 (2.5%)	1 (2.5%)	
	Not specified, n (%)	1 (2.5%)	1 (2.5%)	
EDSS at diagnosis, median (IQR)		2.5 (2.0 - 3.5)	2.5 (2.0 - 3.0)	2.0 (2.0 - 4.0)
EDSS in the previous 24 months, median (IQR)		5.5 (4.50 - 6.5)	5.0 (4.5 - 5.5)	6.0 (4.5 - 6.5)
EDSS in the previous 12 months, median (IQR)		5.5 (4.50 - 6.5)	5.5 (4.5 - 6.5)	6.0 (4.5 - 6.5)
EDSS at baseline, median (IQR)		6.0 (5.0 - 6.5)	5.5 (5.0 - 6.0)	6.5 (4.5 - 6.5)
Number of previous treatments, mean ± SD		1.9 ± 1.21	2.1 ± 1.14	1.8 ± 1.26
Genotype, n (%)	1/1, n (%)	19 (51.4%)	19 (51.4%)	
	1/2, n (%)	7 (18.9%)	7 (18.9%)	
	1/3, n (%)	3 (8.1%)	3 (8.1%)	
	2/2, n (%)	5 (13.5%)	5 (13.5%)	
	5, 2/3, n (%)	0 (0.0%)	0 (0.0%)	
	Unknown, n (%)	3 (8.1%)	3 (8.1%)	
Relapses in the previous 24 months, median (range)		0 (0 – 2)	0 (0 – 2)	0 (0 – 1)
Relapses in the previous 12 months, median (range)		0 (0 – 2)	0 (0 – 2)	0 (0 – 1)

Baseline characteristics and MS history

Table 2 - Factors associated with the change from Fingolimod to Siponimod

	UNIVARIATE OR (95%CI); p value	MULTIVARIATE OR (95%CI); p value
Sex, males vs females	1.00 (0.43 – 2.31); 0.99	-
Age at enrolment (years)	0.96 (0.91 – 1.01); **0.09**	0.96 (0.91 - 1.02); 0.21
Age at onset (years)	1.00 (0.96 – 1.04); 0.90	-
Disease duration (years)	0.98 (0.93 – 1.03); 0.49	
EDSS at baseline	0.69 (0.50 – 0.97); **0.031**	0.62 (0.43 – 0.91); **0.014**
Number of previous DMTs	1.26 (0.90 – 1.76); 0.19	1.53 (1.02 – 2.31); **0.042**
Relapses in the previous 12 months	2.72 (0.70 – 10.59); 0.15	2.92 (0.67 – 12.78); 0.16
Months of treatment with Fingolimod	1.00 (0.98 – 1.01); 0.48	

Factors associated with the change from Fingolimod to Siponimod

Conclusion: Only 40% of SPMS patients treated with fingolimod were switched to siponimod. Lower EDSS and higher number of previous DMTs were associated with the decision to switch to siponimod.
Disclosure: The authors declare no competing interests for this work.

EPO-144

Safety and tolerability of Zadiva® (NanoAlvand Co. brand-generic product of dimethyl fumarate) in Iranian MS population

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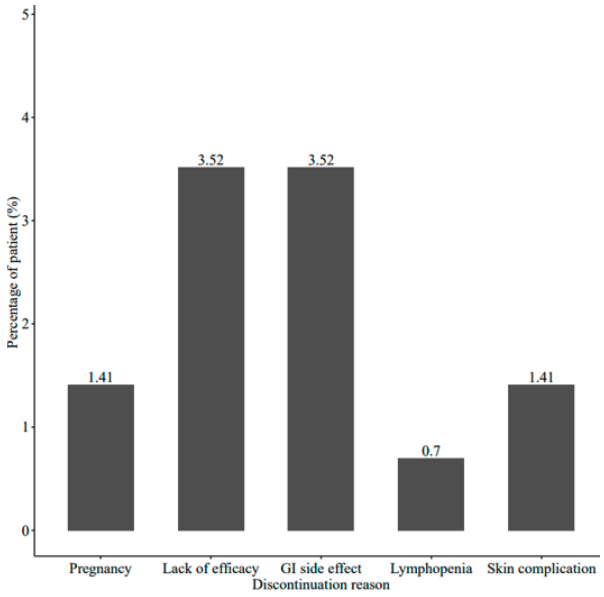
Background and aims: Dimethyl fumarate (DMF) was approved in 2013 to reduce disease activity in relapsing remitting multiple sclerosis (RRMS) patients. Although randomized controlled trials' evidences are high-level, they cannot reflect the clinical context in which drugs are used in reality.
Methods: The study is an observational, retrospective and real-world assessment of the safety and tolerability of Zadiva® in Iranian RRMS patients. Individuals' data in the neurology clinics of a referral university hospital following receiving informed consent were collected. The main objectives of the study were to assess the safety and discontinuation rate of the drug during the follow-up period and the reasons for the discontinuation. Other objectives were the number of patients who experienced a relapse and their EDSS score.
Results: A total of 142 patients with mean age of 33.90 ± 7.76 years were enrolled in the study. During the evaluation, only 15 patients (10.56%) discontinued treatment with the drug. The leading causes for discontinuation were adverse events, lack of efficacy, and pregnancy respectively. Besides, the most common adverse events were flushing (N=34, 23.94%), though no serious adverse event were

reported. The data also demonstrated a significant reduction in the number of patients with relapse, and 90.85% (N=129) of patients were relapse-free at the end of the study. The mean EDSS score changed from 1.64 ± 0.44 to 1.68 ± 0.50 before and after one-year treatment.

Age (yr) Mean ± SD	33.90 ± 7.76
Gender, Female N (%)	126 (88.73)
EDSS score Mean ± SD	1.64 ± 0.44
Duration of disease (yr)* Mean ± SD	4.55 ± 3.82
Previous medication history N (%)	
Interferon beta-1a, IM	50 (35.21)
Interferon beta-1a, SC	21 (14.79)
Interferon beta-1b, SC	9 (6.34)
Glatiramer Acetate	36 (25.35)
Fingolimod	2 (1.41)
Teriflunomide	1 (0.70)
Naive	11 (7.75)
Unknown	12 (8.45)

*Calculated for 139 patients

Demographics and baseline characteristics



Reasons of discontinuation

System Organ Class	Preferred Term Name	No. of Patients (N=142)
Vascular disorders	At least one event	34 (23.94)
	Flushing	34 (23.94)
Gastrointestinal disorders	At least one event	27 (19.01)
	Abdominal pain	23 (16.2)
	Diarrhoea	13 (9.15)
	Dyspepsia	11 (7.75)
	Nausea	9 (6.34)
	Vomiting	2 (1.41)
Skin and subcutaneous tissue disorders	At least one event	17 (11.97)
	Erythema	10 (7.04)
	Rash	4 (2.82)
	Pruritus	4 (2.82)
	Lichenoid keratosis	1 (0.7)
Investigations	At least one event	16 (11.27)
	Transaminases increased	16 (11.27)
Blood and lymphatic system disorders	At least one event	7 (4.93)
	Lymphopenia	6 (4.23)
	Eosinophilia	1 (0.7)
Infections and infestations	At least one event	3 (2.11)
	Varicella zoster virus infection	2 (1.41)
	Tinea versicolour	1 (0.7)
Nervous system disorders	At least one event	2 (1.41)
	Headache	2 (1.41)
Immune system disorders	At least one event	1 (0.7)
	Urticaria	1 (0.7)

Incidence of adverse events classified based on the Medical Dictionary for Regulatory Activities (MedDRA) as the preferred term (PT) and system organ class (SOC)

Conclusion: The results of this study confirmed the acceptable safety and tolerability of Zadiva® in a real-world setting for RRMS patients in addition to its efficacy.
Disclosure: All authors declared there is no relationships, activities and interests related to the manuscript.

EPO-145

Erectile dysfunction in men with multiple sclerosis

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Background and aims: To evaluate the prevalence and predictors of erectile dysfunction in men with multiple sclerosis (mwMS).
Methods: 179 consecutive mwMS (age 37.25±9.48 years, disease duration 7.64±5.54 years) and 32 (33.72±8.53 years) healthy controls (HC) were enrolled. mwMS completed The sexual health inventory for men (IIEF-5), Modified Fatigue Impact Scale (MFIS) (cognitive, physical, and psychosocial subdomain), Beck depression inventory (BDI-2), and The 5-level EQ-5D questionnaire (your health

today question, range from 0-100). HC completed the IIEF-5. We performed a linear regression analysis and statistically significant predictors from the univariable analysis were included in the multivariable regression analysis.
Results: mwMS scored less on IIEF-5 compared to HC (23, range 6-25 vs 24, range 14-25, p=0.017). Erectile dysfunction (defined as IIEF-5 score ≤21) was present in 37.9% of mwMS and 25.8% of HC, p=0.227. In the univariable linear regression analysis age, multifunctional initial presentation of MS, MRI lesions in the brainstem, EDSS, physical, cognitive, and psychosocial domains of MFIS were negative and your health today question of the EQ-5D was a positive predictor of the IIEF-5 score. In a multivariable linear regression analysis age (B=-0.155, 95% CI -0.275- -0.035), the multifunctional initial presentation of MS (B=-7.857, 95% CI -15.625 - -0.089) and cognitive part of MFIS (B=-0.212, 95% CI -0.410 - -0.014) were negative predictors of the IIEF-5 score.
Conclusion: Erectile dysfunction is very frequent in mwMS. Increased age and presentation with multifunctional symptoms at disease onset and cognitive fatigue are negative predictors of the IIEF-5 score.
Disclosure: IA: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals. TG: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals. MKS: received consultation and/or speaker fees from: Sanofi Genzyme, Roche. MH: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals.

EPO-146

Remibrutinib: A Novel BTKi in Development for MS With a Favorable Safety Profile in Various Autoimmune Disorders

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Background and aims: Remibrutinib is a novel, potent, highly selective, covalent, oral Bruton's tyrosine kinase inhibitor (BTKi) currently investigated in Phase 3 trials for treatment of multiple sclerosis (MS; NCT05147220/NCT05156281). This analysis presents an overview of the safety of remibrutinib from Phase 2 clinical trials in various autoimmune disorders.
Methods: Data were collected from final analyses of trials in chronic spontaneous urticaria (CSU), Sjögren syndrome (SjS), and asthma, and interim analysis of open-label extension (OLE) in CSU. Safety assessments comprised of AEs, including serious and AEs of special interest (AESI), vital signs, ECGs, and laboratory parameters.
Results: Overall, 363 patients (267 CSU; 49 SjS; 47 asthma) who received various doses (10–100 mg q.d./b.i.d.) of remibrutinib for 12–52 weeks were included. Among CSU patients, the safety of remibrutinib 100 mg b.i.d. in the 52-week OLE study was comparable to doses in the core study (Table 1). Overall, most frequently reported grouped AEs (≥10%) were infections and infestations, skin, subcutaneous, gastrointestinal, and nervous system disorders. AEs were similar to placebo in core studies except for skin disorders, where post-treatment CSU flares caused an imbalance. There were no increases in infection rates. Other AESI, including bleeding (all minor) and cytopenia were not altered during long-term treatment. No safety concerns were noted in laboratory analyses, ECGs, or vital signs.

Patients, n (%)	Core study		Extension study
	Remibrutinib any dose (n=267)	Placebo (n=42)	Remibrutinib 100 mg b.i.d. (N=183*)
Duration of exposure, weeks, median (IQR)	12 (12.0–12.3)	12 (12.1–12.7)	35 (14.4–52.0)
Patients with ≥1 AE	155 (58.1)	18 (42.9)	105 (57.4)
Discontinued study treatment due to AE(s)	7 (2.6)	0 (0.0)	6 (3.3)
Patients with SAE(s)	5 (1.9)	0 (0.0)	4 (2.2)
Death	0 (0.0)	0 (0.0)	0 (0.0)

*At the time of interim analysis (July 2021).
AE, adverse event; b.i.d., twice a day; CSU; chronic spontaneous urticaria; IQR, interquartile range; N, total number of patients; n, number of patients in each arm; SAE, serious adverse event.

Table 1. Safety and Tolerability of Remibrutinib (10–100 mg q.d./b.i.d.) in the 12-week Core and 52-week Extension Phase 2b Studies in CSU patients

Conclusion: Remibrutinib demonstrated a favorable safety profile and was well tolerated at all doses studied in Phase 2 trials and the 52-week OLE (up to 100 mg b.i.d.), supporting its development in Phase 3 clinical trials in MS.
Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPO-147

ACE and ACE-2 as potential biomarkers in multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is a chronic autoimmune neurodegenerative disease characterized by demyelination in the central nervous system (CNS). It is heterogeneous in terms of clinical expression, histopathological and radiological changes, and response to therapy. Renin-Angiotensin System (RAS) plays a pivotal role in autoimmune inflammation in the CNS. Angiotensin-converting enzyme (ACE) and its homolog ACE-2 are considered two of the major enzymes in the RAS system. The aims of this study were to measure protein levels of ACE and ACE2 in the serum obtained from MS patients and healthy controls, and to find significant associations with demographics and clinical characteristics of patients.
Methods: This was a case-control study that included 87 MS patients and 87 age and sex matched healthy controls. Serum levels of the target markers was measured using human enzyme-linked immunosorbent assay (ELISA) technique.
Results: Median serum ACE and ACE-2 levels were significantly higher in MS patients (220.60 pg/ml and 1867.68 pg/ml, respectively) compared to healthy controls (159.28 pg/ml and 1059.72 pg/ml, respectively) (p-value<0.001). Cut-off values of 188.66 pg/ml for ACE and 1459.03 pg/ml for ACE2 were found to discriminate MS patients from healthy controls (sensitivity = 66.7% and 78.2%, and specificity = 62.1% and 75.9%, respectively). Significant correlations were revealed between serum ACE level and BMI (p-value=0.012) and MS disease duration (p-value=0.002), also between ACE2 level and gender (p-value=0.027).
Conclusion: Serum ACE and ACE-2 can be potential diagnostic biomarkers for MS. However, future prospective studies should focus on investigating their role in predicting response to therapy in MS patients.
Disclosure: The authors declare that there are no conflicts of interest.

EPO-148

Cognitive assessment in a large Argentinian cohort of patient with Multiple Sclerosis

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Background and aims: Cognitive impairment (CI) is a common symptom of multiple sclerosis, with a negative effect on patients' daily lives. **Objectives:** 1-To describe the prevalence of CI and cognitive profile of the PwMS cohort. 2-To compare the cognitive performance of PwMS in relation to Expanded Disability Status Scale (EDSS) and MS duration.
Methods: Cross-sectional study. Measuring instruments: Clinical and cognitive variables were assessed (EDSS, Fatigue severity scale, Beck Depression Inventory, BICAMS battery, PASAT, verbal fluency, 7/24 test). CI was defined as impairment in ≥2 cognitive domains. Parametric and non-parametric statistics were used, p<0.05 was considered significant.
Results: 323 PwMS were recruited. Mean age: 40.71±12.89 years; mean education: 13.43±4.2 years; mean EDSS: 2.05±1.94 (median 2.5 IQR8) and stratified EDSS was 0-3:61.7%; 3.5-8:38.3%; mean MS duration: 8.51±8.29 years; female 62.8%; relapsing-remitting MS (RRMS) 91.6%. Objectives:1)The prevalence of CI at inclusion study was 47.5%. The most affected cognitive domains were: attention and processing speed followed by verbal memory, verbal fluency and visual memory. 2)Patients with EDSS between 3.5-8 presented worse cognitive performance (p<0.05). The PwMS duration >20 years presented worse cognitive performance compared to those of ≤5 years (p<0.05). The group of >20 years presented worse performance than those of 6-10 years (p<0.05). In a multivariable logistic regression model, EDSS was an independent risk factor to reach CI when adjusted for potential confounders (adjusted Odds Ratio(OR) 1.43, 95% confidence interval(CI) 1.09-1.87, p=0.01).
Conclusion: The prevalence of IC in our cohort was similar to previous reports. Disability (EDSS) was an independent predictor of CI.
Disclosure: Nothing to disclose.

EPO-149

Comorbidities among myasthenia gravis patients: a population-based observational study in Denmark, Finland, and Sweden

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune neuromuscular disease. Comorbidities complicate medical management and can be a consequence of MG or its treatment. Here, we assessed the evolution of MG comorbidity burden in Denmark (DK), Finland (FI), and Sweden (SE).

Methods: Data were collected from healthcare registers with almost complete population coverage. Incident MG patients were identified based on ≥2 MG diagnostic codes (ICD-10; G70.0*) in specialty care during 2000–2020, defining first (incident) MG diagnosis as the index date. The presence of comorbidities was assessed based on hospital discharge diagnoses five years before and up to 20 years after the index date. Comorbidities reaching 10% cumulative incidence at 20 years are presented. Cumulative incidences were estimated from the index date onwards regardless of the pre-existence of comorbidity, treating death as a competing risk.

Results: Among 6415 patients, 76% had ≥1 of 41 comorbidities. Difference (%-points) in comorbidities five years prior and five years after the index date was highest for hypertension in FI (+10.9%) and SE (+12%), and osteoporosis in DK (+8.7%) (Figure 1). Across countries, age and sex, highest cumulative comorbidity incidence at 10 and 20 years after index date was observed for hypertension (Figure 2). Similarly, the highest cumulative incidences over 20 years were hypertension followed by malignancies (excluding thymoma) and cataract (Figure 3).

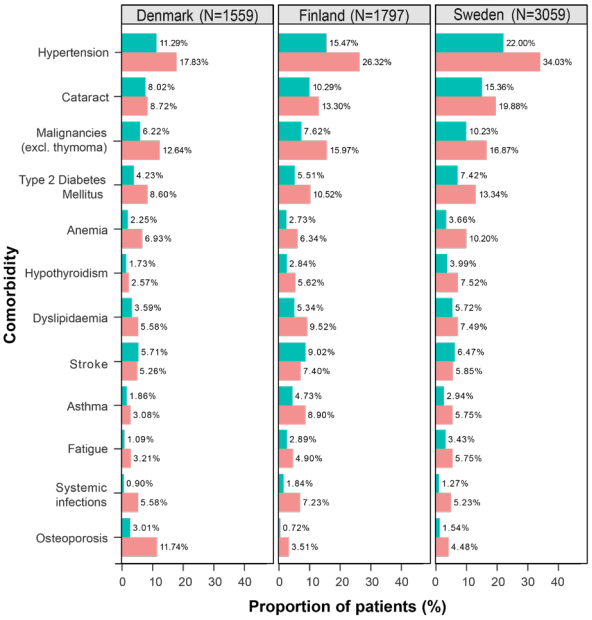

Figure 1: Comorbidities five years prior and five years after the incident myasthenia gravis diagnosis in Denmark, Finland, and Sweden.

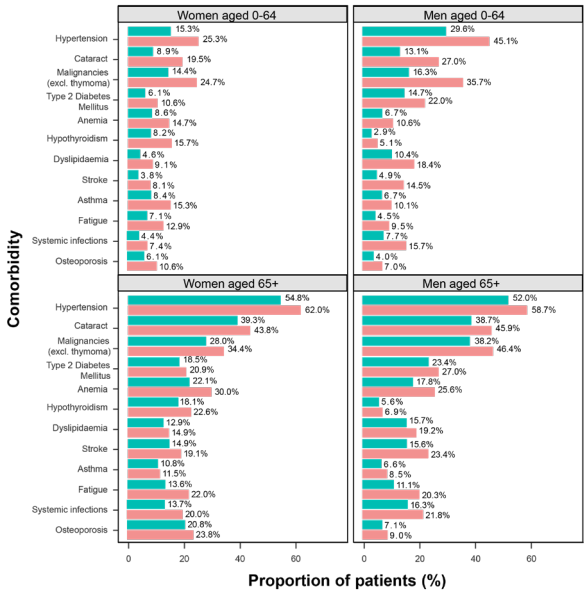

Figure 2: The cumulative incidence of comorbidities at 10 and 20 years on or after the incident myasthenia gravis diagnosis (index date) in Denmark, Finland, and Sweden, by age and sex.

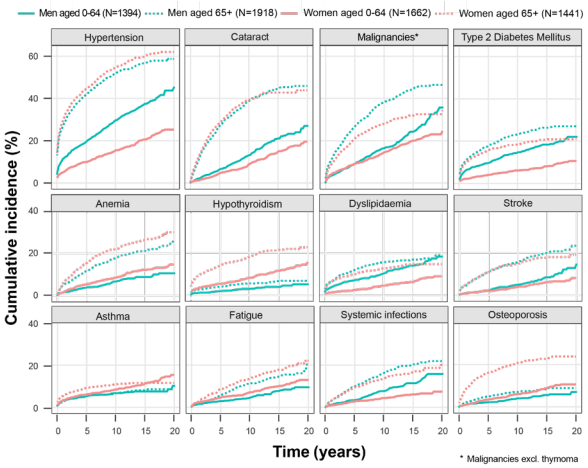

Figure 3: The cumulative incidence of comorbidities during the 20 years on or after the incident myasthenia gravis diagnosis (index date) in Denmark, Finland, and Sweden.

Conclusion: MG is associated with a wide range of comorbidities in a substantial proportion of patients. This highlights the complex management needs of MG patients, to limit comorbidity burden and exacerbation of existing conditions.

Disclosure: Funded by UCB Pharma. John Vissing is Consultant on advisory boards for Roche, Sanofi Genzyme, Sarepta Therapeutics, Novartis Pharma AG,Fulcrum Therapeutics, Biogen, Lupin, Amicus, Regeneron, Argenx BVBA,UCB Biopharma SPRL, Arvinas, ML Biopharma, Atamyo, Horizon Therapeutics, Dyne Therapeutics Research, travel support, and/or speaker honoraria from Sanofi Genzyme, Alexion Pharmaceuticals, Edgewise Therapeutics, Fulcrum Therapeutics, and UCB Biopharma SPRL. Principal investigator in clinical trials for Sanofi Genzyme, Roche, Horizon Therapeutics,Argenx BVBA, Novartis Pharma AG,Alexion Pharmaceuticals, UCB Biopharma SPRL, Genethon, ML Biopharma, Reneo Pharma, Pharnext, Janssen Pharmaceutical, Khondrion, Regeneron, and Dynacure SAS, Janssen Sari Atula travels with pharmacompany: Merck, Speaker in educational sessions by pharma companies: Merck, Roche, Biogen, Novartis, Advisory boards: Biogen, Merck, Roche, Novartis, UCB Pharma Mari Savolainen, employed at UCB Pharma, Espoo, Finland Juha Mehtälä, employee of MedEngine Oy, Finland Laila Mehkri, employee of MedEngine DK ApS, Denmark Tero Ylisaukko-oja, owner of MedEngine Oy and MedEngine DK ApS Didier Pitsi, employed at UCB Pharma, Brussels, Belgium Fredrik Berggren is an employee and stockholder of UCB Pharma, Copenhagen, Denmark Fredrik Piehl has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis.

EPO-150

The Relationship Between Neurofilament Light Chain and B Lymphocyte Chemoattractant and Cognition in Multiple Sclerosis

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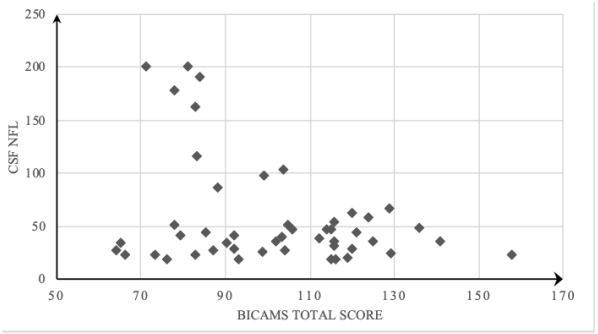
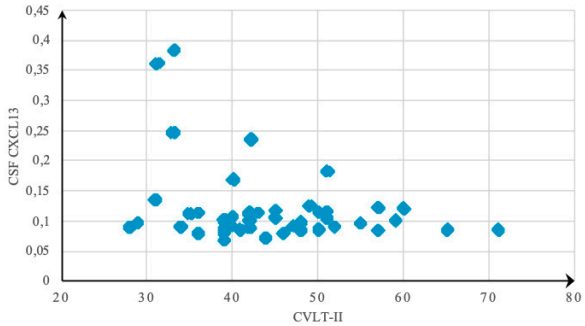
Background and aims: Multiple sclerosis (MS) is a chronic inflammatory, autoimmune, demyelinating disease of the central nervous system. Cognitive impairment can be seen in all stages of MS. This study aims to investigate the relationship between neurofilament light chain (NfL) and B Lymphocyte Chemoattractant (CXCL13) potential biomarkers and cognitive impairment in MS.

Methods: This study included 57 patients diagnosed with Radiologically Isolated Syndrome (RIS), Clinically Isolated Syndrome (CIS), Relapsing-remitting MS (RRMS) and 70 healthy controls. NfL and CXCL13 were studied by The Enzyme-Linked Immunosorbent Assay Method (ELISA) in the patient's cerebrospinal fluid (CSF) and serum samples. These biomarkers were studied just in serum samples in the control group. The Brief International Cognitive Assessment for MS (BICAMS) test was applied to all participants. Serum biomarker levels and cognition tests were compared between the control and patient groups.

Results: A significant negative correlation was found between CSF NfL and BICAMS (p=0.030), and CSF CXCL13 and California Verbal Learning Test-II (p=0.034). Serum NfL and CXCL13 values in the patient group were significantly higher (p=0.043; p<0.001, respectively). A significant positive correlation was found between CSF NfL and CSF CXCL13 (p=0.004). There is a strong relationship between serum and CSF NfL (p=0.002). BICAMS were found to be significantly lower in the patient group (p<0.001).



The correlation between BICAMS and CSF NfL in the patient group



The correlation between CVLT-II and CSF CXCL13 in the patient group

Conclusion: NfL and CXCL13 potential biomarkers are associated with cognitive impairment in MS patients. For this reason, it has been seen that there are promising biomarkers in cognition follow-up and predicting prognosis.
Disclosure: The authors have no conflict of interest. No funds was received.

EPO-151

ASSESSMENT OF SLEEP DISORDERS IN NEUROMYELITIS OPTICA

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Background and aims: Although sleep disorders are frequently reported by neuromyelitis optica (NMO) patients, they are often overlooked. This study aimed to characterize factors that contribute to fatigue and excessive daytime sleepiness in NMO patients.
Methods: Fifty patients with a confirmed diagnosis of NMO and 52 sex and age matched healthy control group were admitted to the sleep laboratory for 2 days to perform 1 night of polysomnography (PSG) and a 5-nap multiple sleep latency test (MSLT) the following day. The results were evaluated with regards to the clinical scales.
Results: Excessive daytime sleepiness was found in 43.1%, and sleep quality was poor in 72.2% of NMO patients. According to the PSG-MSLT, a sleep disorder was found in 92.4% of NMO patients. A diagnosis of hypersomnolence was made in 51.1% of patients, and 5.1% of them were categorized as type 2. Compared to healthy control group, patients with NMO had a lower quality of sleep and higher sleep disorders.
Conclusion: Understanding the mechanism of NMO-associated-sleep disorders is necesary to improve the patient's quality of life. Correction of sleep disorders by effective treatments could be important for reducing fatigue symptoms and improving general state of NMO patients.
Disclosure: Nothing to disclose.

EPO-152

Progression independent of relapse activity drives permanent disability accrual in relapsing multiple sclerosis

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Background and aims: Progression independent of relapse activity (PIRA) occurs frequently in relapsing multiple sclerosis (MS) and is recognized as the most frequent driver of confirmed
Methods: Relapsing-onset MS patients with follow-up >/= 5 years (n=16,130) were extracted from the Italian MS Registry. CDA was defined by an increase in Expanded Disability Status Scale (EDSS) score confirmed at 6 months, and classified per temporal association with

relapses. Sustained disability accumulation (SDA) was a CDA with no EDSS improvement in subsequent visits. Predictors of SDA were assessed using logistic multivariable regression analyses.
Results: Over a follow-up of 11.8+/-5.4 years, 16,731 CDA events occurred in 8,998 (55.8%) patients. Overall, PIRA (n=12,175) accounted for 72.3% of CDA events. SDA occurred in 73.2% of PIRA and 56.7% of RAW (p<0.001). 56.8% of patients transitioned to secondary progressive MS at first PIRA; this proportion progressively increased to 87.5% of transition at fourth PIRA. In the multivariable analysis risk of SDA was associated with PIRA (OR=1.64;95%CI 1.49-1.80,p<0.001), male sex (OR=1.26;95%CI 1.14-1.38,p<0.001), higher EDSS (OR=1.17;95%CI 1.13-1.21,p<0.001) and older age at baseline (OR=1.02;95%CI 1.01-1.03,p<0.001), and shorter exposure to disease modifying therapies (OR=0.43;95%CI 0.38-0.50,p<0.001).
Conclusion: In our population PIRA represents the main driver of disability accumulation in relapsing MS. Compared with RAW it was associated with increasing risk of evolution to secondary progressive MS and permanent disability accrual. Identification of early clinical, radiological and laboratory predictors of PIRA is key to guide personalized treatment decisions.
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EPO-153

Microchimerism and multiple sclerosis: the impact of sex of offspring on maternal clinical and ophthalmological features

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Background and aims: Multiple sclerosis (MS) is a chronic autoimmune disorder characterised by inflammation and neurodegeneration. Several pregnancy-related changes have been accounted for the protective role of gravidity in MS. XX and XY fetal microchimeric cells (fMCs) migrate to maternal blood during pregnancy and survive for decades. However, their biological significance is still unknown. The aim of this study was to investigate the role of the sex of offspring, an indirect marker of fMCs, in clinical and ophthalmological MS features.
Methods: We enrolled 43 female MS patients, including 18 nulliparous (NPp), 19 patients with at least a male son (XYp), and 6 patients with only daughters (XXp). Each patients underwent clinical assessment and optical coherence tomography (OCT) scan. Data for retinal nerve fibre layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL) thickness were extracted.
Results: The risk of MS onset in post-partum was higher in XYp than XXp (OR=4.43, p=0.043). XXp had higher annual relapse rate (0.45±0.30 vs 0.89±0.71, p=0.009), while XYp reached lower scores at Paced Auditory Serial Addition Test (50.26±28.39 vs 65.56±19.11, p=0.039). In the optic nerve, RNFL was higher in XYp than NPp (89.88±18.26 μm vs 97.22±13.65 μm, p=0.049), while no difference was detected between XXp and NPp (p>0.050). Similar trends were found in GCIPL, but they did not reach statistical significance.
Conclusion: Our findings showed different trends between patients with male and female offspring. Being other pregnancy-related changes similar in male and female pregnancies, we hypothesised that XX and XY fMCs could play a role on the biological processes underlying MS.
Disclosure: A Bianchi received Research Grant from the Italian Society of Neurology (Società Italiana di Neurologia, SIN). G Salemi received grants for speaking or consultancies from: Almirall, Biogen, Merck, Novartis, Roche, Sanofi Genzyme. P Ragonese received grants for speaking or consultancies from: Biogen, Bristoll-Myers-Squibb, Merck, Novartis, Roche, Sanofi Genzyme. M Aprile, S Viscomi, G Schirò, R Di Blasio, S Iacono, M Andolina, M Marrale, G La Tona, M Midiri, C Gagliardo, M Vadalà, and VME Bonfiglio do not report any disclosure for the project. authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-154

SF36 in the domain of physical activity predicts confirmed disability progression in people with multiple sclerosis

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Background and aims: To assess whether the Patient reported outcome measure (PROM) scores may predict disease progression in relapsing remitting multiple sclerosis (RRMS) patients within three years of follow-up, and investigate which of PROMs single components is most closely associated with the outcome (progression within three years of follow-up).

Methods: Observational prospective multicenter study. Stable RRMS patients were enrolled consecutively. At the time of enrollment, we assessed EDSS, and all patients completed the following PROMs: Beck Depression Inventory- II (BDI-II), The Treatment Satisfaction Questionnaire for Medications (TSQM), Medical Outcomes Study Short Form 36- Item (SF36), Fatigue Severity Scale (FSS). EDSS was re-assessed three years later for all patients. The outcome measure was defined as the occurrence of confirmed disability progression (CDP) over three years of follow-up. Univariable logistic regression models were performed to study the association between the final score of each test and the outcome. Subsequently, a multivariable model was performed including variables with p-value<0.10 in the univariable analysis.

Results: Demographics and clinicals are reported in Table 1. At the multivariable regression model, SF36-Physical Functioning (SF36-PF) was the only independent variable associated with the outcome. (Table 2) The ROC curve analysis determined a score of 77.5 at SF36-PF sub-scale as the cut-off point resulting in the best combination of sensitivity and specificity (Se=0.65; Sp=0.64) for the occurrence of CDP within three years of follow-up [AUC: 0.66 (0.56-0.75)].

	Overall N=200	Not worsened N=158(79%)	Worsened N=42(21%)	p-value
Age, mean (SD)	39.67(10.29)	39.00(9.95)	42.28(11.27)	0.068
Female, N (%)	123(62%)	95(60%)	28(67%)	0.439
Education, mean (SD)	13.46 (3.22)	13.64(3.25)	12.78(3.06)	0.130
Presence of comorbidities, N (%)	39(20%)	32(20%)	7(17%)	0.602
Disease duration, mean (SD)	10.81(7.89)	10.60(7.71)	11.61(8.61)	0.464
Number of previous relapses, median (IQR)	2(1; 3)	2(1; 3)	2(1; 3)	0.368
Number of therapies, median (IQR)	1(1;2)	1(1; 2)	1(1; 2)	0.396
Therapy, N (%)				
Dimethyl fumarate	45(23%)	35(22%)	10(24%)	0.381
Glatiramer acetate	25(13%)	18(11%)	7(17%)	
Interferon	111(56%)	92(58%)	19(45%)	
Teriflunomide	19(10%)	13(8%)	6(14%)	

Table 1. Characteristics of the patients, overall and based on the outcome. P-values refer to T-test or Mann-Whitney for continuous variables and to Chi-squared test for the categorical ones.

Characteristics of the patients, overall and based on the outcome. P-values refer to T-test or Mann-Whitney for continuous variables and to Chi-squared test for the categorical ones.

Table 2. The association between the final score of each test and the outcome.

			Univariate analysis		Multivariate analysis	
	N	Median (IQR)	OR (95%CI)	p-value	OR (95%CI)	p-value
BDI (10-unit increase)	197	6(2; 11)	1.49(0.98; 2.26)	0.062	1.09(0.59; 2.01)	0.778
TSQM (10-unit increase)	199	52(46; 61)	0.84 (0.63; 1.13)	0.252	----	----
FSS (10-unit increase)	196	28(15; 45)	1.26(1.03; 1.54)	**0.027**	1.10(0.80; 1.51)	0.574
SF36 PF (10-unit increase)	185	90(60; 95)	0.81(0.71; 0.93)	**0.002**	0.82(0.67; 1.00)	**0.046**
SF36 RP (10-unit increase)	185	100(25; 100)	0.94(0.86; 1.02)	0.155	----	----
SF36 BD (10-unit increase)	185	74(51; 100)	0.86(0.75; 0.98)	**0.023**	0.95(0.79; 1.14)	0.572
SF36 GH (10-unit increase)	185	56(42; 72)	0.85(0.71; 1.01)	0.061	0.94(0.74; 1.20)	0.635
SF36 VT (10-unit increase)	185	55(45; 70)	0.85(0.71; 1.03)	0.099	1.19(0.88; 1.62)	0.268
SF36 SF (10-unit increase)	185	75(50; 100)	0.92(0.81; 1.06)	0.245	----	----
SF36 MH (10-unit increase)	185	66(33; 100)	0.99(0.90; 1.09)	0.848	----	----
SF36 RE (10-unit increase)	185	64(52; 80)	0.90(0.74; 1.09)	0.267	----	----

Legend. Beck Depression Inventory- II (BDI-II); The Treatment Satisfaction Questionnaire for Medications (TSQM); Fatigue Severity Scale (FSS); Medical Outcomes Study Short Form 36- Item (SF36): Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Mental Health (MH), Role Emotional (RE).

The association between the final score of each test and the outcome.

Conclusion: RRMS patients scoring higher at SF36-PF subscale present a higher likelihood to experience CDP within the next 3 years.

Disclosure: Nothing to disclose.

EPO-155

A clinical diffusion MRI protocol to simultaneously dissect brain grey and white matter microstructure

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Background and aims: Chronic inflammatory process in MS involves both white matter (WM) and grey matter (GM). Diffusion MRI (dMRI), thanks to advanced signal modelling like the Soma And Neurite Density Image (SANDI) can probe microstructural information from both GM and WM. We propose a 10 minute acquisition protocol that enables to acquire such images on a clinical 3T scanner in both healthy subjects (HS) and MS patients.

Methods: We enrolled 5 HS and 5 relapsing remitting (RR) patients. MPRAGE, FLAIR and multishell dMRI images were acquired on a 3T Siemens Prisma scanner. We compared microstructural maps from diffusion tensor imaging (DTI) and neurites orientation dispersion and density image (NODDI) with neurite, soma and extracellular densities (f-neurite, f-soma, f-extra), apparent soma radius

and intra ed extra neurites diffusivities from SANDI. Mean values of all the metrics in HS WM, MS NAWM, MS WM lesions, HS GM, MS NAGM and MS GM lesions were evaluated.
Results: Repeatability and reproducibility of SANDI was comparable with those of DTI and NODDI (intraclass correlation coefficient, ICC>0.7 and coefficient of determination, R^2>0.7). SANDI showed increase of f-extra in almost all WM lesions, but different f-soma behaviors within lesions and in comparison to NAWM. SANDI allowed an accurate separation in mean values between HS WM/GM and MS patients NAWM/NAGM as well as NAWM, WM lesions and NAGM and GM lesions within MS patients.
Conclusion: Our result suggest that SANDI is a repeatable, reproducible, feasible and a practical method to characterize WM and GM tissues in both HS and MS patients.
Disclosure: M.I. received research grants from NIH, DOD, NMSS, FISM and Roche; and received consulting fees from Novartis, Roche, Merck, SanofiGenzyme, Janssen and Admirall.

EPO-156

Autologous hematopoietic stem cell transplantation in multiple sclerosis: updating outcomes in the Valencian cohort.

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Background and aims: Autologous hematopoietic stem cell transplantation(aHSCT) has been recognized as a therapeutic option for very aggressive multiple sclerosis(MS) patients, although it is not a commonly used technique. The current aHSCT indications are highly activeMS, short duration of disease (≤ 5-10 years) and a suboptimal response to high-efficacy treatments.
Methods: A prospective cohort of 46 consecutive MSpatients undergoing aHSCT between 1999-2022 was included in the analysis. The main indication for transplantation was clinical relapse despite active targeted treatment for at least one year. Efficacy was assessed in patients followed for at least 2 years and toxicity was assessed during the entire follow-up.
Results: The baseline characteristics of the patients were, mean age 36.53 years(SD 9.2), 31 women and 15 men, baseline EDSS of 5(SD 4–6), 33 recurrent MS -11 secondary progressive MS -2 primary progressive MS. 24 patients had gadolinium enhancing lesions(GEL) at baseline. The median time to follow-up was 8 years (2,5-13). 28 patients had lost NEDA3 status at last visit, 8 patients progressed de novo, and 20 required re-initiation of specific treatment. Median EDSS post-aHSCT was 4(SD 3–6.5), we found a median overall EDSS improvement of 0.5(SD -1.5– 1). Malignancies and autoimmune events were infrequent (3 for each group).
Conclusion: aHSCT as an alternative therapy to manage aggressive MS patients is a relatively safe and effective procedure. It is necessary to propose comparative studies with adverse effects and effectiveness between immunomodulatory treatments and aHSCT.
Disclosure: Boix Lago, A. No potential conflict of interest. Gil-Perotín, S. Speaker: Biogen, Merck, Sanofi-Genzyme, Bial; Consultant and advisor: Merck; Research grants: Almirall. Ramió-Torrentà Ll: has received compensation for consulting services and speaking fees from Biogen, Novartis, Bayer, Merck, Sanofi, Genzyme, Roche, Bristol-Myers-Squibb, TEVA, Almirall. Casanova Estruch, B. has received compensation for consulting services and speaking fees from Genzime, Roche, BMS, Jensen, Almirall, Merck-serono.

EPO-157

Thalamus volume as a convenient marker of degenerative-atrophic changes in the brain of multiple sclerosis patients

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Background and aims: In recent years, it has become clear that MS is a disease characterized not only by a demyelinating inflammatory process but also by a neurodegenerative. However, methods for monitoring the progression of neurodegeneration in MS are still in their infancy. The development of easy-to-use methods for assessing neurodegenerative processes in MS would significantly improve diagnostic and prognostic possibilities.
Methods: Randomly selected 17 multiple sclerosis patients and a control group of 20 healthy individuals corresponding to the studied group regarding age and gender were examined in the MS centre of Lviv Regional Clinical Hospital. They underwent an MRI of the brain, followed by a volume analysis of brain structures using the Vol2Brain pipeline with further correction regarding the intracranial cavity volume.
Results: We found that thalamus volume in patients with MS was significantly smaller than in healthy individuals (p=0.002). The most pronounced decrease in thalamus volume in MS patients was associated with an increase in the total number of MS relapses (r=0.633, p=0.006). The decrease in the thalamus volume did not have a statistically significant relationship with the age and duration of the disease. At the same time, thalamus volume in MS patients was closely related to the volume of brain white matter (r=0.752, p<0.001) and other brain structures.
Conclusion: Thalamus volume could be a convenient marker to evaluate general degenerative-atrophic changes associated with MS relapses in the brain of MS patients. Assessing its volume in dynamics can be a good option for monitoring the course of MS.
Disclosure: Nothing to disclose.

MS and related disorders 2

EPO-158

Matching-Adjusted Indirect Comparisons of Diroximel Fumarate, Ozanimod, and Interferon beta-1a for Relapsing MS

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Background and aims: Diroximel fumarate (DRF), ozanimod (OZA), and interferon beta-1a (IFN) are disease-modifying therapies for relapsing multiple sclerosis. No randomised trials have directly compared DRF vs OZA or IFN. We report matching-adjusted indirect comparisons (MAIC) of efficacy for DRF vs OZA and DRF vs IFN.
Methods: Analyses were based on individual patient data from the 2-year, open-label, single-arm, phase 3 EVOLVE-MS-1 study (NCT02634307) of DRF (462mg BID; n=1057), and aggregated data from the 2-year, double-blind, active-comparator, phase 3 RADIANCE study (NCT02047734) of OZA (1mg QD; n=433) and IFN (30µg weekly; n=441). EVOLVE-MS-1 data were restricted (per RADIANCE inclusion/exclusion criteria) and weighted to match baseline characteristics in RADIANCE. Outcomes were compared for annualised relapse rate (ARR), 12-week confirmed disability progression (CDP), 24-week CDP, absence of gadolinium-enhancing (Gd+) T1 lesions, and absence of new/newly enlarging T2 lesions.
Results: After weighting, baseline variables were balanced across groups. ARR outcomes were similar for DRF and OZA but favoured DRF vs IFN. Outcomes for 12- and 24-week CDP favoured DRF vs OZA; 12-week CDP favoured DRF vs IFN, but there was not strong evidence favouring DRF over IFN for 24-week CDP. Compared with OZA and IFN, DRF had higher proportions of patients without Gd+ T1 lesions and patients without new/newly enlarging T2 lesions.
Conclusion: Disability progression and radiological outcomes favoured DRF vs OZA. All clinical and radiological outcomes favoured DRF vs IFN, except for 24-week CDP. Limitations include potential residual confounding due to different study designs and the application of unanchored MAIC since there was no cross-trial common comparator.
Disclosure: Supported by Biogen.

EPO-159

Effectiveness of Dimethyl Fumarate After Switching From Non-Specific Immunosuppressants

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Background and aims: Non-specific immunosuppressants (NSIS) have been used as off-label therapy for the treatment of multiple sclerosis (MS) but most lack controlled phase 3 clinical trials. This study investigated patient outcomes on dimethyl fumarate (DMF), an oral disease modifying therapy with demonstrated clinical effectiveness in treating MS, after switching from NSIS in a real-world setting.
Methods: This retrospective, single arm, observational analysis of patients in the MSBase registry database assessed 18−65 year old relapsing-remitting MS patients with EDSS score 0−6.0 on NSIS treatment, who switched to DMF between 2014 to 2022. NSIS included azathioprine, cyclosporine, cyclophosphamide, methotrexate, mitoxantrone, and mycophenolate mofetil. Annualized relapse rate (ARR), proportion relapse free, time to first relapse (TTFR), 6-month confirmed disability progression (CDP) and improvement (CDI), and DMF discontinuation were assessed prior to switching, and during DMF treatment.
Results: Of 127 patients that switched from NSIS to DMF (Table 1), ARR (95% CI) was 0.17 (0.10, 0.27) during last 12 months on NSIS and 0.12 (0.07,0.19) on DMF; proportion relapse-free was 89% (48/54) and 100% (26/26) at 12 and 24 months of DMF, respectively. DMF discontinuation rate was 18.66/100 person-years (12.49, 26.79) (Table 2); TTFR (95% CI) was 9.01/100 person-years (4.92, 15.11; see Figure); 6-months CDP was 2.57/100 person-years (0.70,6.59); and 6-months CDI was 5.27/100 person-years (1.71, 12.31).

Table 1: Patient characteristics at time of switch from NSIS to DMF

Characteristics at time of switch to DMF	Category	n=127
Age (years), mean (SD)		41.2 (10.0)
Sex, n (%)	Female	106 (83.5)
	Male	21 (16.5)
Disease duration (years), mean (SD)		12.8 (7.8)
Baseline EDSS, median (IQR)		1.5 (1, 2.5)
Country, n (%)	Iran	77 (60.6)
	Turkey	17 (13.4)
	Italy	16 (2.4)
	Czechia	6 (4.7)
	Spain	3 (2.4)
	Lebanon	3 (2.4)
	Australia	2 (1.6)
	Canada	2 (1.6)
	Belgium	1 (0.8)
Duration of pre-switch IS (years)	Mean (SD)	3.9 (3.7)
	Median (IQR)	2.6 (0.9, 6.2)
Treatment gap between NSIS and DMF (months)	Mean (SD)	27.5 (43.0)
	Median (IQR)	6.5 (0.0, 39.1)

EDSS, expanded disability severity score

Table 1: Patient characteristics at time of switch from NSIS to DMF

Table 2: Outcomes in patients who switched from NSIS to DMF

OUTCOME	
ARR (95% CI)	
On DMF	0.12 (0.07, 0.19)
Last 12 months on NSIS	0.17 (0.10, 0.27)
Proportion relapse free, % (n)	
1 year on DMF	88.9% (48/54)
2 years on DMF	100.0% (26/26)
3 years on DMF	100% (15/15)
TTFR[1], (95% CI)	9.01 (4.92, 15.11)
6-month CDP[1], (95% CI)	2.57 (0.70, 6.59)
6-month CDI[1], (95% CI)	5.27 (1.71, 12.31)
DMF discontinuation[1], (95% CI)	18.66 (12.49, 26.79)

[1]Rate per 100 person-years
ARR, annualized relapse rate; CDI, confirmed disability improvement; CDP, confirmed disability progression; DMF, dimethyl fumarate; NSIS, non-specific immunosuppressants;

Table 2: Outcomes in patients who switched from NSIS to DMF

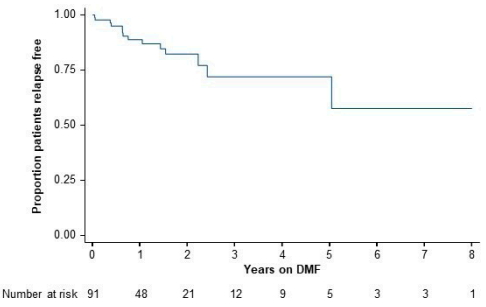

Figure. Kaplan-Meier Curve for Time-to-First-Relapse

Conclusion: These data represent the first analysis of efficacy on DMF after switching from NSIS, and suggest good treatment response to DMF after switching from immunosuppressant medication, although our dataset size is relatively small.

Disclosure: Supported by Biogen.

EPO-160

Safety and Efficacy of Diroximel Fumarate in Older Patients with Multiple Sclerosis from the Phase 3 EVOLVE-MS-1 Study

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Background and aims: Oral diroximel fumarate (DRF) has similar efficacy/safety to dimethyl fumarate in relapsing-remitting multiple sclerosis (RRMS), but improved GI tolerability. Safety/efficacy of DRF was assessed in patients with RRMS aged >=55 years from EVOLVE-MS-1.

Methods: EVOLVE-MS-1 (NCT02634307) was a phase 3, open-label, 96-week study of DRF in adults with RRMS. Safety/efficacy outcomes were compared in older (aged >=55 years) vs younger patients (aged <55 years).

Results: Of 1057 patients, 158 (14.9%) were classified as older (mean [SD], 58.8 [2.9] years) and 899 (85.1%) as younger (mean [SD], 39.6 [9.0] years) (Table 1). Adverse events (AEs) occurred in 139 (88.0%) older and 799 (88.9%) younger patients. AEs led to discontinuation in 16 (10.1%) of older and 69 (7.7%) of younger patients (Table 2), including lymphopenia, GI disorders, MS relapse, and lymphocyte count decrease. Annualized relapse rate reduction from 12 months prior to study to Week 96 of DRF treatment was 89.3% (95% CI: 81.7-93.7) in older and 80.4% (76.9-83.4) in younger patients. Proportions with no evidence of disease activity (NEDA-3), estimated from Kaplan-Meier, were 65.8% (older) and 36.9% (younger). At Week 96, mean (SD) EDSS score change from baseline was 0.09 (0.82; older) and 0.03 (0.66; younger); mean (SD) number of Gd+ lesions decreased 0.1 (0.78; older) and 0.8 (4.05; younger).

Characteristic	< 55 years n=899	≥55 years n=158
Mean (SD) Age	39.6 (9.0)	58.8 (2.9)
Female, n (%)	648 (72.1)	114 (72.2)
Region, n (%)		
Non-US	531 (59.1)	73 (46.2)
US	368 (40.9)	85 (53.8)
BMI (kg/m^2), mean (SD)	26.6 (6.3)	27.1 (4.8)
No. of Gd+ lesions, mean (SD)	1.3 (3.8)	0.2 (1.0)
T2 lesion volume (cc), mean (SD)	12.9 (14.1)	16.5 (14.9)
EDSS score, mean (SD)	2.57 (1.4)	3.39 (1.5)
No. of relapses in previous year, mean (SD)	0.7 (0.8)	0.6 (0.7)
No. of prior DMTs, mean (SD)	1.2 (1.2)	1.5 (1.2)
Time since MS diagnosis (yr), mean (SD)	6.8 (6.6)	12.2 (9.6)

BMI, body mass index; DMT, disease-modifying therapy; EDSS, expanded disability status score; GD, gadolinium endhancing; MS, multiple sclerosis; SD, standard deviation

Table 1. Patient characteristics at enrollment

Classification	< 55 years n=899, n (%)	≥55 years[2] n=158, n (%)
Any TEAE	69 (7.7)	16 (10.1)
Investigations	14 (1.6)	4 (2.5)
Lymphocyte count decreased	6 (0.7)	1 (0.6)
Glomerular filtration rate decreased	0 (0.0)	2 (1.3)
Blood pressure abnormal	0 (0.0)	1 (0.6)
Blood/lymphatic system disorders	10 (1.1)	5 (3.2)
Lymphopenia	9 (1.0)	5 (3.2)
Nervous system disorders	14 (1.6)	1 (0.6)
Multiple sclerosis relapse	11 (1.2)	0 (0.0)
Hemiparesis	0 (0.0)	1 (0.6)
Gastrointestinal disorders	5 (0.6)	2 (1.3)
Anal incontinence	0 (0.0)	1 (0.6)
Irritable bowel syndrome	0 (0.0)	1 (0.6)
Skin and subcutaneous tissue disorders	4 (0.4)	1 (0.6)
Pruritis generalized	0 (0.0)	1 (0.6)
Vascular disorders	5 (0.6)	0 (0.0)
Flushing	5 (0.6)	0 (0.0)
Cardiac disorders	2 (0.2)	1 (0.6)
Hypertensive heart disease	0 (0.0)	1 (0.6)
General disorders and administration site conditions	1 (0.1)	1 (0.6)
Fatigue	0 (0.0)	1 (0.6)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	1 (0.6)
Dyspnoea	0 (0.0)	1 (0.6)

TEAE, treatment-emergent adverse events
[1]Included TEAEs leading to discontinuation in >= 0.5% patients
[2]No infections or neoplasms were found in patients >= 55 years old

Table 2. Summary of adverse events leading to discontinuation

Conclusion: After 96 weeks of DRF treatment, overall benefit/risk ratio was similar in older and younger patients. At baseline, older patients had fewer Gd+ lesions than younger patients and higher EDSS scores. More older patients achieved NEDA-3 versus younger patients.
Disclosure: Supported by Biogen.

EPO-161

Google Maps Timeline: an open-access digital tool to evaluate gait impairment in people with multiple sclerosis

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Background and aims: Gait impairment is common in multiple sclerosis (MS), but difficult to evaluate in clinical practice. We have used Google Maps Timeline (GMT) data to provide direct measurements of the overall walking abilities in MS and validated towards conventional clinical measures.
Methods: This is a proof-of-concept observational study. We collected Expanded Disability Status Scale (EDSS), Time-25 Foot Walking Test (T25FWT), Multiple Sclerosis Walking Scale (MSWS), Fatigue Severity Scale (FSS), European Quality of Life questionnaire (EuroQoL). We used open-access GMT to record the total number of days with walking activity, walking distance, walking time, and walking speed. Each GMT variable was included in a different stepwise linear regression model to select best clinical correlates.
Results: We included 9 pwMS (age 43.1±6.6 years; females 55.6%; disease duration 12.7±3.1 years). Percent of days with recorded walking was associated with lower FSS (Coeff=-1.14; 95%CI=-1.95, -0.33; p=0.01), and higher MSWS (Coeff=0.73; 95%CI=0.01, 1.46; p=0.04). Average daily walking distance was associated with shorter T25FWT (Coeff=-150.58; 95%CI=-278.00, -23.15; p=0.02), lower EDSS (Coeff=-171.91; 95%CI=-296.65, -47.18; p=0.01), and higher EuroQoL (Coeff=10.20; 95%CI=0.40, 20.00; p=0.04). Average daily walking time was associated with shorter T25FWT (Coeff=-0.06; 95%CI=-0.11, -0.01; p=0.03). Higher walking speed was associated with lower FSS (Coeff=-0.02; 95%CI=-0.04, -0.01; p=0.04).
Conclusion: GMT parameters were associated with conventional clinical measures, providing actual estimates of daily walking activities in MS. Extension to a larger sample, validation towards other clinical/MRI measures, and longitudinal evaluation are warranted.
Disclosure: The authors declare no competing interests.

EPO-162

Multiple Sclerosis and SARS-CoV2 pandemic: a population based study.

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Background and aims: Environmental factors, in particular infections, are risk factors for Multiple Sclerosis disease activity. Aim of the study was to evaluate the impact of the SARS-COV2 pandemic on disease activity in the MS population from the Italian MS Registry (RISM).
Methods: We compare the incidence of clinical/radiological disease activity occurring during the pandemic phase (Jan 2020-Jul 2021) and the pre-pandemic period (Jan 2018-Jul 2019) in the MS population followed during boths periods, according to different regions of residence. We investigated potential differences in the neurological functional system affected.
Results: 18669 out of 72959 patients had visits registered in the pre-pandemic and pandemic periods and were analysed. 4312 relapses were registered in 3306 patients (17.7%, relapse rate (RR)=0.23) in the pre-pandemic period, while 1206 relapses were reported for 1054 patients (5.6%, RR=0.06) in the pandemic period (chi-square test, p<0.0001). The exploration of potential differences in functional system involved was limited by the different number of missing data between the two preiods. A total of 38182 MR data were reported for 14382 patients in the pre-pandemic period while 20329 MR data were reported for 9849 patients in the pandemic: 2194 (5.7%) and 912 (4.5%) gadolinium-positive scans were respectively recorded in the 2 period (chi-square, p<0.0001).

Conclusion: A reduced disease activity was observed during the pandemic period compared to the pre-pandemic: this may be ascribed to an overall decrease in the risk of infections as results of lockdown, social distancing, isolation strategies and hygiene measures, supporting the role of viral infections as triggers of inflammation in MS.
Disclosure: Nothing to disclose.

EPO-163

Testing the Padova Emotional Dataset of Facial Expressions in Multiple Sclerosis: a neuropsychological-MRI study

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Background and aims: Social cognition can be altered in multiple sclerosis-patients (MS), even from the early stages of the disease[1]. We aimed to study in a group of recently-diagnosed relapsing-MS and controls the Padova Emotional Dataset of Facial Expressions (PEDFE), a new facial emotion recognition (FER) test in which patients are asked to recognize the type and genuineness of different genuine or posed emotions[2].
Methods: PEDFE was acquired in 32 relapsing-MS (<2 years from diagnosis) and 32 controls, by calculating the emotion-type (ET) and emotion-genuineness (EG) scores. Patients also underwent clinical, neuropsychological evaluation and MRI. Brain segmentation of regional grey matter (GM) atrophy and white matter (WM) lesion probability map were obtained and Spearman correlations with FER scores were evaluated, setting $p<0.05$.
Results: Recently-diagnosed MS and controls did not show significant differences at PEDFE scores, but ET and EG scoring displayed different patterns in MS. ET correlated with executive performances at PASAT-3/PASAT-2 ($p=0.01$) and SRT ($p=0.01$) and with GM thickness in many cortical frontal, parietal and temporal regions (Fig.1). Conversely, EG correlated with WLG ($p=0.01$) and with GM thickness in cingulum isthmus and different subcortical areas (Fig.2). Macroscopic WM-lesion load did not affect our results (Fig.3).

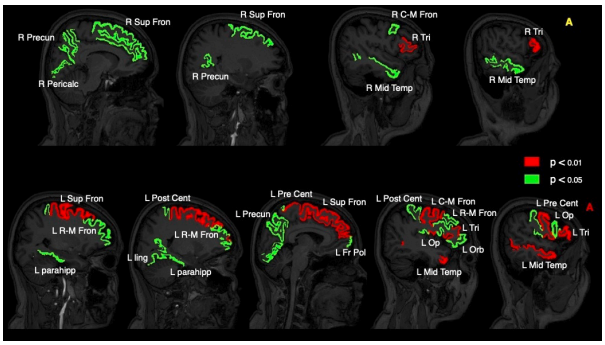

Fig.1: Spearman correlations between ET scores and cortical GM thicknesses [A: anterior]

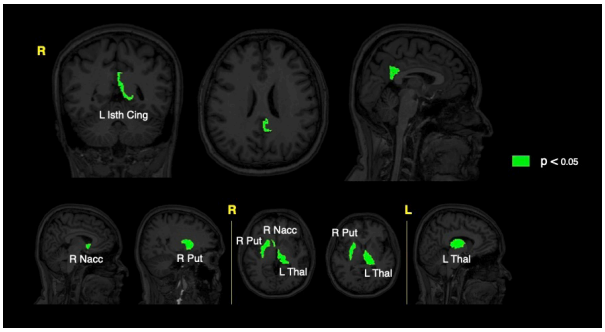

Fig.2: Spearman correlations between EG scores and cortical GM thicknesses and subcortical volumes [R: right; L: left]

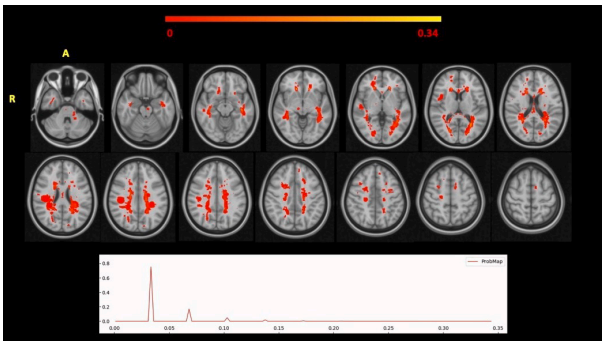

Fig.3: WM macroscopic lesions probability map; data are expressed as percentages from 0 up to 34% [A: anterior; R: right]

Conclusion: PEDFE may represent a valid tool to assess FER in MS and to detect early alterations in social cognition. As an adding value, the PEDFE possibly distinguishes different anatomical structures involved in FER, with ET scores that are mostly linked to executive and memory functions, while EG scores that are more related to the limbic system functioning.
Disclosure: All authors declare no disclosures.

EPO-164

Validation of the RoAD score in an Italian cohort of people with Relapsing Multiple Sclerosis

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Background and aims: Scoring the risk of future disability in Multiple Sclerosis(MS) is a big challenge of today's clinical practice. Recently, the Risk of Ambulatory Disability(RoAD) Score was proposed as an useful tool to predict individual prognosis and optimize treatment strategy for MS patients. The score includes both baseline factors and one-year outcomes on platform treatment with a score of ≥4 as the best cut-off score for the risk of reaching EDSS score≥6. In this study, we evaluated the performance of RoAD score in our cohort of long-term RMS patients.
Methods: We analysed a dataset of RMS patient from our MS centre who started platform injectable disease modifying therapies (DMTs) with at least 10 years of follow-up.
Results: 255 patients met all inclusion criteria and were included in the analysis. Median RoAD score was 2 with 61(24%) patients having a RoAD score≥4. At 10-year follow-up, 42(16.5%) patients reached a confirmed EDSS score≥6. The best RoAD score cut-off for estimating the risk of EDSS score≥6 was 4 with an AUC of 0.77 (IC 0.70-0.85, p<0.01).
Conclusion: In our study we confirmed a RoAD score≥4 as the best cut-off score for discriminating patients at higher risk of reaching the disability milestone of EDSS score≥6. This study confirmed that RoAD score could represent a valuable tool to help the clinician in the assessment of long-term prognosis in patients treated with platform injectable DMTs as first-line treatment.
Disclosure: Nothing to disclose.

EPO-165

MSCopilot® Real Life Data Show Influence of Multiple Sclerosis Phenotypes and Disability Levels on Functional Parameters

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Background and aims: We describe the evolution and potential influences of phenotypes (relapsing-remitting or progressive) and the Expanded Disability System Status Scale (EDSS) score on four main functional parameters, walking, dexterity, cognition and low-contrast visual acuity, in patients with multiple sclerosis (PwMS), assessed in real life using MSCopilot®, a clinically validated software medical device.
Methods: MSCopilot® database was analysed from 2017-Oct to 2022-Apr and 1047 females/473 males (mean age 41.3±12), having consented, were included. Patients were split by phenotypes and EDSS levels (<3.5 or ≥3.5). PwMS performed the four unsupervised digital assessments following embedded tutorials.
Results: A significant group effect was found in MS phenotypes resulting in a decreased performance in walking, dexterity and cognition (p<0.05). These parameters were also significantly impaired in PwMS with an EDSS≥3.5 (p<0.05). No specific interaction was found between low-contrast visual acuity and phenotypes or EDSS. Compared to baseline and over three time points, 26.4% and 23.1% of patients had a sustained worsening (<10%) of their dexterity and walking capacity respectively.
Conclusion: In PwMS, impairment of three functional parameters, measured in real-life via MSCopilot®, relate to a more severe course and degree of disability. Visual acuity was not influential, which could be explained by an optic neuritis history or a lesser influence over the EDSS. This novel insight opens new avenues for phenotype discrimination and disability progression prediction, two unmet needs in the PwMS care pathway.
Disclosure: L. Carment, L. Diouf, L. Ahamada, A. Plaud, L. Klaeyle, S. Zinai, S. Bieuvelet are employees of Ad Scientiam, A. Tourbah is a member of its scientific committee and received honoraria for lectures, travel grants and research support from Biocara, Hikma, Novartis, Roche.

EPO-166

Plasma exchanges in acute relapses of inflammatory demyelinating diseases: a multicenter study

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Background and aims: Plasma exchange (PE) can improve recovery of patients with severe relapses of CNS demyelinating diseases (CNS-DD). We aimed to 1)assess the effectiveness and 2)identify predictors of improvement to PE.

Methods: Retrospective, non-interventional study, including patients receiving PE at 3 Spanish hospitals between 2012-2021 who met: 1)severe relapse of CNS-DD unresponsive to methylprednisolone; 2)≤3 months until PE administration; 3)5-10 exchanges administered. Improvement at 6 months after PE was defined as: return to pre-relapse Expanded Disability Status Scale (EDSS) score; or decrease ≥1 or 1.5 points for patients with EDSS nadir ≤7.5 or ≥8, respectively; or improvement in ≥2 lines on the visual acuity chart for patients with optic neuritis (ON). Uni and multivariate logistic regression models were used to determine factors associated with improvement.
Results: Ninety patients were included (66% female, median (IQR) age: 42(32-51.8) years, EDSS 5.0(4.0-7.0) at PE initiation). Most frequent diagnosis were multiple sclerosis (49%), idiopathic CNS-DD (28%) and AQ4-positive NMOSD (16%). Relapses phenotype were myelitis (36%), ON (23%), multifocal/disseminated forms (22%), brainstem/cerebellum (10%) and pseudotumoral (8.9%). In one center, 32 patients received 200 mg of rituximab pre- and post-PE. Median time between MTP-PE was 18(7-34) days. A median of 7(6-7) exchanges were administered. Improvement was achieved by 77% of patients. Younger age (p=0.04) and lower pre-relapse EDSS (p=0.01) were independently associated with improvement, while etiology, relapse phenotype, number of exchanges or rituximab were not.
Conclusion: PE produced a marked improvement in a large proportion of patients with severe CNS-DD relapses, particularly younger patients, and those with lower baseline disability.
Disclosure: The authors report compensation for consulting services and speaker honoraria: JLCG from Bayer, Sanofi, Biogen and Bial. JM from Sanofi. FRJ from Sanofi and Bial. SSM from Biogen, Bristol Myers Squibb, Merck, Novartis, Roche, Sanofi, and Teva. EM from Biogen, Merck,Novartis, Roche, Almirall, and Sanofi-Genzyme. MS from Roche and Biogen. EMH from Biogen-Idec. LCF rBiogen, Bristol Myers Squibb, Janssen, Merck-Serono, Novartis, Sanofi, Roche and Teva. JEML from Biogen, Bristol-Myers-Squibb, Merck, Novartis, Roche and Sanofi. YB from Merck-Serono, Biogen-Idec, Sanofi, Brystol-Myers and Roche. AS from Merck-Serono, Biogen-Idec, Sanofi, Novartis, Roche, Janssen, and Alexion. SL from Biogen Idec, Novartis, TEVA, Genzyme, Sanofi and Merck. ES received travel reimbursement from Sanofi. ELS received travel reimbursement from Sanofi and ECTRIMS. EF received funding for an ECTRIMS Clinical Training Fellowship Programme. The remaining authors have no conflict of interest to declare.

EPO-167

Relationship of disease severity and the diffusion along the perivascular space in multiple sclerosis

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Background and aims: The glymphatic system in multiple sclerosis has not been thoroughly explored yet. Recently it was suggested that this 'waste clearance' system can be examined by measuring the diffusion along the perivascular space index.
Methods: DTI parameters of 107 MS patients were calculated with FSL's DTIFIT, followed by registration to the common space without creating the skeleton. ALPS index was calculated using two ROIs along the periventricular white matter (Taoka et al. 2017). Using linear regression model the EDSS score was correlated with the ALPS index with different nuisance regressors and tested on a test and training set. Based on EDSS (>=1.5 and <1.5) two groups were created to compare the ALPS indices.
Results: EDSS and DTI-ALPS showed weak correlation (rho=-0.19, $p<0.0478$). The linear regression model revealed that DTI-ALPS index did not contribute significantly to the patients' EDSS (beta: -0.33, p=0.73), however, disease duration was the only significant contributor to EDSS (beta: 0.083, $p<0.001$). Testing the model on the unseen dataset it achieved an R2=0.239. The DTI-ALPS index of the patients with higher EDSS was significantly lower ($p=0.011$, $\alpha=0.05$).
Conclusion: According to our results there is only a weak relationship between the DTI-ALPS index and the clinical disability due (i) scanner reference-based diffusion directions should probably be replaced by fibre-based reference frame; (ii) registration issues should be resolved by TBSS approach, using the voxels only in a skeleton; (iii), thus the connection between the DTI-ALPS index and the glymphatic system should be further investigated.
Disclosure: Image processing, statistical analysis.

EPO-168

The analysis of miRNAs in CSF identifies upregulation of miR-146a in patients with early diagnosed multiple sclerosis

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Background and aims: Recently microRNAs (miRs) have been proposed as possible disease biomarkers in Multiple Sclerosis (MS) field. Few studies have focused on cerebrospinal fluid (CSF) miRs, although these might be more relevant to understanding disease regulation.
Methods: This is a case-control study performed at the Department of Medical and Surgical Sciences, University of Foggia, Italy. Patients have not been yet exposed to disease modifying therapies (DMTs) and had received a confirmed diagnosis of relapsing remitting MS (RRMS). We analyzed the CSF expression of 6 miRs by using Quantitative Real-Time PCR, comparing RRMS to HCs, with a 2:1 ratio. Subsequently, the differentially expressed miRNAs, were further tested with receiving operator curves (ROC). We aimed to explore possible role of CSF miRs as disease biomarker at the time of diagnosis.
Results: A total of 32 patients were enroled, 67.7% female, mean age 32±12.5. MiR-146a had higher levels in RRMS patients when compared to HCs ($p<.01$). The ROC curve indicated that both miR-146a could be considered as biomarkers with an area under the curve of 0.772 ($p=.003$; 95% CI: 0.610–0.935).
Conclusion: Our study suggested CSF miR-146a as possible disease biomarkers in early diagnosed RRMS patients, not yet exposed to DMTs.
Disclosure: The authors have nothing to disclose related to this poster.

EPO-169

A registry study of highly active disease modifying therapies in relapsing remitting MS motor and psychiatric outcomes

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Background and aims: The United Kingdom MS Register (UKMSR) is an online registry recording patient-reported outcomes (PROs) from >15,000 people with MS (pwMS) and clinical data from 46 NHS centers nationwide with 12 years of follow-up. This study examined the real-world efficacy of highly and normally active DMTs versus no treatment.
Methods: Psychiatric and motor symptoms were assessed using MSIS-29 questionnaires, answered <6 months after the previous and >2 weeks from the last questionnaire. Patients were separated into a highly active (HA), normally active (NA) and no treatment (NT). Patients were propensity matched on a 1 to 1 ratio for age, gender, time since disease diagnosis and treatment length. Kaplan Meier cumulative time to event analysis was performed on the time to a clinically significant event defined as a 6-point change in MSIS-29 score
Results: In total, 800 patients with Relapse Remitting MS (RRMS) met the inclusion criteria. Over four-years of follow up from baseline patients on HA-DMTs showed a statistically significant improvement in motor ($p < 0.0008$) and psychiatric symptoms ($p = 0.047$). There was no difference found in worsening of motor ($p = 0.27$) or psychiatric symptoms ($p = 0.96$). There was no significant difference in worsening or improvement when NA-DMTs were compared to NT.
Conclusion: These investigations demonstrated that RRMS patients on HA-DMTs had a statistically significant improvement in psychiatric and motor symptoms compared to NT. These results suggest that HA-DMTs have beneficial effects in improving psychiatric symptoms beyond their established efficacy in improving motor symptoms.
Disclosure: This project was supported by the United Kingdom MS Register, Imperial College London and The University of Swansea.

EPO-170

Journey of MS Patients in Turkey; a questionnaire based survey

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Background and aims: MS is a chronic neurodegenerative disease that is one of the most important causes of disability in young adults. In this study, it is aimed to highlight all the obstacles in the MS journey of the patients and to collect information for solution suggestions.
Methods: The online survey, in which a total of 2176 MS patients participated between November 11, 2022 and December 16, 2022, was evaluated by making analysis and statistics according to the questions.
Results: 57% patients have numbness and/or weakness in an arm or leg before being diagnosed. Physicians perform additional examinations and tests for 71% of patients

receiving MS treatment, and It takes an average of 6.4 weeks. 29% of the patients who received MS treatment did not have an attack requiring cortisone, but of the remaining 71%, 18% had a single attack requiring cortisone and 17% had more than 4 attacks requiring cortisone. 53% patients were hospitalized during the attack and they stated that they stayed in the hospital for an average of 9 days. Since 57% (n=2097) of the patients who continued the treatment showed high disease activity, their treatment was changed with the decision of the physician. In 72% of them, it was stated that the reason was ineffectiveness against the treatment they used, while the problems of compliance with the treatment they used in 23%.

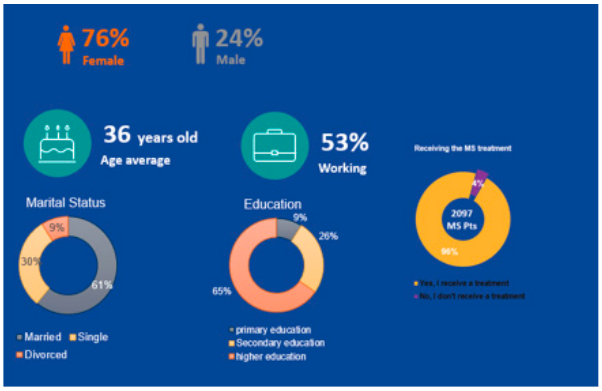
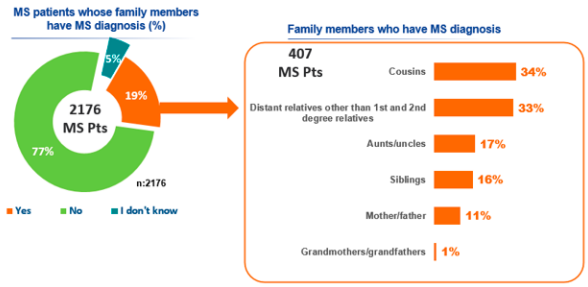
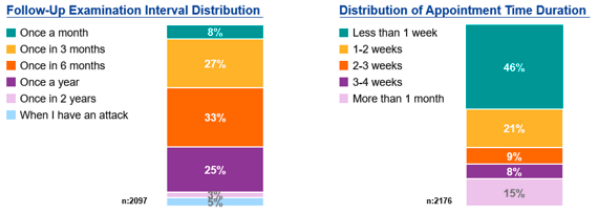


Figure 1: A total of 2176 patients participated in our study. The female-male ratio in the patients participating in the study was 76% and 24%, respectively. and the average age is 36 years. 65% of the patients who participated in the survey are graduates



Patients have MS diagnosis for averagely 8 years. (between 1984 and 2022). 1 of 5 MS patients' family members have MS diagnosis.1/3 of them are cousins and 1/3 of them are distant relatives who are other than 1st and 2nd degree relatives.



While ¼ of the MS patients receiving treatment went to the follow-up examination every 6 months, 27% of them stated that they went to the follow-up examination every 2 years. 85% of patients can make an appointment with their neurologist within 1 month.

Conclusion: Discussion: This Questionnaire gave an idea about how physicians can support MS patients living in Turkey with their problems detected during their journey.
Disclo.ure: This study was funded by Novartis Pharma Turkey

EPO-171

Journey of MS Patients in Turkey; a questionnaire based survey- Nurse Support Evaluation

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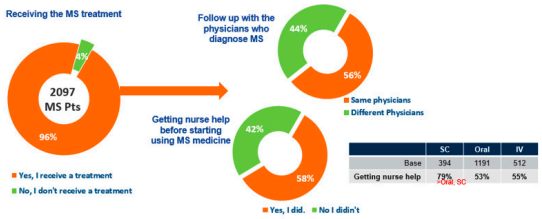
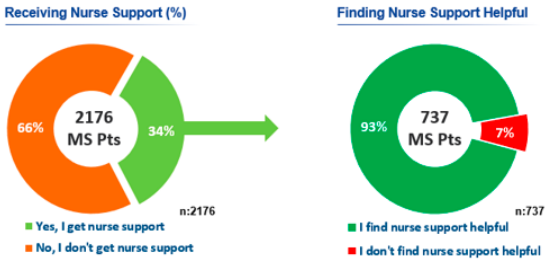
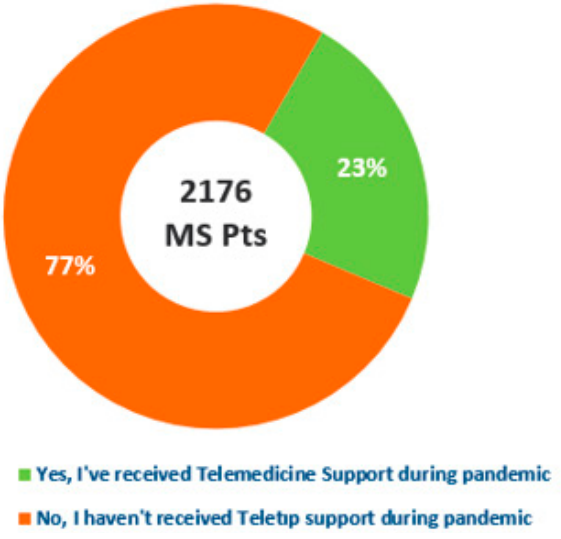
Background and aims: In this study, it was aimed to evaluate the frequency and satisfaction of the nurse support that MS patients received during their MS treatment and the telemedicine support they received during the pandemic period, according to the treatment groups.
Methods: It is an online survey study conducted by the MS Association of Turkish in which a total of 2176 MS patients participated between 11 November 2022 and 16 December 2022
Results: Almost ¼ of MS patients have received telemedicine service during Covid19 pandemic.Ratio of MS patients received Telemedicine Support during Covid19 pandemic is higher among IV and oral patients compared to SC patients. Female-male ratio was similar in patients receiving telemedicine service (22%, 23% retrospectevely) it was found to be unrelated to the educational status of the patients.



A total of 2176 patients participated in our study. 96% of MS patients receive MS treatment. 56% of patients who receive MS treatment continue follow up with the physicians who diagnose 58% of patients got nurse support before starting using MS



34% of all patients receive clinical nurse support (IV patients receive nurse support more than SC patients.) and 93% of these patients find this support helpful. This result did not differ between sc, oral, iv treatments (90%, 92%, 95%, retrosp



Those who have received telemedicine Suport during Pandemic

Conclusion: Studies have shown that telemedicine offers a supportive alternative to face-to-face visits. here has been a huge increase in the use of telemedicine during the COVID-19 pandemic . Nurses play an important role in coordinating the care of patients with multiple sclerosis (MS) throughout their disease course in a complex treatment setting. This information may support the role of nurses in the multidisciplinary management of MS, facilitating shared decision making.

Disclosure: This study was sponsored by Novartis Pharma Turkey

EPO-172

Effect of disease-modifying treatment on coronavirus disease 2019 vaccination in patients with multiple sclerosis

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Background and aims: Coronavirus disease 2019 (COVID-19) vaccination while receiving disease-modifying-treatment (DMT) with B-cell depleting agents or sphingosine-1-phosphate receptor modulators (S1PRMs) has repeatedly been associated with a dampended humoral and/or cellular immune response in patients with multiple sclerosis (MS),[1] but it remains unknown whether this translates into a decreased clinical protection against severe forms of the infection.

Methods: Since March 2020, demographics and infectious outcome of patients with MS who developed COVID-19 have been collected at the Belgian National MS Center in Melsbroek. Patients were considered to be 'protected by vaccination' if they were (a) fully vaccinated and (b) tested positive for COVID-19 in the period ranging from 14 days to 6 months after the last administered vaccine dose.[2]

Results: On December 19, 2022, we have identified 450 cases of COVID-19 in 436 individual patients (Table 1). Hospitalisation and mortality rates resulting from the infection were 10.0% and 2.2%, respectively. Being 'unprotected by vaccination' was associated with a worse COVID-19 outcome (i.e., hospitalisation and/or death) in the total cohort (OR 3.93, 95% CI 2.03-7.97, $P < 0.001$) and after exclusion of patients on B-cell depleting agents or S1PRMs (324 infections, OR 7.74, 95% CI 3.37-19.86, $P < 0.001$) but not in those on B-cell depleting agents (Table 2). The S1PRMs subgroup was considered too small (23 infections) for a meaningful analysis.

Table 1: Characteristics of the total cohort of COVID-19 infections

Infections, *N* (individual patients)	**450 (436)**
Mean age, years (SD)	54 (13)
Sex, *N* females (%)	304 (67.6)
Mean MS disease duration, years (SD)	23 (12)
Clinical MS subtype, *N* with progressive disease (%)	239 (53.1)
DMT, *N* (%)	264 (58.7)
Fully vaccinated, N (%)	345 (76.7)
Protected by vaccination at time of COVID-19, *N* (%)	271 (60.2)

Table 2: Variables used in the multivariate logistic regression models

Dependent variable (outcome)
- COVID-19 outcome (hospitalisation and/or death versus ambulatory care)
Independent variables (predictors)
- Age (years)
- Sex (male versus female)
- Clinical MS subtype (progressive versus relapsing)
- Disability (Expanded Disability Status Scale scores)

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2. Fiolet T, Kherabi Y, MacDonald CJ, Ghosn J, Peiffer-Smadja N. Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review. Clin Microbiol Infect. 2022;28(2):202-221; doi: 10.1016/j.cmi.2021.10.005.

Conclusion: Overall, COVID-19 vaccination protects against a worse infectious outcome in patients with MS but we were not able to confirm this effect in those on DMT with B-cell depleting agents.

Disclosure: The authors have no conflicts of interest relevant to this study.

ePosters

Sunday, July 02 2023
Ageing and dementia 2

EPO-173

Identification of pre-frailty in the elderly through serum metabolomics and its impact on Parkinson's disease phenotype

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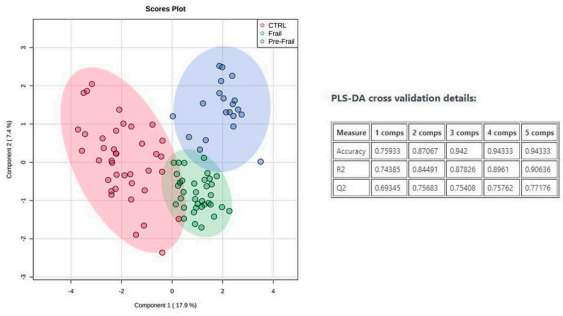
Background and aims: Pre-frailty is a potentially reversible condition increasingly common with aging. However, whether it represents a continuum between healthy and frail status or a well-defined clinical entity is still unclear. Here, we attempted to better characterize pre-frailty using serum metabolomics in a large cohort of elderly subjects without neurodegenerative diseases. Next, we sought to investigate the impact of concurrent pre-frailty on elderly subjects with Parkinson's disease (PD).
Methods: We recruited 96 elderly non-PD subjects and classified them as non-frail, pre-frail, and frail based on Fried criteria. Untargeted metabolomics was carried out using Nuclear Magnetic Resonance (1H-NMR) on serum samples. Partial least-squares discriminant analysis and Pathway enrichment analysis were used to identify metabolites and biochemical pathways discriminating the three groups. Next, 83 mild-stage PD patients underwent Fried classification and assessment of motor and non-motor domains, ADL and QoL.
Results: Serum metabolomics identified three distinct clusters for non-frail (n=39), pre-frail (n=20), and frail (n=37) non-PD, with pre-frails showing the most evident separation from other groups. Multivariate analyses revealed L-Serine, Betaine, and Histidine as the most discriminating molecules. Pathway analysis pointed to dysregulation of amino acid metabolism, first of all, Serine-Glycine ($p<0.001$). In PD, pre-frail (n=25) patients showed intermediate levels of motor, ADL, QoL, and psychiatric impairment compared to both non-frail (n=45) and frail (n=13) subgroups (all FWER-adjusted $p<0.05$).



Measure	1 comps	2 comps	3 comps	4 comps	5 comps
Accuracy	0.75933	0.87067	0.942	0.94333	0.94333
R2	0.74385	0.84491	0.87826	0.8961	0.90636
Q2	0.69345	0.75683	0.75408	0.75762	0.77176

Fig. 1. Partial least squares-discriminant analysis (PLS-DA) score plot and cross validation results showing a clear clusterization of pre-frail serum metabolomics profile compared to non-frail and frail subgroups. CTRL = non-frail controls.

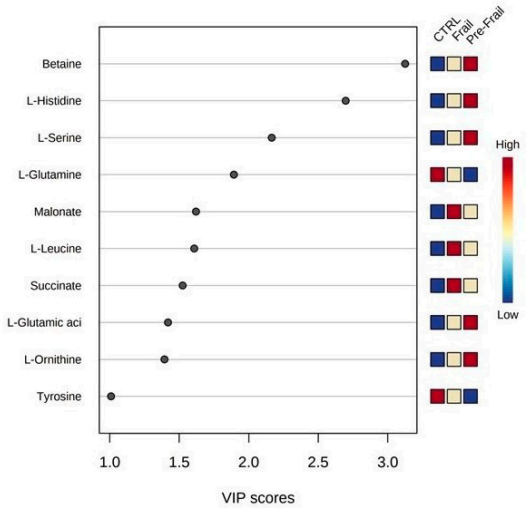


Fig. 2. Variable Importance in the Projection (VIP) score generated from PLS-DA showing Betaine, L-Histidine and L-Serine as the best discriminating molecules (VIP score > 2) between pre-frail, frail and non-frail subjects.

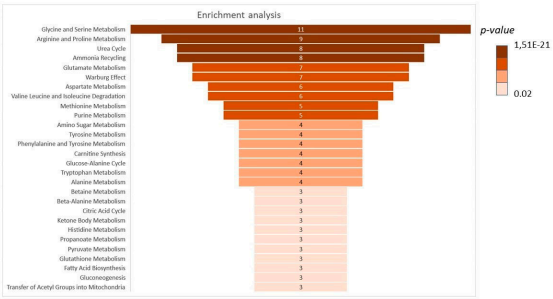


Fig. 3. Pathway enrichment analysis showing dysregulation of several amino acid pathways in frail and pre-frail subgroups, firstly Serine-Glycine metabolism. Further dysmetabolism is related to energy and reactive oxygen species pathways.

Conclusion: We identify L-Serine pathway dysregulation as a distinctive signature of pre-frailty in the elderly. In PD, pre-frailty status significantly affects both clinical phenotype and QoL, representing a potentially modifiable factor to be targeted with specific interventions.

Disclosure: This study was financially supported by Fondazione Cariplo (Call 2017 – Scientific Research "Biomedical research on aging-related diseases", grant no. 2017-0575).

EPO-174

Abstract withdrawn

EPO-175

The role of sleep structure analysis in the recognition of cognitive decline

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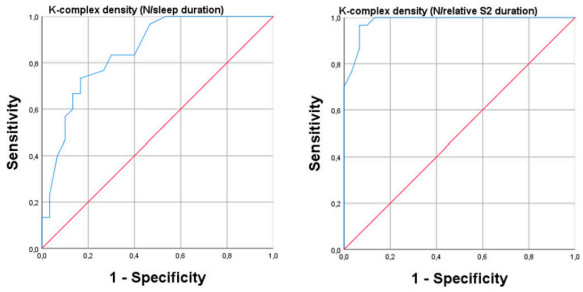
Background and aims: Alzheimer's disease (AD) effective treatment is absent due to difficulties in early differential diagnosis. Sleep-wake disturbances are common in AD, even at early stages. Our aim is to study the potential role of micro- and macrostructural sleep changes as early differencial diagnostic tools.

Methods: We involved 30 individuals with AD, and 30 controls. Sleep structure was examined with 24-hour Holter electroencephalograph (EEG), followed by visual evaluation. For microstructural analysis K-complex detection was used. Brain magnetic resonance imaging (MRI) and neuropsychological tests were also performed. 32 patients with mild cognitive impairment (MCI) and 46 healthy controls were also involved. Spearmann correlation and ANCOVA analyses were used for statistical evaluation.

Results: A rearrangement of sleep stages was observed in AD. Significant decrease was found both in K-complex densities avaraged for total sleep (F: 0.216; $p<0.001$) and for S2 sleep (F: 0.386; $p<0.001$). Based on the MRI examination, significant positive correlation was found between right caudal anterior gyrus cingulate thickness and both type of K-complex densities (total sleep: $r=0.458$; $p=0.042$; S2 sleep: $r=0.472$; $p=0.036$). In the MCI patient group, there was a significant reduction in right caudal anterior gyrus cingulate thickness (2.53±0.2 mm vs. 2.42±0.3 mm; $p=0.004$; Cohen's d: 0.353), showing the potential of K-complex analysis in early recognition.



ROC curve was used for testing the diagnostic abilities of K-complex densities. AUC=0.85 for K-complex density averaged for whole sleep duration and AUC=0.98 for K-complex density averaged for S2 sleep duration. AUC: area under the curve

Conclusion: Macro- and microstructural sleep changes were

significantly observed in AD which may be good markers of neurocognitive status. K-complex density is significantly decreased in AD, which raises the possibility that it may have a great impact in the preclinical detection of AD.
Disclosure: Nothing to disclose.

EPO-176

Genetic association between ADAM17 gene polymorphisms and risk of Alzheimer's disease: a case-control association study

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Background and aims: ADAM17 (a disintegrin and metalloproteinase 17) is a sheddase that participates in the proteolysis of several substrates playing a key role in Alzheimer's disease (AD), like amyloid precursor protein and Nerve Growth Factor Receptor (NGFR/p75NTR). The general aim of this study is to characterize the association between ADAM17 gene Single Nucleotide Polymorphisms (SNPs) and AD risk.
Methods: This case-control association study was conducted in a Southern Italian cohort consisting of 147 AD patients and 114 age- and sex-matched controls. Seven tag-SNPs were selected and genotyped with TaqMan SNP genotyping assays. The associations between these tag-SNPs and AD risk were assessed by logistic regression models.
Results: The variability of rs12692385 and rs11690078 polymorphisms was related to the AD onset. Subjects who were homozygous for the T allele of the rs12692385 polymorphism had 2.15 higher probability to develop AD than subjects carrying a single copy of the C allele (p=0.011). A significant effect was also detected for the rs11690078 polymorphism for which carriers of the T allele showed a significant reduced risk to develop AD with respect to those who were homozygous for the C allele (OR=0.24, p=0.011). A borderline effect was also detected for rs12464398 polymorphism for which carriers of the C allele showed a reduced risk to develop AD with respect to those who were homozygous for the T allele (OR=0.58, p=0.065).
Conclusion: Our results reveal a new role of ADAM17 gene in AD from a genetic perspective. ADAM17 gene tag-SNPs analysis should be considered for the genetic screening of AD.
Disclosure: Nothing to disclose.

EPO-177

Genetic variants in the NGFR/p75NTR gene predict cognitive impairment and functional decline in Alzheimer's disease

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Background and aims: Alzheimer's Disease (AD) is the most widespread neurodegenerative disorder. AD is commonly categorized as either early onset (EOAD) or late onset (LOAD) based on an age cutoff, typically 65 years. Previously, we have shown that Single Nucleotide Polymorphisms (SNPs) of the Nerve Growth Factor Receptor (NGFR/p75NTR) gene could represent risk factors both for EOAD and LOAD. The principal aim of this study is to better characterize the association between NGFR/p75NTR gene SNPs with AD, considering cognitive impairment and functional decline.
Methods: This study was conducted on 295 AD patients (109 EOAD and 186 LOAD) recruited at the Regional Neurogenetic Centre (CRN) – ASPCZ of Lamezia Terme (CZ, Italy). Nineteen tag-SNPs were selected within the entire NGFR/p75NTR gene and genotyped using TaqMan SNP genotyping assays on DNA extracts prepared from blood samples. The associations between these tag-SNPs, cognitive impairment (MMSE scores) and functional decline (ADL and IADL scores) were assessed by linear and logistic regression models after adjustment for gender, APOE genotype and level of education.
Results: The variability of two investigated polymorphisms was correlated with MMSE score only in LOAD patients. The variability of other polymorphisms was significantly associated with ADL and IADL scores in both EOAD and LOAD patients.
Conclusion: Our results reveal a new role of NGFR/p75NTR gene in the cognitive impairment and functional autonomy of both EOAD and LOAD patients. NGFR/p75NTR gene tag-SNPs analysis should be considered for the genetic screening of AD.
Disclosure: This work was supported by funds granted by the Italian Ministry of Health Ricerca Finalizzata 2018:SG-2018-12366233.

EPO-178

Apathy and unawareness of apathy differ in neural pathways in prodromal Alzheimer's disease: an FDG-PET study

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Background and aims: The discrepancy in apathy ratings between patients with amnestic MCI and their informants predicts transition to Alzheimer's disease(AD) dementia as a measure of disease awareness. We investigated whether the metabolic changes linked to discrepant estimations differ topographically from those in the frontal-subcortical circuits typically connected to apathy.
Methods: 29 individuals with amnestic MCI and an intermediate-to-high likelihood of AD progressing to dementia over an average of two years were retrospectively chosen (21 F;age 76.2±4.9 years;education 8.7±4.0; MMSE score 25.9.2±1.5). All participants completed at baseline an extended neuropsychological assessment including the Apathy Evaluation Scale (AES) to measure apathy, either patients' self-(AES-S) or informant-reported(AES-I), and [18F]-FDG-PET analysis. Patients' self-ratings were subtracted from caregivers' estimations to produce a "Discrepancy" score. We identified the various regions of correlation of AES-S, AES-I, and "Discrepancy" with brain metabolism using voxel-based analysis of [18F]-FDG-PET images(multiple regression analysis, nuisances:age, MMSE score).
Results: The "Discrepancy" in the bilateral hippocampal gyri and thalami, right posterior cingulate cortex, and putamen, and the AES-S score in the left cingulate, precentral, superior frontal cortices, and right medial frontal area were found to correlate with metabolic levels negatively. The two subgroups of patients split according to the degree of the "Discrepancy" (median score=6) showed no differences in cognitive functioning.
Conclusion: Our findings are consistent with the relationship between frontal network activity and the degree of apathy in MCI-AD patients. In contrast, regardless of the amount of cognitive impairment, the "Discrepancy" between patients' self- and informant-estimated apathy is linked to limbic areas typically involved in memory functioning.
Disclosure: Nothing to disclose.

EPO-179

Language and biomarker profile of data-driven subtypes of mixed semantic-logopenic primary progressive aphasia

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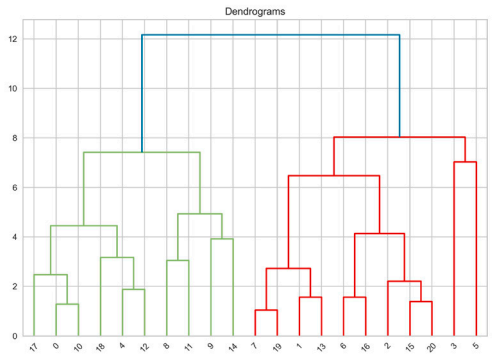
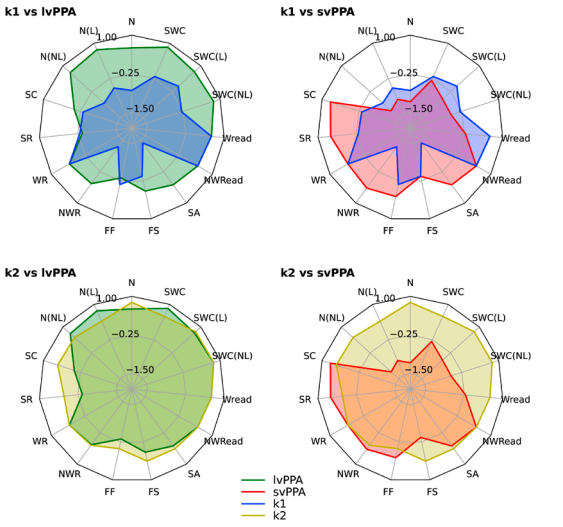
Background and aims: A variable amount (6–41%) of primary progressive aphasia (PPA) cases did not fulfill criteria for prototypical variants and are defined as mixed PPA (mPPA). Patients with mPPA are poorly characterized. We aimed to detail linguistic and biomarker profiles of patients with mixed semantic-logopenic PPA (s/lv-PPA).
Methods: We considered 56 patients with diagnosis of PPA: 12 semantic variant (svPPA), 23 logopenic variant (lvPPA) and 21 s/lvPPA. All patients underwent neuropsychological and language evaluation, CSF concentration of Aβ42, Aβ42/Aβ40, phosphorylated tau and total tau measurement. Reduction of dimensionality was performed by principal component analysis (PCA). We used Agglomerative Hierarchical Clustering (HCA) as unsupervised learning algorithms.
Results: Five principal components were defined based on language tests and were used to run an HCA identifying two clusters: k1 (n=10) and k2 (n=11) (Fig. 1). k1 group had lower Aβ42/Aβ40 ratio ($p=0.018$, $\eta2=0.40$) and higher t-tau ($p=0.012$, $\eta2=0.35$) and p-tau ($p=0.023$, $\eta2=0.34$) concentrations than k2. Moreover, k1 group had lower scores in test assessing for semantic fluency ($p=0.021$, $\eta2=0.27$), naming ($p=0.003$, $\eta2=0.42$), single word comprehension ($p<0.001$, $\eta2=0.59$) and semantic association ($p=0.001$, $\eta2=0.58$) than k2 group. Linguistic profile of k1 was more similar to svPPA and the one of k2 was more similar to lvPPA (fig.2).



Dendrogram from Agglomerative Hierarchical Clustering



SWC = singleword comprehension, SWC(L) = single word comprehension (living), SWC(NL) = single word comprehension (non-living), WRead = word-reading, NW Read = non-word-reading, NWR = non-word repetition, WR = word repetition, SR = sentence repetition, SC = sentence comprehension, SA = semantic association, FF = phonemic fluency, SF = semantic fluency, N = naming, N(L) = naming (living), N(NL) = naming (non-living)

Comparison between clusters and prototypical PPA variants

Conclusion: Based on language features, we identified two s/lvPPA subtypes showing different AD biomarkers profile. Interesting the subtypes with a CSF biomarker profile showed a linguistic profile more consistent with svPPA. This result might suggest the existence of a linguistic spectrum influenced by AD pathology across mPPA.

Disclosure: The authors declare no commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-180

Blood-CSF barrier impairment and regional brain atrophy in prodromal and overt AD and DLB

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Background and aims: Alzheimer's disease (ADdem) and Lewy body dementia (DLB) are characterized by cholinergic impairment and regional brain atrophy. In DLB, overlapping AD associates with greater atrophy). However, other factors may play role in atrophy and clinical impairment. Choroid plexus (CP), part of blood-CSF barrier, regulates inflammation and monitors CSF synthesis, composition, and circulation. Association between blood-CSF barrier impairment and regional atrophy, and effect of AD biomarkers, is unknown in prodromal and overt AD and DLB.

Methods: 108 participants (n=30 prodromal AD, n=24 ADdem, n=10 prodromal DLB, n=20 overt DLB, n=24 unimpaired controls, CN) had clinical, MRI and CSF tests. FreeSurfer algorithm and cholinergic basal forebrain ROIs measured CP and nucleus basalis of Meynert (NBM) volumes and regional cortical thickness. From CSF, AD biomarkers and albumin quotient (QAlb), proxy of blood-CSF barrier impairment, were derived. MANOVA adjusted for age, sex assessed the associations between atrophy and blood-CSF barrier; mediation analysis assessed how the CSF AD biomarkers mediated this relationship.

Results: CP volume was larger and NBM volume was smaller in both DLB and AD compared to CN, and CP increased from prodromal to overt dementia. Larger CP was associated with smaller NBM in AD and DLB. Larger CP was associated with abnormal QAlb, and with abnormal AD biomarker levels. Abnormal AD biomarker levels mediated association between larger CP, abnormal AlbQ and regional atrophy.

Conclusion: Impaired blood-CSF barrier is associated with greater regional atrophy including cholinergic regions in prodromal and overt AD and DLB.Investigation into blood-CSF barrier as additional potential treatment target may be beneficial.

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EPO-181

Abstract withdrawn

EPO-182

Abstract withdrawn

EPO-183

A comparison of cerebral amyloid angiopathy in the cerebellum and occipital lobe from routine autopsies

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Background and aims: The occipital lobe is most frequently and severely affected by cerebral amyloid angiopathy (CAA). CAA can also occur in the cerebellum, although less frequently than in the cerebral lobes. Until recently, there have been limited studies assessing cerebellar CAA. In the present study, we semiquantitatively compared the frequency and severity of CAA in the cerebellum and occipital lobe.
Methods: We reexamined the senile changes in approximately 440 autopsied brains in our institute. We selected 60 subjects in whom the CAA were observed in the occipital lobe. Five-micrometer-thick paraffin-embedded brain sections were immunostained with monoclonal anti-amyloid-β (Aβ) peptides 17–24 (4G8) and monoclonal anti-phosphorylated tau (AT8) antibodies.
Results: In the 60 subjects with CAA-positive occipital lobe, cerebellar CAA was observed in 29 subjects (48.3%), and the severity of cerebellar CAA was relatively mild compared with occipital lobe CAA. Capillary CAA was observed in the occipital lobe of 12 subjects and the cerebellum of three subjects. CAA-related vasculopathies were observed in the occipital lobe of 15 subjects and the cerebellum of two subjects–the severity of CAA-related vasculopathy was mild in both of these subjects. Aβ plaques were observed in the occipital lobe of 54 subjects (90%) and the cerebellum of 16 subjects (26.7%)–the severity of Aβ plaques in the cerebellum was mild compared with the occipital lobe.
Conclusion: We confirmed that cerebellar CAA is frequently observed in the cerebellum, but with a lower severity than CAA in the occipital lobe. Clinicians should pay more attention to cerebellar CAA.
Disclosure: The authors declare no conflicts of interest for this study.

EPO-184

Dependency as a result of AD across disease stages measured by activities of daily living

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Background and aims: Alzheimer's disease (AD) is a progressive disease causing cognitive dysfunction, reduced ability to perform activities of daily living (ADLs), and behavioural changes. The study objective is, to describe neuropsychiatric symptoms and ability to conduct ADLs among cognitively unimpaired participants and AD.
Methods: Data from the National Alzheimer's Coordinating Center (NACC) Uniform Data Set were used for this study. The NACC collects annual follow-up data from participants seen at participating Research Centers. Participants with unimpaired cognition, clinically diagnosed MCI or dementia due to AD were included. ADLs were assessed at each visit using the NACC-Functional Assessment Scale (FAS) and neuropsychiatric symptoms using the Neuropsychiatric Inventory Questionnaire (NPI-Q).
Results: The study included participants with unimpaired cognition (13,692 [48.5%]); MCI due to AD (7,075 [25.1%]); and dementia due to AD (7,453 [26.4%]). Participants responses to individual NACC-FAS questions demonstrate that impact on ADLs may emerge as early as the MCI stage. For example, 0.4% of cognitively unimpaired participants were dependent on others when traveling out of the neighbourhood, driving, or arranging to take public transportation compared to 8.0%, 47.4%, 85.5% and 94.9% of participants with MCI due to AD, mild, moderate, and severe AD dementia, respectively. Similarly, 0.3% of cognitively unimpaired participants reported severe anxiety compared with 1.5%, 3.5%, 7.6% and 7.5% of participants with MCI due to AD, mild, moderate and severe AD dementia, respectively.
Conclusion: These data demonstrate that deterioration of ADLs and emergence of psychiatric symptoms are apparent as early as the MCI stage in AD continuum and increase with disease progression.
Disclosure: Nothing to disclose.

EPO-185

Cortical morphological dissimilarities as potential biomarkers of Alzheimer disease and late mild cognitive impairment

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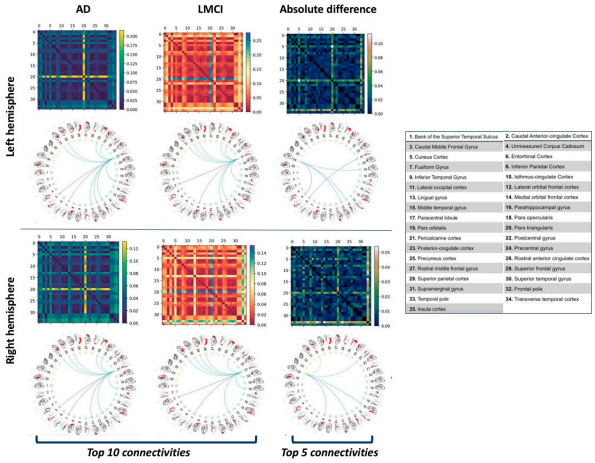
Background and aims: Deep learning methodologies have achieved great progress regarding classification of neurological disorders and yet, failed to learn efficiently from connectomic brain graph data. Graph neural networks(GNNs) have provided learning by considering the connectivity of regions of interests (ROIs) which extracts a deeper interpretation of the brain networks. In this study, we implemented a GNN model to extract the biomarkers distinguishing Alzheimer's disease(AD) from late mild cognitive impairment(LMCI).
Methods: We used a dataset with 70 subjects(35 AD,35 LMCI) from the Alzheimer's Disease Neuroimaging Initiative(ADNI) database GO public dataset. The networks are derived from maximum principal curvature, mean cortical thickness, mean sulcal depth, average curvature measurements and cortical surface area. The cortical surface is reconstructed from T1-weighted MRI using the FreeSurfer and each view is defined with 35 ROIs by Desikan-Killiany atlas. The weight of the entry denotes the strength of connectivity between given ROIs.
Results: The top 10 connectivities within the right hemisphere pinpoints that Pericalcarine cortex(PrC) and precuneus connectivity is specific to AD patients and could be considered as a discriminative biomarker of AD(Figure1), a fact that has been established using functional MRI. Dissimilarities of the connections of the the PrC with the inferior parietal cortex(IPC) and with the caudal middle frontal gyrus(CMFG) represent fingerprints of LMCI.
Conclusion: Dissimilar morphological connectivity and functional connectivity are intertwined. The concept of cortical morphological connectivity exceeded the morphology-cortical-region-based approach providing accurate biomarkers: The PrC with precuneus as a distinctive connectivity in AD and PrC with the IPC and with the CMFG in LMCI.
Disclosure: Arwa Rekik and Oben Özgür are first authors.



Representation of the top 10 most discriminative connectivities within the left and the right hemispheres seperately, in AD and LMCI along with the absolute difference matrices between AD and LMCI illustrated with the top 5 connectivities.

EPO-186

Different CSF tau measures and their association with traditional CSF and PET biomarkers in a memory clinic population

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Background and aims: Alzheimer's Disease (AD) is characterized by abnormal deposition of amyloid (A) and tau (T) proteins in the brain. A and T can be measured by using PET, cerebrospinal fluid (CSF) and blood. Several CSF pTau epitopes have been described and could be more specific for the different stages of the disease. The present study aims to assess the association between several pTau epitopes and Tau368, the traditional CSF and PET biomarkers and global cognition.
Methods: The following CSF biomarkers were quantified using single molecular arrays developed at the University of Gothenburg from 112 subjects (49 cognitively-unimpaired,55 MCI,8 demented) of the Geneva Memory Center: pTau181, pTau212, pTau231, pTau217, Tau368 (analyzed as Tau368/tTau). Subsets of: n=84 underwent an amyloid PET; n=48 a tau PET; n=63 a lumbar puncture (traditional biomarkers: Aβ42, pTau181, tTau); n=109 a MMSE. A Kruskal-Wallis test was used to assess the differences in levels of CSF tau measures among diagnostic

groups; Pearson correlation to assess the association between CSF tau measures and traditional CSF and PET biomarkers and cognition.
Results: pTau181, pTau212, pTau231, pTau217 but no Tau368/tTau were able to differentiate disease stages ($p<0.005$). All CSF pTau epitopes and Tau368/tTau strongly correlate with traditional CSF biomarkers ($R>0.5;p<0.001$) and PET biomarkers ($R>0.6;p<0.05$). All CSF pTau epitopes and Tau368/tTau can differentiate A+/A- and T+/T- assessed through PET and they all correlate with MMSE ($R>0.3;p<0.005$).
Conclusion: Further analyses are needed to investigate the prognostic value of different CSF pTau epitopes across disease stages. However, they seem to identify AD patients and they strongly correlate with traditional AD biomarkers.
Disclosure: HZ has served at scientific advisory boards and/or as a consultant for Abbvie, Acumen, Alector, Alzinova, ALZPath, Annexon, Apellis, Artery Therapeutics, AZTherapies, CogRx, Denali, Eisai, Nervgen, Novo Nordisk, Optoceutics, Passage Bio, Pinteon Therapeutics, Prothena, Red Abbey Labs, reMYND, Roche, Samumed, Siemens Healthineers, Triplet Therapeutics, and Wave, has given lectures in symposia sponsored by Cellectricon, Fujirebio, Alzecure, Biogen, and Roche, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program (outside submitted work). KB has served as a consultant, at advisory boards, or at data monitoring committees for Abcam, Axon, BioArctic, Biogen, JOMDD/Shimadzu. Julius Clinical, Lilly, MagQu, Novartis, Ono Pharma, Pharmatrophix, Prothena, Roche Diagnostics, and Siemens Healthineers, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program, outside the work presented in this abstract. FR, AJM, AL, VG, GBF declare that they have no competing interests.

EPO-187

Attitudes toward seeking professional help among patients with early Alzheimer´s disease

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Background and aims: Limited information is available on the active process of seeking professional help when patients with Alzheimer's disease (AD) perceive cognitive impairment in the early stages. The aim of this study was to assess the phenomenon of help-seeking in early AD and to identify associated factors.
Methods: A multicenter, non-interventional study was conducted including patients of 50–90 years of age with prodromal or mild AD, a Mini-mental State Examination (MMSE) score ≥22, and a Clinical Dementia Rating-Global score (CDR-GS) of 0.5-1.0. A battery of self-report instruments was used to evaluate different patients´ psychological and behavioral domains. A multivariable logistic regression analysis was conducted.
Results: A total of 149 patients were included. Mean age (SD) was 72.3 (7.0) years and 50.3% were female. Mean disease duration was 1.4 (1.8) years. Ninety-four (63.1%) patients sought help when they realized their symptoms, mostly from neurologists (71.3%). Patients with help-seeking attitudes were mostly female (60.6%) with a CDR-GS score of 0.5 (91.5%) and had a greater awareness of diagnosis, poorer quality of life, more depressive symptoms, and more severe perception of their condition than their

counterparts. Lack of help-seeking attitudes was associated with male gender (OR=0.33 [95%CI 0.15, 0.69], p=0.003), a low awareness of diagnosis (OR=0.96 [95%CI 0.92, 0.99], p=0.015), and the perception of non-threatening illness (OR=0.32 [95%CI 0.15, 0.71], p=0.005) in the multivariable analysis after adjustment for confounders.

Conclusion: These findings should be considered when developing strategies to promote positive attitudes towards professional help-seeking in patients with cognitive impairment at earlier stages.

Disclosure: This study was funded by Roche Farma SA, Spain (Medical Department) Alberto Villarejo-Galindo discloses honoraria from a consulting/advisory role with KRKA, Kern Pharma, Exeltis, Esteve, Roche, AbbVie, Schwabe, Neuraxpharm, Nutricia, and Alter. Antonio del Olmo-Rodríguez discloses honoraria from a consulting/advisory role with Alter, Biocross, Biogen, KRKA, Esteve, Schwabe, Nutricia, and Lilly. Emilio Franco-Macías discloses honoraria from a consulting/advisory role with Kern Pharma, Esteve, Roche, and Neuraxpharm. Mercè Boada discloses honoraria from a consulting/advisory role with Grifols, Araclon Biotech, Roche, Lilly, Merck, Biogen, Zambon, Novo-Nordisk, Bioiberica, Biogen, Eisai, Servier, and Schwabe Pharma; funding sources with Life Molecular Imaging, Bioiberica, and Schwabe; and grants from CIBERNED, EU/EFPIA, Instituto de Salud Carlos III (ISCIII), Fundación La Caixa, and Grífols. Albert Lleó discloses honoraria from a consulting/advisory role with Grifols, Fujirebio-Europe, Novartis, Roche, Otsuka, Nutricia, Zambón, Biogen, Lilly, and KRKA. Co-author of a patent on markers of synaptopathy in neurodegenerative diseases (EP18382175.0, PCT/EP2019/056535). Elena García-Arcelay and Jorge Maurino are employees of Roche Farma SA Spain. The rest of authors declare no potential conflict of interest.

Motor neurone diseases

EPO-188

A longitudinal evaluation of early sleep and respiratory impairment in ALS patients

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Background and aims: ALS is a neurodegenerative disease characterised by motor neuron death. 30% present a bulbar onset, while 70% a spinal one. Extra-motor systems involved in ALS include circuits regulating sleep; the early identification of sleep impairment and his better definition could improve patient's quality of life (QoL). One of the most important prognostic factors in ALS is respiratory impairment. It's early recognition and an early starting of non-invasive ventilation (NIV) allow a prolongation of survival.
Methods: Between August 2021 and July 2022 we enrolled 45 ALS patients and 45 healthy controls (HC). At baseline and at month six, patients underwent neurological examination, polysomnography (PSG), arterial blood gases (ABG), spirometry and filled sleep and respiratory questionnaire (RLSRS, STOP-BANG, ISI, ESS, PSQI, PIRS, MEQ, STAI, BDI). SPSS software was used for data analysis.
Results: At baseline, ALS patients without respiratory symptoms showed an increase of AHI-index and of ODI-index compared to HC (respectively, p=0.001 and p=0.04). Contrarily, spirometry and ABG were not so altered. Longitudinally we observed a significant worsening of PSG parameters ($p<0.05$). Patients who started nocturnal-NIV (15 out of 45) showed a significant improvement of PSG parameters. At baseline we also observed an excess of periodic limb movement in ALS vs HC (p=0.01). Direct correlation between progression rate of disease and both AHI and ODI (r=0.546 and r=0.442 $p<0.05$).

Sex (M/F)	ALSFRS (± SD)	FVC (± SD)	FEV1 (± SD)	AHI (± SD)	ODI (± SD)	PLMS (± SD)
25/20	39,2 ± 4,6	92 ± 21	93 ± 23	18,5 ± 15,5	13,3 ± 11,0	22,5 ± 31,6

Demographic and clinical data of ALS patients

Conclusion: This preliminary study showed the presence of respiratory and sleep impairments in ALS patients since the beginning of the disease. Their identification is fundamental for an early treatment and for an improvement of QoL.
Disclosure: I have nothing to disclose.

EPO-189

Role of TDP-43 in the diagnosis and phenotypic characterization of ALS: comparison between CSF and plasma data.

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Background and aims: Background: the diagnostic work-up for Amyotrophic Lateral Sclerosis (ALS) diagnosis is complex and often associated with diagnostic delay. Scientific research focused on the neurodegeneration biomarkers that can anticipate the diagnosis and phenotypically characterize patients is necessary. Among these, TDP-43, which accumulates in the neuronal cytoplasm in most ALS patients, is one of the most promising. This study aimed to compare the data obtained from the cerebrospinal fluid (CSF) and blood TDP-43 dosage and to correlate the results obtained from the assays with clinical and laboratory data.
Methods: Methods: 14 patients were recruited, and CSF and serum TDP-43 were determined by the ELISA method. Clinical-phenotypic and functional data (ALSFRS-R, BMI, FVC%), blood chemistry, and genetic data were also collected.
Results: Results: a strong negative correlation (r=-0.70; p=0.03) was observed between CSF and serum levels. There was also a significant positive correlation (r=0.67; p=0.03) between CSF and Creatine phosphokinase (CPK) and a negative correlation (r=-0.90; $p\leq0.01$) between serum TDP-43 and CPK values. Patients with the bulbar phenotype appear to show lower levels of CSF TDP-43 compared to spinals (p=0.04); moreover, there was a positive correlation between CSF TDP-43 and the bulbar subscore of the ALSFRS-R (r=0.67; p=0.03). Correlating with the genetic data, the patient carries the lowest absolute CSF TDP-43 concentration within the cohort characterizes a SOD1 mutation.
Conclusion: Conclusions: data from this study support the utility of TDP-43 as a biomarker in ALS, both at CSF and plasma levels, also showing significant correlation with clinical and genetic data.
Disclosure: Nothing to disclose.

EPO-190

Upper motor neuron involvement in ALS: a correlation between neurophysiological and metabolic brain pattern.

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Background and aims: In Amyotrophic Lateral Sclerosis (ALS) diagnostic work-up, the involvement of lower motor neurons (LMNs) is easily demonstrated by electromyography; on the contrary, finding markers of upper motor neuron (UMN) suffering is harder. Transcranial magnetic stimulation (TMS)-induced motor-evoked potentials (MEPs) are one of the proposed markers of (sub)clinical UMN damage. Our study aimed to verify a possible correlation between the metabolism brain pattern and the MEPs findings for highlighting the UMN damage.

Methods: A total of 20 ALS patients who underwent FDG-PET and TMS-MEPs at diagnosis were retrospectively enrolled in the study. Patients were enrolled between 2018 and 2022 at the ALS Tertiary Center, Novara, Italy. For each patient, we collected clinical-phenotypical variables. We measured the motor latency, amplitude, and central motor conduction time (CMCT) for TMS-MEPs from the upper and lower limbs. For FDG-PET, following a validated voxel-based Statistical Parametric Mapping procedure, we obtained hypometabolism maps at the single-subject level, correlating the regional hypometabolism with clinical and neurophysiological values.

Results: Of enrolled patients, the mean age was 57.2±12.63 years (30% bulbar, 70% spinal onset). 14/20 patients (70%) had abnormal MEPs in at least one limb: 8/20 (40%) had unreliable MEPs, and 12/20 (60%) had delayed CMCT. We observed a direct correlation between lower limbs CMCT and precentral, frontal superior, and supplementary motor areas (r=0.65,p=0.05;r=0.76,p=0.02;r=0.72,p=0.03). For the upper limbs, the correlation is limited with the supplementary motor area (r=0.78,p=0.02).

Conclusion: Our data suggest an essential single and additive role of TMS-MEPs and FDG-PET in highlighting the UMN suffering in ALS patients at diagnosis.

Disclosure: Nothing to disclose.

EPO-191

Electrodiagnostic Findings in Facial Onset Sensory and Motor Neuronopathy (FOSMN)

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Background and aims: FOSMN is a rare clinical syndrome initially described in a seminal case series of five patients who presented with facial sensory deficits, followed by motor deficits, evolving rostro-caudally. Clinical, genetic and neuropathological data strongly suggest that FOSMN is a rare phenotype of amyotrophic lateral sclerosis (ALS). Herein, we review the published electrodiagnostic data for FOSMN and report detailed electrophysiological data from two cohorts (n=10) with this syndrome, proposing a specific approach to electrodiagnostic testing in patients who present with facial sensory symptoms.

Methods: Blink Reflexes, Electromyography, Nerve Conduction Studies, Somatosensory Evoked Potentials, Threshold Tracking Transcranial Magnetic Stimulation.

Results: Findings on standard electrophysiological assessment were in broad agreement with those published: blink reflexes were abnormal in all but one patient (Figure 1); SNAPs were reduced but CMAPs preserved; mixed acute and chronic neurogenic change was identified on needle EMG in bulbar and cervicothoracic muscles in approximately 50% of patients. In addition, upper limb SEP central conduction times were increased (n=4) and progressed on repeat testing (n=3) (Figure 2), and upper motor neuron dysfunction was revealed by several measures [ipsilateral MEPs (n=1); reduced short interval intra-cortical inhibition on threshold-tracking TMS (n=2); absent beta-band intermuscular coherence (n=3)].

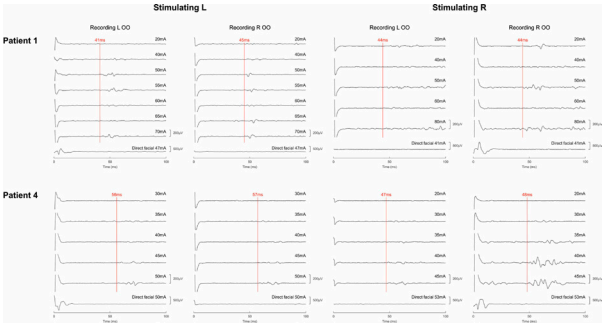

Figure 1: Illustrative examples of blink reflex responses acquired from 2 patients.

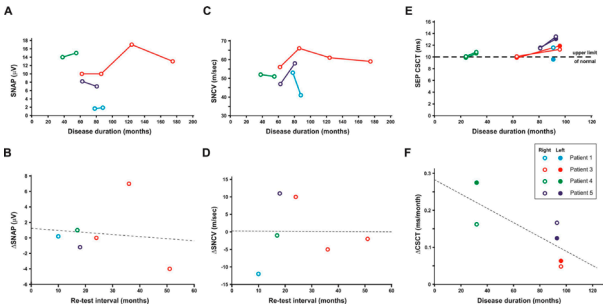

Figure 2. Changes in sensory nerve action potential (SNAP) amplitudes, sensory nerve conduction velocities (SNCVs) and upper limb somatosensory evoked potentials (SEPs).

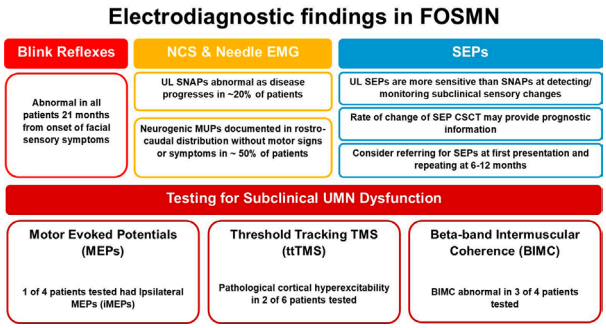

Figure 3. Summary of electrodiagnostic findings in facial onset sensory and motor neuronopathy (FOSMN).

Conclusion: Electrodiagnostic investigation of FOSMN should include blink reflex testing, SEPs and tests of upper motor neuron function (Figure 3). The combination of progressive lower motor neuron disease and upper motor neuron disease on neurophysiological investigation provides further support for the contention that FOSMN is a rare phenotypic variant of ALS.

Disclosure: Hugo M De Oliveira is supported by a National Institute of Health Academic Clinical Lectureship

EPO-192

Transcriptome signature in Amiotrophic Lateral Sclerosis (ALS) phenotypes

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Background and aims: Unmet needs for ALS patients includes both the identification of criteria for clinical stratification, and the discovery of reproducible biomarkers. We aim to identify a transcriptome signature in homogenous MND sub-groups obtained using specific phenotype classification.

Methods: We have stratified n=48 newly-diagnosed sporadic ALS patients by Chiò et al (JNNP, 2011) criteria, and enrolled n=19 age-matched healthy controls. We have isolated PBMCs, performed RNA sequencing, and compared the transcriptome profiles for all the subjects compared to healthy controls.

Results: We have collected the following phenotypes: n=12 classic, n=10 bulbar, n=7 flail arm, n=10 flail leg, n=9 pyramidal. We have observed a different gene expression between patients and controls ($p<0.05$), particularly for the flail leg subgroup (fig. 1). Moreover, bulbar phenotype has been characterized by a great number of altered genes ($p>0.05$). Finally, we have noticed a single gene altered in all the phenotypes (Y-RNA, a component of the Ro60 ribonucleoprotein involved in cellular response to interferon-alpha and in regulation of gene expression) while the other genes seem to be phenotype-specific (fig. 2), and many of them are involved in inflammatory pathways.

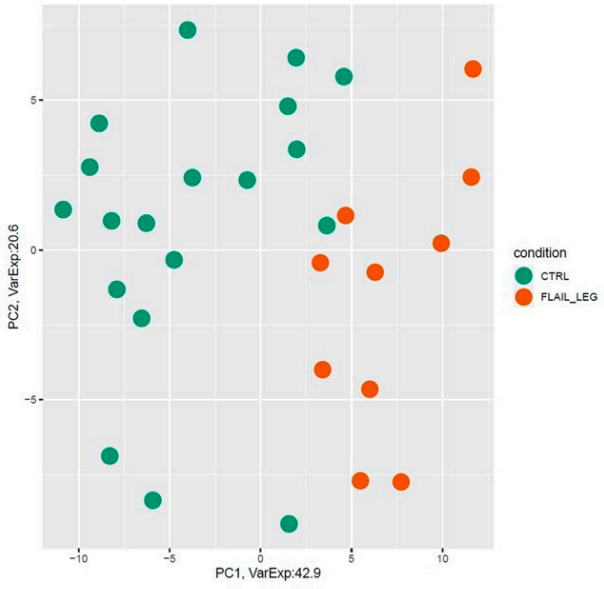

Figure 1. Principal Component Analysis of sALS patients' RNA-sequencing (flail leg phenotype)

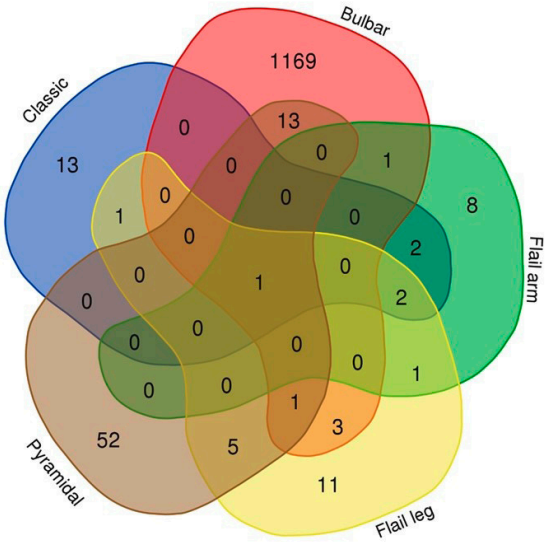

Figure 2. Venn diagram showing common deregulated genes among phenotypic groups.

Conclusion: The identification of phenotype-specific pathogenic mechanisms could be pivotal for the study of progression biomarkers. Future development of this work will regard the longitudinal evaluation of transcriptomic patterns.

Disclosure: The authors declare no competing interests. this work was supported by grants of the Italian Ministry of Health to Luca Diamanti (2021-2022).

EPO-193

Hidden hints from routine blood analyses in patients with amyotrophic lateral sclerosis

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Background and aims: There is an unmet need in amyotrophic lateral sclerosis (ALS) to provide specific biomarkers for the disease. Due to their easiness and reproducibility, we aimed to investigate whether routine blood parameters may provide useful clues for phenotypic classification and prognosis.

Methods: We analysed a large inpatient cohort of 836 ALS patients who underwent deep phenotyping in terms of clinical upper (UMN) and lower (LMN) motor neuron scores and active and chronic denervation scores. Disability and disease progression rate were measured through the revised ALS functional rating scale (ALSFRS-R) and its changes during time. Cox regression analysis with relative hazard ratios (HR) was performed to assess potential survival associations.

Results: Creatinine showed significant correlations with LMN damage (r=0.38), active (r=0.18) and chronic (r=0.24) denervation and baseline ALSFRS-R (r=0.33). CPK, ALT, and AST correlated with ongoing (r=0.35, 0.27, 0.24) and chronic (r=0.37, 0.20, 0.19) denervation, respectively while albumin and CRP significantly correlated only with LMN score (r=0.20 and 0.17). Disease progression rate showed correlations only with chloride (r= -0.19) and potassium (r= -0.16). After adjustment for known prognostic factors, creatinine (HR 0.86, 0.81–0.92), AST (HR 1.02, 1.01–1.02), total proteins (HR 0.70, 0.57–0.86), LDH (HR 0.998, 0.997–0.999) and chloride (HR 0.95, 0.92–0.99) were independently associated with survival in ALS.

Conclusion: creatinine is a reliable biomarker for ALS, associated with clinical features, disability and survival. Markers of muscle damage and inflammation correlate with neurophysiological and clinical scores, respectively. Chloride and potassium were significantly associated with progression rate and survival.

Disclosure: Nothing to disclose.

EPO-194

Association between retinal vascularization and disease severity in Amyotrophic Lateral Sclerosis

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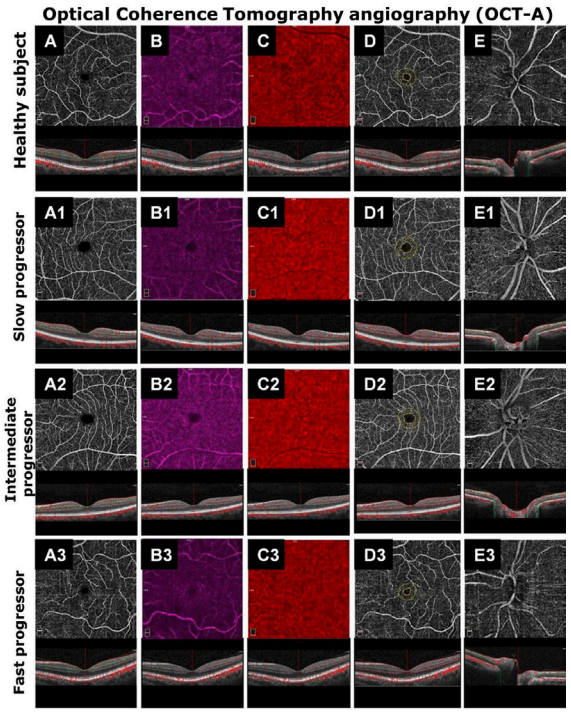
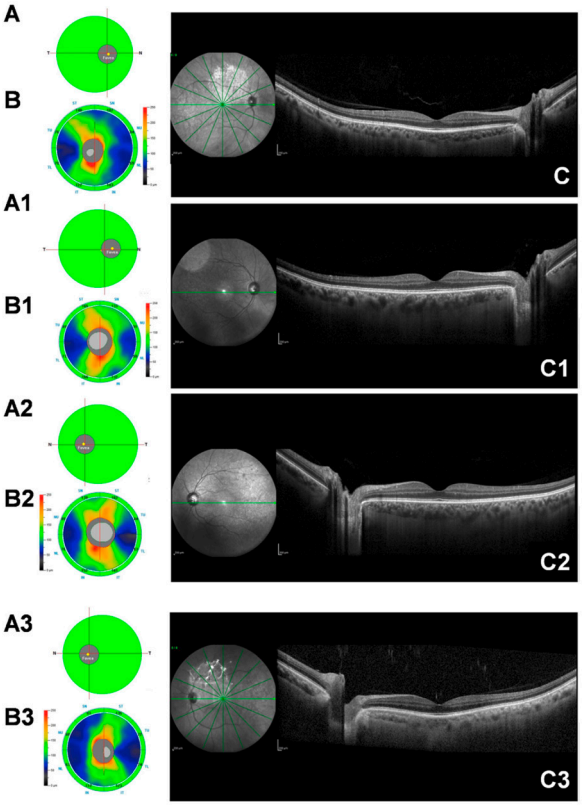
Background and aims: Alterations in retinal vascularization and neural density have been found in many neurodegenerative diseases, however conflicting results are described in Amyotrophic Lateral Sclerosis (ALS). The aim of the present study was to analyse retinal layers and vascularization using structural and Optical Coherence Tomography angiography (OCT-A) in ALS patients classified according to disease severity.
Methods: We enrolled 48 ALS patients, classified into three groups: slow progressors (n=10), intermediate progressors (n=24) and fast progressors (n=14) according to the disease progression rate, and 45 healthy controls. For structural-OCT we evaluated the Subfoveal Choroidal Thickness (SFCT), Ganglion Cell Complex (GCC), Retinal Nerve Fiber Layer (RNFL). Regarding the OCT-A we assessed the vessel density (VD) in Superficial and Deep Capillary Plexuses, Radial Peripapillary Capillary Plexus, Choriocapillary and the Foveal Avascular Zone (FAZ) area.
Results: Structural-OCT did not show any significant differences in GCC and RNFL thicknesses between patients and controls, and among the three ALS groups. The SFCT was significantly greater in patients compared with controls, interestingly the SFCT was thicker in patients with slow and intermediate disease progression than in those with fast disease progression. OCT-A did not reveal any significant results. Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) and disease duration did not correlate with any of OCT parameters, except for SFCT with ALSFRS-R.



OCT-A exam did not show any significant differences in GCC and RNFL thicknesses between patients and controls, and among the three ALS groups



The SFCT was statistically greater in patients compared with controls. The SFCT was thicker in patients with slow and intermediate disease progression than in those with fast disease progression (Figure 2a, 2b and 2c).

	Disease Duration	ALSFRS-r	SCP	DCP	CC	RPC	FAZ	GCC	RNFL	SFCT
Disease Duration	1									
ALSFRS-r	−0.1149	1								
SCP	0.0707	0.1413	1							
DCP	−0.1326	0.2561	0.3858	1						
CC	−0.1048	0.0976	0.2002	0.1941	1					
RPC	−0.0103	0.0760	0.4693	0.0301	0.2016	1				
FAZ	0.2218	−0.2739	−0.1753	0.0719	−0.0130	−0.0080	1			
GCC	0.0843	0.2179	0.4119	0.1434	0.1148	0.3980	−0.1272	1		
RNFL	0.0701	0.2469	0.3771	0.3122	0.1507	0.4082	0.1271	0.6505	1	
SFCT	0.2443	0.7526	0.0728	0.0827	0.0472	−0.1978	−0.0603	0.0754	0.0009	1

Pearson's correlations between OCT measures and clinical findings represented as visual matrix form with color coding based on strength and sign of correlations. Note the positive significant relationship between ALSFRS-r and SFCT.

Conclusion: This study demonstrated the possible association between higher SFCT and disease activity in SLA, likely due to inflammatory vascular phenomena. OCT could be a useful biomarker in management of this neurodegenerative disease.
Disclosure: Nothing to disclose.

EPO-195

Study of non-neuronal cell populations in an experimental model of Spinal Muscular Atrophy

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Background and aims: Spinal muscular atrophy (SMA) is a rare neuromuscular disorder caused by survival motor neuron (SMN) protein insufficiency. The SMNΔ7 is a widely used rodent model exhibiting SMA type II disease.
Methods: Triple transgenic FVB.Cg Grm7Tg (SMN2)89Ahmb Smn1tm1Msd Tg(SMN2*delta7) 4299Ahmb/J mice were euthanized on postnatal day 13 after clinical and neuromuscular evaluation. Spinal cord (L1-L5) was harvested and paraffin sections were used for immunohistochemistry and immunofluorescence of microglia (Iba1, iNOS). Frozen tissue was used for western blot for SMN protein.
Results: Smn1-/-SMN2+/+SMNΔ7+/+(SMNΔ7) mice exhibited increased activation of Iba1+ cells in contrast to Smn1+/+SMN2+/+SMNΔ7+/+(healthy control / HC) mice (87.5±5.43 vs. 60.1±4.17 respectively, $p<0.05$) and same trend was observed for iNOS+ cells in SMNΔ7 mice (26± 0.656) in contrast to HC mice (15.9±0.229), $p<0.0001$. SMNΔ7 mice exhibited reduced weight (4.83±0) compared to HC (2.93±0), $p<0.05$. Upon Tail suspension test SMNΔ7 mice exhibited neuromuscular impairment (1.778±0.49) in contrast to healthy controls (3.944±0.03), as well as upon hind limb suspension test (SMNΔ7 mice (2.167±0) vs. HC (4.0±0), $p<0.05$). SMNΔ7 mice exhibited decreased levels of SMN protein (0.255± 0.0347) compared to healthy siblings (1±0), $p<0.05$.
Conclusion: Preliminary data support that late stage SMNΔ7 mice, manifested with neuromuscular impairment in hind-limbs and verified by reduced presence of SMN protein, exhibit increased activation of M1 microglia.
Disclosure: The present study is funded by Biogen in the frame of Investigator Initiated Trial (IIT) [GR-SMG-11658] entitled "Non-neuronal cellular elements of the Central Nervous System and structural biomarkers in an experimental model of Spinal Muscular Atrophy".

EPO-196

Cdk5 inhibition in the SOD1G93A transgenic mouse model of ALS suppresses neurodegeneration and extends survival

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Background and aims: Deregulated cyclin-dependent kinase 5 (Cdk5) activity closely correlates with hyperphosphorylated tau, a common pathology found in neurodegenerative diseases. Previous postmortem studies had revealed increased Cdk5 immunoreactivity in amyotrophic lateral sclerosis (ALS); hence, we investigated the effects of Cdk5 inhibition on ALS model mice and neurons in this study.
Methods: In vitro study, motor neuron cell lines and primary neuronal cultures with wild-type superoxide dismutase 1 (SOD1) or SOD1G93A were compared for the expression of proteins involved in tau pathology, neuroinflammation, apoptosis, and neuritic outgrowth. In vivo study, SOD1G93A mice and non-transgenic (TG) mice were intrathecally injected with adeno-associated virus 9 (AAV9)-scramble (SCR)-short hairpin RNA (shRNA) or AAV9-Cdk5-shRNA at the age of 5 weeks. Motor function and longevity were evaluated, and the tissues were collected from 90-day-old or 120-day-old mice.
Results: Neurons with SOD1G93A showed increased phosphorylated tau, attenuated neuritic growth, mislocalization of SOD1, and enhanced apoptosis, all of which were reversed by Cdk5 inhibition. SOD1G93A mice treated with AAV9-Cdk5-shRNA showed significantly delayed disease onset ($p < 0.001$), delayed rotarod failure ($p = 0.032$), and prolonged survival ($p = 0.007$) compared with those treated with AAV9-SCR-shRNA. The brain and spinal cord of SOD1G93A mice intrathecally injected with AAV9-Cdk5-shRNA exhibited suppressed tau pathology, neuroinflammation, apoptosis, and an increased number of motor neurons compared to those of SOD1G93A mice injected with AAV9-SCR-shRNA.

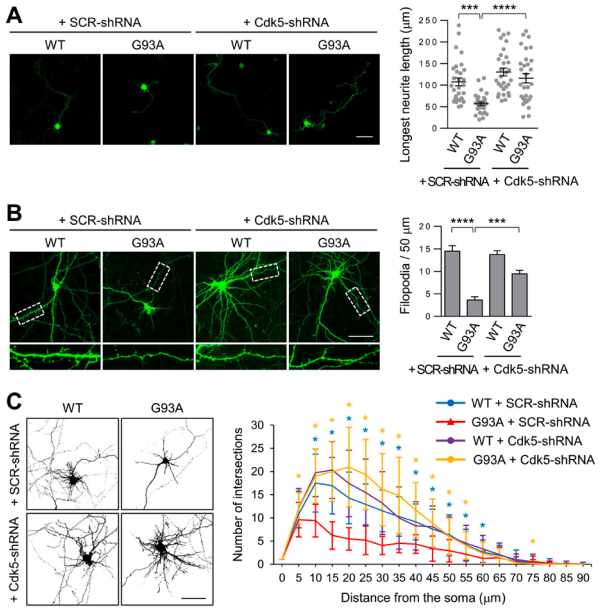

Fig. 1. Cdk5 knockdown promotes neuronal development in primary neuronal cultures with SOD1G93A.

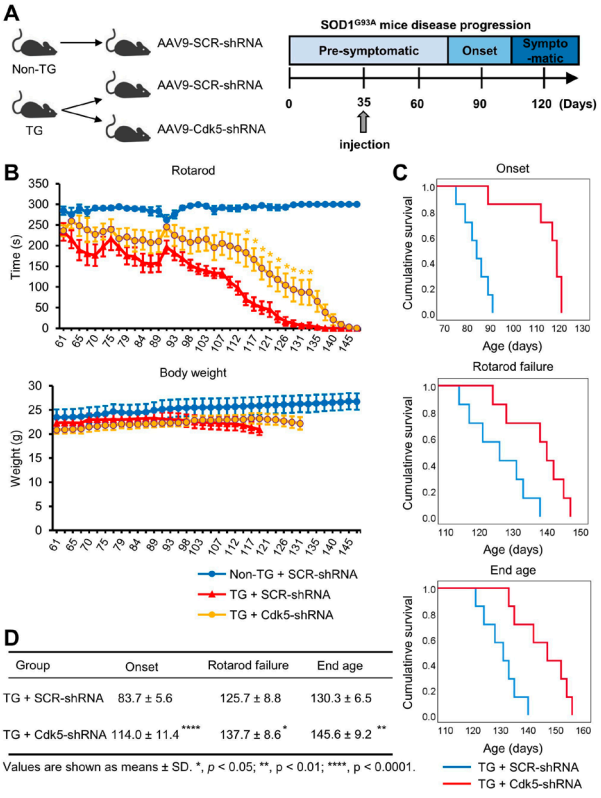

Fig. 2. In vivo study of non-transgenic (TG) and TG mice with or without Cdk5 knockdown.

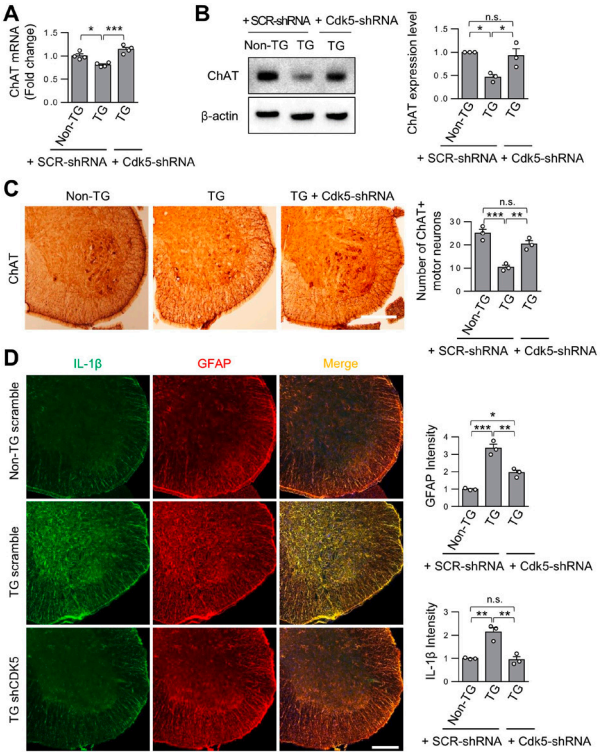

Fig. 3. AAV9-Cdk5-shRNA inhibits motor neuron degeneration and neuroinflammation in spinal cord of 120-day-old SOD1G93A transgenic mice.

Conclusion: Cdk5 inhibition could be an important mechanism in the development of a new therapeutic strategy for ALS.

Disclosure: Nothing to disclose.

EPO-197

Upper Motor Neuron Involvement Examined by Triple Stimulation in Amyotrophic Lateral Sclerosis

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Background and aims: The diagnosis of ALS requires the presence of lower (LMN) and upper (UMN) motor neuron involvement. LMN involvement is demonstrated by clinical and EMG findings whereas UMN neuron signs are dependent on the clinical examination. Even though such signs often are ambiguous, no electrophysiological methods are currently included in the diagnostic criteria for UMN involvement.
Methods: To evaluate the importance of transcranial magnetic stimulation (TMS) including the triple stimulation technique (TST) to detect upper motor neuron (UMN) involvement in ALS we examined 144 consecutive ALS patients at the time of diagnosis. EMG was carried out in all patients to assess LMN affection. TST was performed in both arms and conventional motor evoked potentials (MEP) in the legs to assess central motor conduction time (CMCT).
Results: The TST in the arms showed a central conduction abnormality in 63% of 142 patients (2 patients had no cortical responses), while only 15% had prolonged CMCT. In the legs, prolonged CMCT was found in 50% of patients. The overall sensitivity to detect UMN dysfunction was 77%. In pure clinical LMN involvement, the TST increased the sensitivity to detect UMN involvement by a factor of 4.7. The combined TST and conventional MEP disclosed a central abnormality in 62% of pure LMN patients.
Conclusion: TMS with TST is a sensitive method to detect corticospinal dysfunction in ALS. This TMS protocol is applicable in the clinical routine supporting the proposal that MEP abnormalities are a reliable marker of UMN damage and could be incorporated into diagnostic criteria for ALS.
Disclosure: Nothing to disclose.

EPO-198

Priorities of SMA adult patients and their HCPs toward evaluation. First results of a French qualitative study

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Background and aims: This work aims to study the assessment needs of adults with spinal muscular atrophy (SMA) and healthcare professionals (HCPs) using qualitative methods. SMA assessment is important for guiding care and objectifying the effects of treatments. However, little is known about the assessment needs of patients.
Methods: A scientific committee of SMA specialists designed a qualitative study. 18 patients and 30 HCPs were needed to reach saturation according to the purposive sampling method. Recruiting (ongoing) is carried out in 8 specialized centers. Interview guides were set around: 1) patients' role, 2) practice of HCPs, 3) changes of practice since the treatments. Semi-structured interviews are conducted by a sociologist and analyzed using grounded theory.
Results: After 3 months, 14 patients and 18 HCPs were interviewed. Patients report: 1) living an unstable disease that might evolve unpredictably. 2) trying to control their environment to achieve an acceptable life balance, which is cumbersome. 3) fear of losing meaningful gestures on

which their acceptable life balance is based. 4) asking for care oriented towards the preservation of their life balance. 5) expecting evaluations that accurately reflect their situation. HCPs report: 1) diverse assessment practices according to the patient's needs, the level of disability, the requirements of research protocols and the resources of their center. 2) tinkering with measures for patients with severe disabilities due to few validated assessments.

		N=14
SEX	female	6
	male	8
AGE	minimum	29 y.o.
	maximum	63 y.o.
	median	38,5 y.o.
	mean	43,5 y.o.
	standard deviation	11,6y.o.
SMA TYPE	Ib	2
	II	5
	III	7
INFERIOR LIMB MOTOR FUNCTION	non ambulant (electric wheelchair)	10
	non ambulant (manual wheelchair)	2
	ambulant	2
UPPER LIMB MOTOR FUNCTION	severely impaired	6
	impaired	5
	normal	3
RESPIRATORY FUNCTION	no ventilation	9
	non invasive ventilation	3
	invasive ventilation	2

Table 1. Patients' characteristics

		N=18
HEALTHCARE PRACTITIONERS FROM SMA SPECIALIZED CENTERS	Neurologists	4
	Pulmonologists	1
	Physical and Rehabilitation Medicine Specialists	3
	Occupational Therapists	2
	Physiotherapists	4
	Psychologists	1
	Nurses	1
	Adaptated Physical Activity Specialists	1
	Social Workers	1

Table 2. HCPs' characteristics

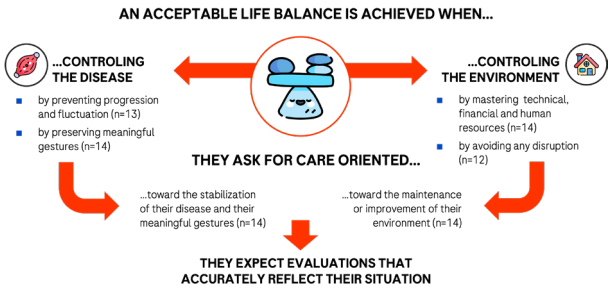

Figure 1. Patients' perspective regarding the preservation of an acceptable life balance

Conclusion: This unprecedented work highlights the preservation of meaningful gestures as an important goal for adults with SMA and the needs for reliable and feasible assessment.

Disclosure: Funding: Roche France SAS

EPO-199

The Phase 3 RESILIENT Study: Taldefgrobep Alfa in Spinal Muscular Atrophy

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Background and aims: Spinal muscular atrophy (SMA) is a progressive, debilitating, genetic condition that results from deficient survival of motor neuron (SMN) protein. Patients experience muscular atrophy and motor neuron loss. Despite the use of SMN upregulators, many patients continue to experience muscle weakness that impairs function and quality of life. Myostatin inhibitors have shown promise in increasing muscle mass and function when administered along with SMN upregulators in murine SMA models. Taldefgrobep alfa (BHV-2000) targets the myostatin pathway directly by lowering myostatin and also blocking downstream signaling. Supported by extensive nonclinical data and an established safety profile in patients with neuromuscular disease, RESILIENT (NCT05337553) will study the efficacy and safety of taldefgrobep as an adjunctive therapy along with SMN upregulators in patients with SMA.

Methods: RESILIENT is a phase 3, randomized, placebo-controlled trial with a 48-week double-blind phase and optional 48-week open-label extension. Patients with SMA (aged 4–21 yrs) will receive weight-based 35 mg or 50 mg weekly subcutaneous injections of taldefgrobep vs matching placebo. Patients must have genetically confirmed 5q autosomal recessive SMA with SMN2 copy number and plan to remain on the same SMN upregulator regimen throughout the study. Patients who have previously received treatment with a myostatin inhibitor are excluded. The primary outcome measure is change in the 32-item Motor Function Measure from baseline to Week 48.

Results: Study recruitment is in progress.

Conclusion: This phase 3 study aims to investigate the efficacy and safety of taldefgrobep as an adjunctive treatment with SMN upregulators in patients with SMA.

Disclosure: LL, IQ, CB, SD, DC, JM, and VC are employed by and hold stock/stock options in Biohaven.

EPO-200

Allelic variants at atypical parkinsonism loci influence phenotypic variability in amyotrophic lateral sclerosis

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Background and aims: Among the group of atypical parkinsonisms, progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) share common genetic, pathological, and clinical features with the frontotemporal dementia (FTD)/amyotrophic lateral sclerosis (ALS) spectrum. Here, we investigated whether genetic risk factors for PSP and CBD might influence phenotypic variability in ALS.

Methods: We extracted genotype data of 16 single nucleotide polymorphisms (SNPs) associated with PSP and CBD from a cohort of 865 ALS patients. For each SNP, demographic and clinical features were compared across genotypes by additive, dominant, and recessive genetic models.

Results: The minor alleles of the rs2011946 (CXCR4), rs12203592 (IRF4) and rs7035933 (GLDC) SNPs were associated with reduced survival. The major allele of rs1768208 (MOBP) was correlated with reduced age at onset and higher frequency of classical ALS phenotype, whereas the minor one with cognitive impairment. Bulbar onset was overrepresented among the homozygotes for the major allele of rs7571971 (EIF2AK3). More severe behavioral symptoms were found in carriers of the minor alleles of rs242557 (MAPT H1c), rs759162 (EGFR) and rs199533 (NSF), as well as the major one of rs2011946 (CXCR4). The homozygotes of the rs759162 (EGFR) minor allele showed also higher lower motor neuron involvement and an increased progression rate.

Conclusion: Overall, our study provides evidence that genetic risk factors for PSP and CBD contribute to phenotypic variability of ALS patients, thus further supporting the hypothesis of a common neurodegenerative pathway linking the FTD/ALS spectrum and 4R-tauopathies.

Disclosure: Nothing to disclose.

EPO-201

Abstract withdrawn

Cerebrovascular diseases 2

EPO-202

Gender-specific relationship between homocystein levels and carotid atherosclerosis in apparently healthy individuals

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Background and aims: Several epidemiological studies have shown that hyperhomocysteinemia is a risk factor for cardiovascular disease and stroke in both men and women, presumably by accelerating vascular atherosclerosis. However, the contribution of gender for homocysteine-driven atherosclerosis is still matter of controversy.
Methods: In this study we aimed to investigate the gender-specific effects of homocysteine serum levels on indicators of carotid atherosclerosis (i.e. intima–media thickness (IMT) and plaque characteristics) in apparently healthy individuals. For this, recruited individuals aged ≥18 years underwent comprehensive medical history collection, physical examination, blood sampling, and carotid Doppler-Duplex ultrasound.
Results: The study included 300 apparently healthy subjects with a mean age of 49.9±14.5 years, including 180 (60%) women and 120 (40%) men. High levels of homocysteine were observed in 166 (55%) subjects, with comparable women to men ratio. Seric homocysteine levels significantly correlated with IMT ($r=0.18$, $p<0.001$), number of carotid plaques ($r=0.24$, $p<0.001$), and total plaque area ($r=0.25$, $p<0.001$) in women but not in men. Subjects with elevated homocysteine displayed higher values of IMT ($t=-2.6$, $p=0.008$), higher number of carotid plaques ($Z=-2.5$, $p=0.01$), and higher total plaque area ($Z=-2.5$, $p=0.008$) compared to subjects with normal homocysteine levels. Seric levels of homocysteine yielded an AUC of 0.68 (95% CI 0.54-0.82) and 0.64 (95% CI 0.57-0.71) in discriminating women with normal/abnormal IMT and women with/without plaques, respectively.
Conclusion: Our findings suggest that only women show a specific association between seric homocysteine levels and carotid atherosclerosis, considered a subclinical marker of stroke risk.
Disclosure: Nothing to disclose.

EPO-203

Economic evaluation of direct oral anticoagulants for stroke prevention in Spain: systematic review

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Background and aims: Direct oral anticoagulants (DOAC) have proven efficacy for preventing stroke in patients with non-valvular atrial fibrillation (NVAF). Limitations in economic resources and the expense of many new treatments make it necessary to allocate health spending as effectively as possible. The aim of this study was to perform a systematic review of the cost-effectiveness analysis of DOAC in the prevention of stroke in patients NVAF in Spain.
Methods: A systematic search in Pubmed, Embase, Cochrane, Web of Science and MEDES databases was carried out from January 2010 to March 2020 to identify Spanish economic evaluations of DOAC in the prevention of stroke in patients with NVAF.
Results: Ten published economic evaluations through Markov models were identified, all of them were conducted from the National Health Service (NHS) perspective, and 6 also included the societal perspective. The most studied drug was apixaban (n=7). Incremental cost-effectiveness ratios (ICER) were within the willingness-to-pay thresholds in Spain (€25,000–€30,000) in all cases. ICER when DOAC were compared alone to VKA was €17,581 for dabigatran, €12,825 for apixaban, €11,247 for rivaroxaban, and €11,518 for edoxaban. ICER of apixaban versus aspirine was €6,289. One model compared dabigatran, apixaban and rivaroxaban to VKA (ICER of €6,397, €8,039, and €29,957 respectively) and each other (dabigatran was the dominant alternative, followed by apixaban). Four models compared apixaban to the other DOAC and showed that it is cost-effective from NHS perspective (median ICER of €4,972.76).
Conclusion: DOAC are cost-effective therapeutic alternatives for stroke prevention in patients with NVAF in Spanish economic evaluations.
Disclosure: Nothing to disclose.

EPO-204

The Burden of Stroke Mimics Among Hyperacute Stroke Unit Attendees with Special Emphasis on Migraine

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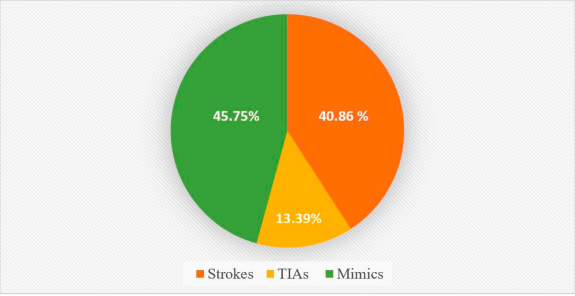
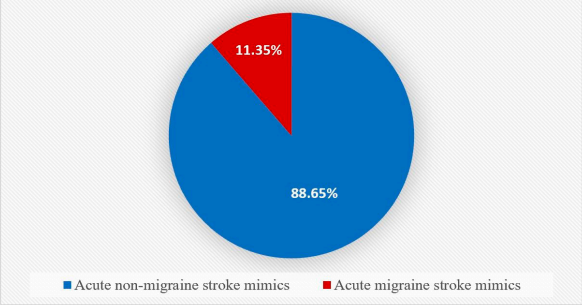
Background and aims: The hallmark of a stroke is the sudden onset of focal neurological impairment. Since many treatments for acute stroke are time dependent, it is important to find acute ischemic insults as rapid as possible. On the other hand, stroke overdiagnosis, formerly known as stroke mimics, may result from the pressure to make quick diagnostic and therapeutic judgments. The main goals of this study are to look at the prevalence of stroke mimics on the stroke pathway and how many of them are migraines.
Methods: A retrospective service evaluation was conducted at the hyperacute stroke unit of the Royal Hallamshire Hospital in the United Kingdom. The total admissions from 2013 to 2022 were collected and the number of stroke mimics was evaluated in each year. Then a one-year sample of stroke mimics was extracted to look for the types of each mimic.
Results: During the last ten years, 45.75% of the stroke pathway patients (26,573) were stroke mimics, with an increment of up to 55% in the last two years. During these ten years, migraine stroke mimics accounted for 11.35% of admissions. The three most common mimics in a one-year sample of the stroke pathway patients were migraine (14.70%), functional neurological disorders (7.17%), and peripheral neuropathies (6.66%). Seizures, syncope, and metabolic derangements were reported as a mimic in 4.17%, 3.14%, and 1.77%, respectively.



The diagnosis of all patients presented to HASU in the last 10 years



The burden of migraine stroke mimics over 10 years

Stroke Mimics Diagnosis	Frequency	Percentage
Migraine	373	14.70%
Functional neurological disorders	182	7.17%
Guillain Barre syndrome and other peripheral neuropathies	169	6.66%
Headaches excluding migraine	148	5.83%
Unknown diagnosis	144	5.67%
Spinal cord and disc lesions	135	5.32%
Facial palsy	126	4.96%
Vestibulocochlear disorders	115	4.53%
Unspecified dizziness	110	4.33%
Seizures	106	4.17%
Disorders of skin sensations	105	4.14%
Ophthalmological disorders	102	4.02%
Unspecified speech disorders	87	3.42%
Syncope and hypotension	80	3.14%
Parkinson disease and related movement disorders	60	2.36%
Systemic infections	55	2.16%
Myopathy and myasthenia gravis	52	2.05%
Anaemia and fatigue	51	2.01%
Multiple sclerosis and other demyelinating diseases	48	1.89%
Nutritional deficiencies and Metabolic derangements	45	1.77%
Brain tumours	41	1.61%
Undiagnosed brain disorders	37	1.45%
Alzheimer disease and other dementia	33	1.30%
Motor neuron disease and spinal muscular atrophy	32	1.26%
Head trauma	28	1.10%
Brain infections	24	0.94%
Cerebellar ataxia	18	0.70%
Postoperative complications	12	0.46%
Gastro-intestinal swallowing disorders	10	0.39%
Hypertensive encephalopathy	4	0.15%
Drugs side effects	4	0.15%

The type of stroke mimics in a one year sample

Conclusion: About half of hyperacute stroke unit attendees were stroke mimics rather than actual strokes and the most common mimics were migraines.
Disclosure: The authors declares that they do not have an conflicts of interests.

EPO-205

Relationships between serum Neurofilament Light Chain and blood inflammatory markers in acute ischemic stroke patients

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Background and aims: Serum neurofilament Light chain (NfL) is a reliable biomarker of axonal injury in many neurological disorders, including stroke. We aimed to study the relationship between NfL and blood inflammatory markers, comprising interleukin-6 (IL6).
Methods: In this longitudinal prospective observational study we included patients with acute ischemic stroke fulfilling these criteria: >18y, onset <24h, NIHSS >1, pre-stroke mRS=0–1, evidence of acute stroke at neuroimaging. Exclusion criteria: >80y, TIA, previous stroke/traumatic head injuries, other neurological disease, immunosuppression before stroke, eGFR<30mL/min, pregnancy. Patients were treated as standard of care, routine blood tests done upon admission. IL6 and NfL serum concentrations were determined with Ella Automated Immunoassay System on samples collected within 24h from onset (T0), after 3–5 days (T1) and 7+2 days (T2).
Results: We included 21 patients (16 males, mean age 61[±17.23]); 66.7% with minor, 23.8% moderate, 9.5% severe stroke. Median values were IL6=6.98 pg/mL (IQR 6.93), NfL=25 pg/mL (IQR 47). IL6 did not change across time-points, while NfL was higher at T2vs.T0 (p=0.006). IL6 and NfL correlated with each other at all time-points. Both biomarkers positively correlated at T0 with CRP (IL6 p<0.001; NfL p=0.002) and negatively with lymphocytes (IL6 p<0.005; NfL p=0.04). NfL retained significancy also at T1 and T2 for CRP, and at T1 for lymphocytes.
Conclusion: Increased NfL serum concentrations are associated with blood inflammatory markers in the acute setting of ischemic stroke. These preliminary results are part of a larger Study to identify a biomarker panel to better characterize the physiopathological complexity and clinical evolution of ischemic stroke patients.
Disclosure: Nothing to disclose.

EPO-206

Transient Hypertension in Transient Global Amnesia: a single center observational study

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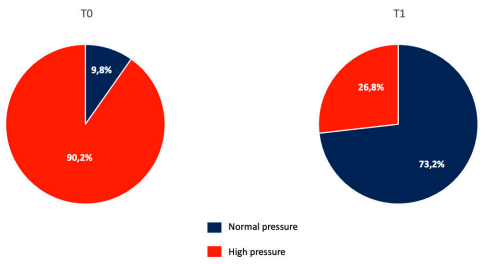
Background and aims: Transient Global Amnesia (TGA) is a syndrome with an unclear pathophysiologic mechanism. Different hypotheses and trigger factors have been proposed [1]. This study aimed to evaluate the incidence of arterial hypertension in patients with TGA to identify its causative role in support of the vascular hypothesis.
Methods: We retrospectively examined data of patients affected by TGA according to Hodges and Caplan criteria [2], who were admitted to the Neurology Unit of the University of Messina, from December 2012 to December 2020. Blood pressure (BP) was recorded on admission and at 24 hours after the TGA onset. High BP was defined as a systolic BP≥140 mmHg and/or a diastolic BP≥90 mmHg.
Results: We selected 41 patients, 22 males (53.7%). The mean age at the TGA attack was 63.3 years. A hypertension history was present in 27 patients (67.5%). On admission, 37 patients (90.2%) had a high BP, SBP was 160.85±26.05 mmHg and DBP was 88.15±14.93 mmHg. At 24 hours, 11 (26.8%) had a high BP, SBP was 124.88±15.47 mmHg and DBP was 74.17±9.54 mmHg. A significant decrease in SBP and DBP was observed comparing BP at the two different time points (p-value <0.0001).



Blood Pressure in T0 and T1

Conclusion: This study described BP trend in TGA patients. We observed an admission high BP during the TGA attack, whereas BP was normal at 24 hours. Our analysis showed a significant difference between T0 and T1, providing further evidence of transitory high BP as possible TGA trigger.
Disclosure: In the interest of transparency, I disclose all relationships/activities/interests related to this manuscript.

EPO-207

Clinical determinants of late diagnosis and recurrence in patients with stroke associated with antiphospholipid syndrome

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Background and aims: Antiphospholipid syndrome (APS) is characterized by arterial or venous thrombosis, in the presence of antiphospholipid antibodies. Stroke is one of its most common complications. Objectives: to characterize APS associated with stroke, clinical determinants of late diagnosis, treatment and recurrence, and compare them with APS with non-stroke manifestations.
Methods: Retrospective cohort study of patients diagnosed with APS between 2018–2022 with and without stroke. Descriptive and comparative analysis of different variables and comparative study using chi-square, t-tests, and non-parametric tests when applicable.
Results: 88 patients were included, 42 of which had stroke. 52.3% were women, mean age at diagnosis was 56-year-old (20-84, SD=16.9). The most frequent vascular risk factors (VRFs) were hypertension, dyslipidemia, and smoking. In 48% of the cases, stroke was the first event. The most common presentations were ischemic stroke (59.5%), TIA (19%), and cerebral venous thrombosis (16.7%). APS diagnosis was made in the first stroke episode in 54.8%. 40.5% had recurrency and it was correlated with hypertension (p=0.002) and diabetes (p=0.032). APS was more likely to manifest with stroke in men (p=0.002) and those with more VRFs, particularly smoking habits (p=0.029). Patients with stroke were less likely to be diagnosed with APS in the first event (p=0.001), start anticoagulation in the first episode (p=0.002) and have a higher number of recurrent events (p=0.001).
Conclusion: Prompt diagnosis, risk-factor control, particularly smoking cessation, and anticoagulation are crucial to prevent stroke and its recurrence in patients with APS. APS remains a challenging diagnosis and requires a high suspicion, particularly in patients with recurrent strokes.
Disclosure: Nothing to disclose.

EPO-208

5-Year survival and cognitive changes in patients with cerebral small vessel disease

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Background and aims: Cerebral small vessel disease(cSVD)is a common disease of the adults and elderly with a high contribution to disability and mortality. Research objective: to investigate the five-year survival,cognitive and MRI changes in patients with cSVD and cognitive impairment(CI).
Methods: 54 patients with cSVD,CI and the widespread white matter hyperintensity(WMH) were observed prospectively during 5 years (average age were 60.51±6.76, women – 37 (20%)). 22 patients undergo an extended examination with an interval of 5 years. Cognitive functions with the definition of the type of CI, diagnostic MRI signs, volumes of WMH,white and gray matter, cerebrospinal fluid(CSF), microstructural changes of the brain were assessed (Fig1). Relationships between cognitive and MRI indicators were clarified.
Results: Over 5 years, the mortality rate was 14% and dementia acquired in 14%. Increasing severity of CI is noted in the domain of executive functions and memory with rising of mixed type of CI.WMH and CSF volume widening, reducing the volume of white matter and axial diffusion in the corpus callosum were exposed (Table1). CSF volume was correlated with Stroop test results and delayed memory (r=0.803 and r=-0.701), white matter atrophy (r=-0.256), and the last one – with axial diffusion in the corpus callosum (r=-0. 560, Table2).

Parameter	CSVD 2016/2017 n=22 mean±SD	CSVD 2021/2022 n=22 mean±SD	p
Volume of white matter hyperintensity(sm^3)	29,80±20,40	36,57±21,83	**<0,05**
Total volume of grey matter (sm^3)	608,88±44,55	609,91±47,55	0,76
Total volume of white matter (sm^3)	493,36±41,27	460,12±45,31	**<0,05**
Volume of cerebrospinal fluid (sm^3)	343,04±74,50	374,57±83,71	**<0,05**
Axial diffusion, 10^{-3} (mm^2/sec)			
Corpus callosum	1,306±0,20	1,307±0,17	**<0,05**
Cingulate gyrus	2,191±0,25	2,017±0,20	0,217
Abbreviations: CSVD – cerebral small vessel disease.			

Table 1. MRI parameters in patients with CSVD in dynamic

	Test of «memorizing 10 words», delayed playback	Stroop test	White matter volume	Volume of CSF	Volume of white matter hyperintensity (WMH)	Axial diffusion in the corpus callosum
Test of «memorizing 10 words», delayed playback	1					
Stroop test	**-,792****	1				
Volume of white matter	,315	-,138	1			
Volume of CSF	**-,701****	**,803****	**-,256***	1		
Volume of white matter hyperintensity (WMH)	-,353	,444	-,215	,420	1	
Axial diffusion in the corpus callosum	-,393	,289	**-,560***	,336	,407	1

Table 2. Correlation between cognitive tests results and MRI parameters in dynamic

Conclusion: cSVD with widespread WMH is characterized by high mortality and an increase in dementia. The general cognitive level and MRI signs have insufficient sensitivity in assessing disease progression over a 5-year period. The Stroop test, memory (delayed reproduction of the 10-word test) and the transition to a mixed type of CI reflect the progression of CI and can be used for dynamic assessment. cSVD in the advanced stage affects the deterioration of cognitive functions through atrophy and changes in CSF circulation.

Disclosure: The study was supported by Grant No.22-15-00183 of the RussianScienceFoundation; https://rscf.ru/project/22-15-00183.

EPO-209

Blood pressure control and stroke outcome at Douala General Hospital

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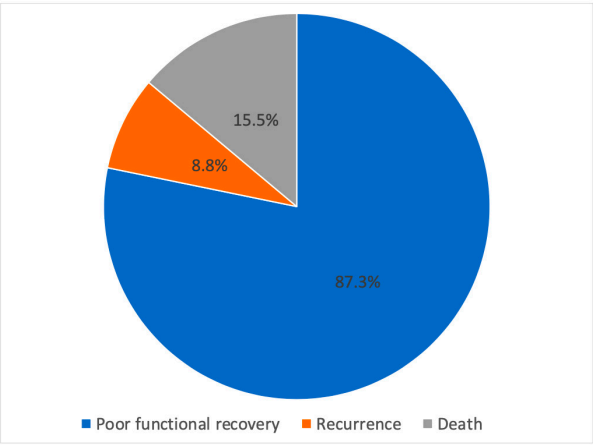
Background and aims: Hypertension (HTN) is the major risk factor for the occurrence of strokes. Uncontrolled hypertension is a predictive factor for poor outcome during the first episode and recurrence stroke.

Methods: We conducted a retrospective cohort study using stroke records from January 1, 2010 to March 1, 2019 at the HGD. We included all patients aged 21 and over who admitted for a first stroke confirmed by neuroimaging and followed up for 3 years. All patients with chronic kidney disease, sub-arachnoid hemorrhage or cerebral veinous thrombosis were excluded. We collected data (sociodemographic, clinical presentation, investigations, treatment and outcome) according to our survey sheet and analyzed using SPSS 26.0 software and a p value <0.05 was considered statistically significant.

Results: 517 patient files were included with an average age of 58.4±13.4 years (men = 58.8%). The prevalence of poor BP control was 81%. The predictive factors of poor BP control were de novo post-stroke hypertension (p<0.001) and de novo post-stroke diabetes (p=0.008). The factors associated with mortality in patients with poor BP control were: Barthel index≤60 (p<0.001), occurrence of vascular dementia (p=0.036), low level of education (p=0.017).



Outcome of stroke patients with poor blood pressure control

Conclusion: Hypertension is not controlled in more than 4 stroke patients out of five in our setting. Hypertension or diabetes discovered during the first stroke would promote poor BP control. Functional dependence, dementia and low level of education would increase the risk of death in stroke patients with poor BP control.

Disclosure: Nothing to disclose.

EPO-210

Prevention strategy of patients with concomitant atrial fibrillation and intracranial stent after acute ischemic stroke

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Background and aims: Intracranial stenosis treatment in the long-term in patients with atrial fibrillation (AF) remains unknown. There is no scientific evidence that confirms that the strategy validated in the AUGUSTUS trial (AF and acute myocardial infarction) can be applied to patients with AF and intracranial stents. We present our experience.
Methods: Retrospective study with prospective gathering of patients with ischemic stroke treated in our hospital with intracranial stent within 2017-2022. Demographic, clinical and radiological variables were gathered. We compared security and efficacy among patients with and without AF.
Results: Twenty-seven patients with intracranial stent were included (74.1% males, median age of 67.18±16.85, 59.2% with hypertension, 44.4% with dyslipidemia, 25.9% diabetic, 33.3% had AF (55.5% with recent diagnosis). Eighteen patients had permeable stent in the early control (100% of "Augustus like" AF group vs 80% of "no Augustus like" AF group vs 62.5% of AF group, p=0.032) and 6 patients died (0% of "Augustus like" AF group vs 33.3% of "no Augustus like" AF group vs 16.6% of no AF group, p 0.081). The most frequent strategy in the AF group was the combination of antiplatelet monotherapy and anticoagulation therapy. In the follow-up, 2 patients presented stent occlusion, both in no AF group (p=0.55). One patient from the "Augustus like" AF group had a major hemorrhagic complication. No patients had new ischemic events.
Conclusion: In our series, the combination of one antiplatelet and anticoagulation in secondary prevention strategy for patients with AF and intracranial stent resulted effective and safe in our experience.
Disclosure: Nothing to disclose.

EPO-211

Hemorrhagic transformation and non-CNS complications after iv. thrombolysis: a brain and body autopsy study

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Background and aims: The intravenous thrombolysis is a significant advancement in the treatment of acute ischemic stroke. Since imaging and detailed clinical examination of stroke patients is not always possible in the agony phase, only the autopsy can provide us reliable data about the frequency of complications.
Methods: Between 2007–2017, 1.426 venous lysis were performed in our department and we had access to the clinical and brain/body autopsy data of 98 (6,9 %) patients treated with iv. lysis 0.9 mg/kg rt-PA, following the international guideline, but died during the clinical period.
Results: We diagnosed 20 hemorrhagic transformation (HT) (20.4%) on the last CT before death: P1:4 P2:8 H1:1 H2:3 (in 4 cases, bleeding occurred in the non-ischemic brain area). On brain autopsy we diagnosed other 26 patients (26.5%), whose HT occured between the period of the last premortal CT and death. We compared the clinical data of patients with HT complications (46) with those, whose brain autopsy did not show HT (52). Admission INR 1.03[0.93–1.04], 1.05[0.96–1.09] P:0.043 and lower platelet count 188, 4 [150.0–227.0] 226.6 [171.0–264.0], p=0.011 increased the risk of a HT. During the autopsy, 2 malignant tumors, 4 thromboembolic complications (+3 aortic thrombus), and 10 pneumonias were detected, but not diagnosed premortal.
Conclusion: The brain and body autopsy provide more reliable data on complications of iv. thrombolysis patients with fatal outcome. The correlation between INR/platelet and increased risk of HT and/or fatal outcome is of clinical importance and need further investigations.
Disclosure: None. Supported by the grant of ELKH-DE CerebrovascularHemor Research Group.

EPO-212

Comorbid conditions in COVID-19 associated ischemic stroke

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Background and aims: To study the relationship between COVID-19 associated ischemic stroke and comorbid conditions.
Methods: We analyzed 176 cases of hemispheric IS.The patients were divided into two groups.The main group consisted of 72 patients with hemispheric IS and laboratory-confirmed coronavirus infection.The control group consisted of 104 patients with hemispheric IS who did not have a history of COVID-19.
Results: In both groups, the following comorbid diseases of the cardiovascular continuum were analyzed: arterial hypertension was the most common of them and had the same prevalence in both groups (94 and 98%,respectively). Atherosclerosis was also a common risk factor; in the group of patients who had undergone COVID-19, it was detected in 57% of cases (n=41), and in the control group it was statistically significantly more common in 82%(n=85) of cases ($p<0.002$). Diabetes mellitus as a risk factor for the development of IS significantly prevailed in the group of patients with concomitant COVID-19 (16%) compared with the control group (7%)($p<0.037$). Atrial fibrillation in both groups was detected in the same number of patients(19%). IHD (history of acute myocardial infarction or angina pectoris) in the group of patients with COVID-19 was observed in 37%(n=27) of cases, while in patients without this infection it was detected in 32%(n=33) of cases ($p<0.077$).
Conclusion: The results obtained showed that diabetes mellitus was significantly more common in patients with stroke in combination with COVID-19,which can be explained by the role of endothelial dysfunction in the pathogenesis of COVID-19 associated stroke, which most likely determines the course of IS.
Disclosure: Nothing to disclose.

EPO-213

Glycated Albumin and IL-10 are associated with Obesity in Hyperacute Ischemic Stroke

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Background and aims: There is growing interest in the use of new biomarkers such as glycated albumin (GA). In contrast to glycated hemoglobin (HbA1c), GA showed an inverse correlation with prestroke obesity status, but data are limited for ischemic stroke (IS).
Methods: We explored the association between GA and body mass index (BMI) and investigated inflammatory cytokines to support the academic background. In total, 155 patients with hyperacute IS (HIS) between 2011 and 2019 were included. To identify the association between GA and BMI, patients were divided into four groups according to BMI quartiles. Levels of inflammatory cytokines, including IL-1β, IL-10, IL-6, TNF-α, and TNF-R1, were determined by ELISA using a ProcartaPlex multiplex immunoassay.
Results: The mean age of the 155 patients was 68±12 years, and 67.1% were men. The lowest BMI group had higher GA levels (GA 2T and 3T=80%) (p-value=0.017), and these U-shaped associations were maintained only for small vessel occlusion etiology (p-value=0.004). Plasma IL-10 levels were positively correlated with BMI and showed a U-shaped pattern (p-value=0.001).
Conclusion: GA levels and BMI had U-shaped associations with HIS. IL-10, which acts as a protective cytokine for cardiovascular disease, may play a novel role in this association. Although GA is an emerging favorable clinical marker of cardiovascular outcomes, obesity status should be considered when interpreting these associations.
Disclosure: Nothing to disclose.

EPO-214

Occlusion Pattern and Clinical Outcome in Acute Large Vessel Occlusion with Intracranial Stenosis

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Background and aims: To investigate whether angiographically defined occlusion location could affect the periprocedural and clinical outcomes of the acute middle cerebral artery (MCA) occlusion associated with intracranial atherosclerotic stenosis (ICAS) and the rescue stenting response.
Methods: We reviewed consecutive patients with acute MCA occlusion associated with ICAS who underwent intracranial stenting and balloon angioplasty after initial mechanical thrombectomy. Patient demographic findings, baseline characteristics, clinical outcomes, and periprocedural complications including in-stent thrombosis and re-occlusion were compared according to the anatomical occlusion location. The occlusion location was divided according to the presence of the proximal MCA stump in enrolled ICAS patients.
Results: Of 44 patients, 30 (68.4%) were classified as having a stump group. When initial NIHSS was compared between the groups, the without stump group was more severe than the with stump group (14.0 (8.0–17.0) vs. 7.5 (6.0–13.0) p=0.044), and received intravenous thrombolysis was more prevalent in the without stump group (71.4% vs. 16.7%, p=0.001). There were no significant differences in procedure time, technique, and devices. However, the successful revascularization rate was significantly lower in the without-stump group (57.1% vs. 100%, p=0.001). Additionally, the immediate re-occlusion rate after the first endovascular reperfusion therapy was a higher tendency in the without-stump group (71.4% vs. 36.7%, p=0.068). However, no significant association was found between periprocedural complications including intracerebral hemorrhage and mortality.
Conclusion: Angiographically presented MCA occlusion without stump in patients with ICAS, predicts complicated intracranial stenting and poor clinical outcome.
Disclosure: Funding This work was supported by a research grant from Jeju National University Hospital in 2022 Competing interests The authors declare that they have no competing interests.

EPO-215

Acupuncture for Spontaneous Intracerebral Hemorrhage; A Systematic Review and Meta-analysis

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Background and aims: This is a systematic review and meta-analysis of randomized clinical trials (RCTs) to figure out the efficacy of acupuncture treatment for patients with spontaneous intracerebral hemorrhage (s-ICH).
Methods: We searched publications in MEDLINE via Pubmed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), CiNii, and several Korean databases. After eligibility assessment, 14 studies that compared acupuncture treatment added to western conventional treatment with only western conventional treatment for s-ICH were included in this systematic review and meta-analysis.

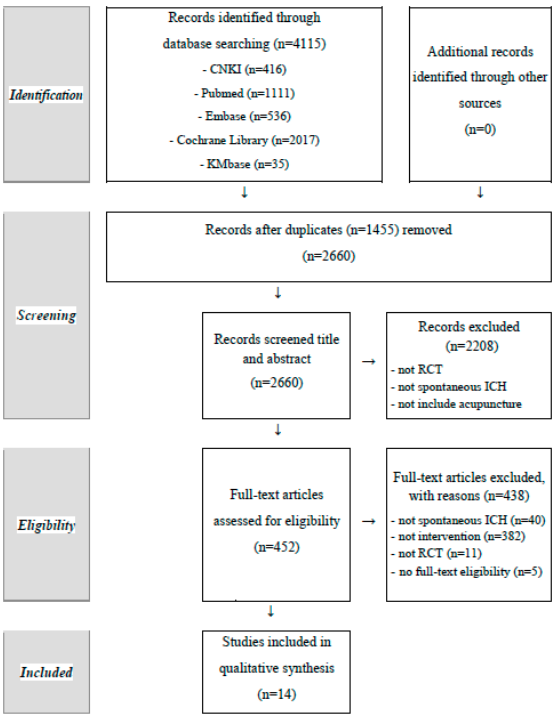

Figure 1. Flow chart of study selection

Fig 1. Flow chart of study selection

Results: The pooled meta-analysis showed the statistical significance in Chinese Stroke Scale (CSS) score [MD 3.61, 95% CI 2.82–4.40], Fugl-Meyer assessment (FMA) score of lower extremity [MD 4.30, 95% CI 3.50–5.11], Barthel Index [MD 8.58, 95% CI 5.95–11.21], and clinical efficacy rate (CER) [n=557, RR 3.51, 95% CI 2.39–5.16]. Subgroup analysis also showed the significant effect of acupuncture treatment in CSS scores of acute phase [MD 3.20, 95% CI 2.26–4.14] and subacute phase [MD: 3.89, 95% CI: 2.34–5.44] and CER of acute phase [n=144, RR: 2.59, 95% CI: 1.30–5.18] and subacute phase [n=228, RR 2.38, 95% CI 1.21–4.68]. There were similar results in hypertensive intracerebral hemorrhage, which is a subgroup of s-ICH.

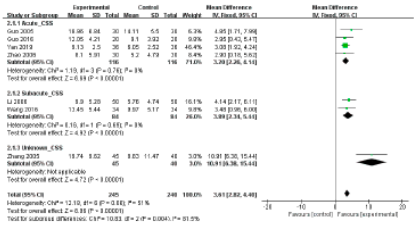

Figure 2. Forest plots of meta-analysis of CSS on acute and subacute phase. Comparison; acupuncture plus western conventional treatment vs western conventional treatment alone

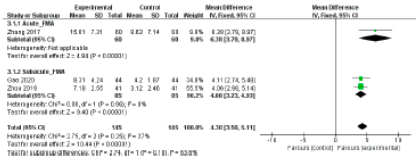

Figure 3. Forest plots of meta-analysis of FMA of lower extremity on acute and subacute phase. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone

Figure 4. Forest plots of meta-analysis of BI. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone.

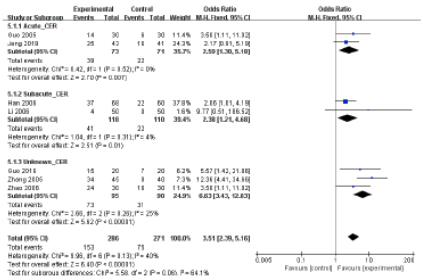

Figure 5. Forest plots of meta-analysis of modified CER on acute and subacute phase. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone

Result 1; meta analysis

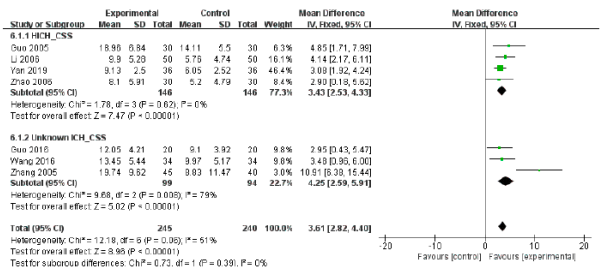

Figure 6. Forest plots of meta-analysis of CSS on ICH. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone

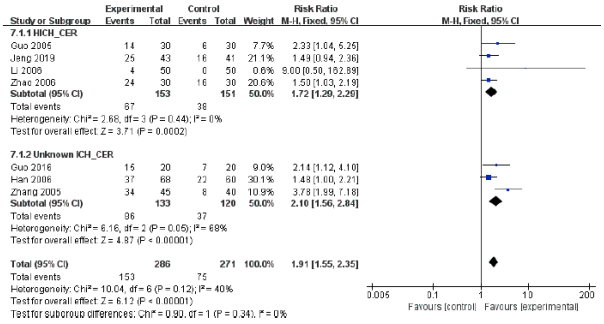

Figure 7. Forest plots of meta-analysis of modified CER on ICH. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone

Result 2; meta analysis

Conclusion: Acupuncture appeared to be effective in neurological impairment in s-ICH. Also, acupuncture helps not only recovering motor function, but also improving activities in daily living.

Disclosure: There are no financial conflicts of interest to disclose.

EPO-216

Deficit in topographical orientation - relation to the affected cerebral hemisphere after stroke

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Background and aims: About 90% of stroke survivors have sequels and cognitive impairment is the most prevalent one. Injury to cortical and subcortical right structures may impair topographic orientation with impact on daily living activities. The aim of this study was to estimate the frequency and characterize impairments of topographic orientation in patients, in a chronic phase, after stroke.
Methods: In this observational cross-sectional case-control study, we performed a subjective (Questionnaire on Everyday Navigational Ability) and an objective assessment of topographic orientation, through topographical tests. In the stroke group, we apply others tests to evaluate the perceptual-cognitive and functional deficits and its impact.
Results: 44 stroke patients (left stroke group, n=23; right stroke group, n=21) and 44 control individuals matched for gender, age and schooling were included. There was a significative difference of subjective assessment of topographical disorientation between the stroke group and the controls. Complaints were more frequent in the right stroke group (42.9%) compared to the left stroke group (8.7%) and to controls (2.3%). Furthermore, right stroke group performance was significantly worse (21.5 points) on the topographical location test, a test of allocentric orientation, than the others. The score on topographic imagery test and topographic location test of patients with neglect was significantly worse compared to patients without neglect.
Conclusion: This indicates a higher frequency of topographic impairment in subjective complaints and objective performance in patients with right hemisphere lesions. Neglect may partially mediate these impairments. Our work reinforces the need to evaluate topographical orientation after right hemisphere stroke.
Disclosure: There isn't relation of interest related to this manuscript.

Muscle and neuromuscular junction disorder 2

EPO-217

Treatment differences between Black and non-Black patients with gMG receiving eculizumab in the United States

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Background and aims: Racial inequities have been observed in healthcare access and treatment. Myasthenia gravis (MG) is a rare autoimmune neuromuscular disease resulting in muscle weakness and functional impairment affecting 6.2% of Black patients in a US-based registry. This study explored differences in treatment and care approaches between Black and non-Black patients with generalized MG (gMG) receiving eculizumab in the USA.

Methods: This retrospective analysis of data from an observational study used physician-reported electronic medical record data from adults (≥18 years) with gMG from 14 sites in the USA. gMG status and treatment 2 years before and 2 years after eculizumab initiation were analysed for Black and non-Black patients.

Results: Black patients (n=19) were predominantly female, diagnosed at a younger age, had a longer time from diagnosis to initiation of eculizumab, and initiated eculizumab with higher disease severity compared with non-Black patients (n=100; Table 1). More Black patients were treated in academic centres and had commercial insurance compared with non-Black patients (Table 1). Prior to eculizumab initiation, prednisone, pyridostigmine and long-term intravenous immunoglobulin were prescribed less frequently, and rituximab prescribed more frequently in Black patients than non-Black patients (Figure 1). At eculizumab initiation, fewer Black patients received prednisone and non-steroidal immunosuppressive therapy than non-Black patients, but more were receiving long-term plasma exchange (Figure 2).

Characteristic	Black patients (n = 19)	Non-Black patients (n = 100)	All patients (N = 119)
Sex at birth, n (%)			
Male	3 (15.8)	45 (45.0)	48 (40.3)
Female	16 (84.2)	55 (55.0)	71 (59.7)
Age at gMG diagnosis, years, mean (SD)	33.3 (15.7)	53.8 (20.0)	50.5 (20.7)
Race, n (%)			
White	0 (0.0)	96 (96.0)	96 (80.7)
Black	19 (100.0)	0 (0.0)	19 (16.0)
Asian	0 (0.0)	2 (2.0)	2 (1.7)
American Indian/Alaskan Native	0 (0.0)	1 (1.0)	1 (0.8)
Other	0 (0.0)	1 (1.0)	1 (0.8)
AChR antibody status tested, n (%)	18 (94.7)	100 (100.0)	118 (99.2)
Seropositive	16 (84.2)	98 (98.0)	114 (96.6)
Seronegative	1 (5.3)	1 (1.0)	3 (2.5)
Unknown	1 (5.3)	1 (1.0)	1 (0.8)
Insurance status, n (%)[a]			
Medicare	6 (31.6)	56 (56.0)	62 (52.1)
Medicaid	3 (15.8)	7 (7.0)	10 (8.4)
Commercial	13 (68.4)	40 (40.0)	53 (44.5)
Military	0 (0.0)	2 (2.0)	2 (1.7)
Information not provided	0 (0.0)	1 (1.0)	1 (0.8)
Time from diagnosis to eculizumab initiation, years, mean (SD)	10.2 (10.0)	7.5 (9.8)	7.7 (9.8)
Age at initiation of eculizumab therapy, years, mean (SD)	43.2 (12.9)	61.1 (17.0)	57.7 (17.7)
MG-ADL score before eculizumab initiation, mean (SD)[b]	9.3 (4.8)	7.7 (3.6)	8.0 (3.8)
Primary setting, n (%)			
Academic medical centre	15 (78.9)	50 (50.0)	65 (54.6)
Large PCP (> 10 physicians) owned by a hospital	0 (0.0)	10 (10.0)	10 (8.4)
Large PCP (> 10 physicians)	0 (0.0)	23 (23.0)	23 (19.3)
Medium-sized PCP (6–10 physicians) owned by a hospital	2 (10.5)	13 (13.0)	15 (12.6)
Medium-sized PCP (6–10 physicians)	2 (10.5)	3 (3.0)	5 (4.2)
Solo practice	0 (0.0)	1 (1.0)	1 (0.8)
Region, n (%)			
Midwest	2 (10.5)	34 (34.0)	36 (30.3)
Northeast	0 (0.0)	2 (2.0)	2 (1.7)
South	14 (73.7)	47 (47.0)	61 (51.3)
West	3 (15.8)	17 (17.0)	20 (16.8)

Table 1. Patient characteristics at baseline and primary setting of care and region of treatment

[a]Categories not mutually exclusive. [b]Most recent score before initiation of eculizumab.

AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; PCP, private community practice; SD, standard deviation.

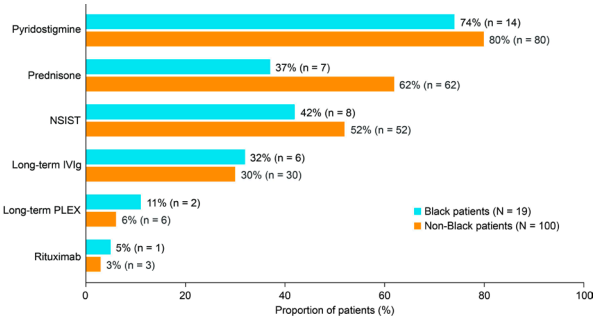

Fig. 2. Patients receiving concomitant therapies at eculizumab initiation
Note: proportions may exceed 100% because patients could have been receiving more than one treatment.
IVIg, intravenous immunoglobulin; NSIST, non-steroidal immunosuppressive therapy; PLEX, plasma exchange.

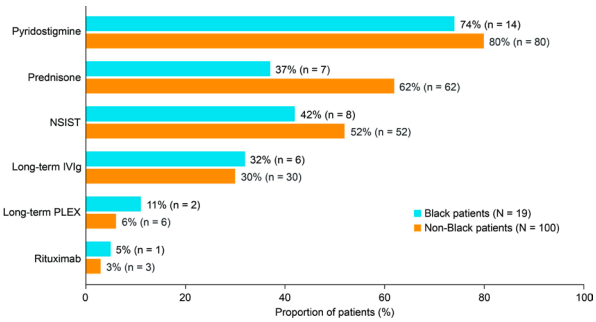

Fig. 2. Patients receiving concomitant therapies at eculizumab initiation
Note: proportions may exceed 100% because patients could have been receiving more than one treatment.
IVIg, intravenous immunoglobulin; NSIST, non-steroidal immunosuppressive therapy; PLEX, plasma exchange.

Conclusion: In clinical practice in the USA, race-based differences were observed in the care and treatment of patients with gMG receiving eculizumab; these differences may indicate health inequities and warrant further investigation.

Disclosure: AAH has received research support from Alexion, AstraZeneca Rare Disease, argenx, Cabealetta Bio, Genentech, Immunovant, Pfizer, Regeneron Pharmaceuticals, UCB Pharma, and Viela Bio (part of Horizon Therapeutics). He has also received fees from Alexion, AstraZeneca Rare Disease, argenx, Immunovant, Regeneron Pharmaceuticals, and UCB Pharma. JFH has received research support (paid to his institution) from Alexion, AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, US), the Muscular Dystrophy Association, the Myasthenia Gravis Foundation of America, the National Institutes of Health (including the National Institute of Arthritis and Musculoskeletal and Skin Diseases, and the National Institute of Neurological Disorders and Stroke), the Patient-Centered Outcomes Research Institute (PCORI), Ra Pharmaceuticals (part of UCB Pharma), and Takeda Pharmaceuticals. He has also received fees from Alexion, AstraZeneca Rare Disease, argenx, Immunovant, Ra Pharmaceuticals (part of UCB Pharma), Regeneron Pharmaceuticals, and Viela Bio (part of Horizon Therapeutics), and nonfinancial support from Alexion, AstraZeneca Rare Disease, argenx; Ra Pharmaceuticals (part of UCB Pharma), and Toleranzia AB. AK and BM are employed by, and own stocks in, Alexion, AstraZeneca Rare Disease. MM is a member of a Scientific Advisory Committee for Alexion, AstraZeneca Rare Disease.

EPO-218

Epilepsy in Dystrophinopathies: Series and review of the literature

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Background and aims: Cognitive and behavioral difficulties occur in approximately a third of patients with Duchenne muscular dystrophy. The aim of our study was to assess the prevalence of epilepsy in a cohort of 222 DMD patients.

Methods: We report the data obtained in 142 DMD patients with mutations from a tertiary neuromuscular center in Istanbul, Turkey.

Results: Epileptic seizures were found in 14 of the 222 DMD patients (6.3%). The age of onset ranged from 3 months to 16 years (mean 7.8). Seizures were more often focal epilepsy (n=6), generalized tonic–clonic seizures (n=4) or absences (n=4). They were present in 12 of the 149 boys with normal IQ (8.1%) and in two of the 73 with mental retardation (2.7%). In two cases the parents did not report any past or present history of seizures but only 'staring episodes' interpreted as a sign of 'poor attention'. In both patients EEG showed the typical pattern observed in childhood absence epilepsy.

Patient no.	Age at 2022 (yr)	Age at onsetof seizures	History of febrile seizure	Family history of epilepsy	Genetics	Seizure type	EEG	Treatment	GMFSC
1	13 yr	5 yr	no	no	del. 48-49	generalized	generalized epileptiform abnormality	LEV	1
2	9 yr	12 m	yes	no	del. 45-50	generalized	theta waves	PHB	2
3	24 yr	7 yr	no	no	del. 49-54	generalized	N	LEV	5
4	10 yr	18 m	yes	no	del. 42-43	generalized	N	-	2
5	9 yr	12 m	yes	no	del. 45-54	generalized	N	LEV	2
6	13 yr	3 yr	yes	no	del. 47-50	generalized	generalized epileptiform abnormality	LEV	2
7	15 yr	2 yr	yes	no	del 23-44	generalized	N	CBZ	1
8	8 yr	12 m	no	no	del. 45-57	generalized	N	PHB	1

Summary of patients

Conclusion: Our results suggest that the prevalence of epilepsy in our study (6.3%) is higher than in the general pediatric population (0.5–1%). The risk of epilepsy does not appear to increase in patients with mental retardation.

Disclosure: Nothing to disclose.

EPO-219

Long-term safety, efficacy & self-injection satisfaction with zilucoplan in myasthenia gravis: RAISE-XT interim analysis

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Background and aims: Long-term data from RAISE-XT (NCT04225871), a Phase 3, multicentre, open-label extension study, will enhance our understanding of the safety, efficacy, and self-injection satisfaction of zilucoplan, a C5 complement inhibitor with dual mechanism of action, in patients with generalised myasthenia gravis (gMG).

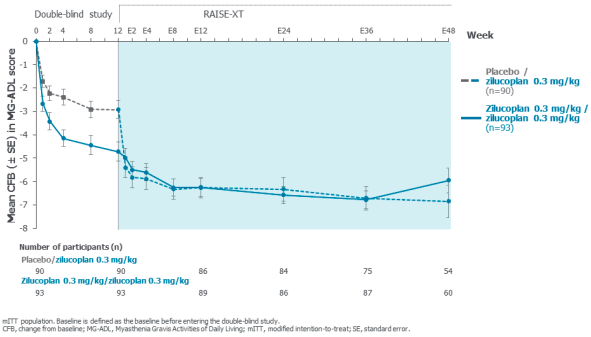
Methods: Adults (aged 18–75 years) with gMG who completed a qualifying zilucoplan study (Phase 2 NCT03315130/Phase 3 NCT04115293 [RAISE]) self-administered daily subcutaneous injections of zilucoplan 0.3 mg/kg. Primary outcome: incidence of treatment emergent adverse events (TEAEs). Secondary efficacy outcomes included change from qualifying study double-blind baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) score. The Self-Injection Assessment Questionnaire (SIAQ; domain scores 0–10; higher scores indicate more positive experience) was completed by US patients directly after self-injection and measured patient satisfaction with self-injection.

Results: At data cut-off (8 September 2022), 200 patients had enrolled in RAISE-XT. Median (range) exposure was 1.2 (0.11–4.45) years. TEAEs occurred in 188 (94.0%) patients; 64 (32.0%) patients experienced a serious TEAE (Table). Mean (standard deviation) changes from double-blind baseline in MG-ADL score continued to decrease through Extension Week 12 and were maintained through to Extension Week 48 (Week E48) for the zilucoplan and placebo-switch groups: −5.95 (4.14) and −6.85 (5.13) at Week E48, respectively (Figure 1). In the SIAQ domain of satisfaction with self-injection, median score was 8.20 (range: 3.9–10.0; n=63; Figure 2).

	All zilucoplan doses (N=200)
Any TEAE, n (%)	188 (94.0)
Serious TEAE, n (%)	64 (32.0)
TEAE resulting in permanent withdrawal from IMP, n (%)	17 (8.5)
Treatment-related TEAE, n (%)	67 (33.5)
Severe TEAE, n (%)	57 (28.5)
TEAEs leading to death, n (%)	4 (2.0)

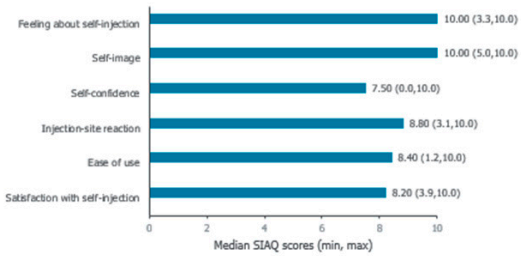
Safety set.
IMP, investigational medicinal product.

Table: Overview of TEAEs



mITT population. Baseline is defined as the baseline before entering the double-blind study.
CFB, change from baseline; MG-ADL, Myasthenia Gravis Activities of Daily Living; mITT, modified intention-to-treat; SE, standard error.

Figure 1: Mean CFB in MG-ADL score to Week E48



All zilucoplan doses, n=63.
For the domain of 'Satisfaction with self-injection', scores ≥8 are indicative of high or very high satisfaction.

Figure 2: SIAQ reported outcomes

Conclusion: In this interim analysis of RAISE-XT, zilucoplan demonstrated a favourable long-term safety profile and sustained efficacy through to Week E48. High satisfaction rates with self-injection were reported. Funding: UCB Pharma.

Disclosure: This study was funded by UCB Pharma. Detailed author disclosures will be provided in the oral/poster presentation.

EPO-220

Longitudinal MGFA-PIS evaluation in a large Italian cohort of patients with Myasthenia Gravis

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Background and aims: Myasthenia Gravis Foundation of America Post-Intervention Status (MGFA-PIS) is the most frequently used outcome measure in myasthenia gravis (MG) to define response to treatment. However, data from literature focused on the MGFA-PIS at the last follow-up, without considering modifications over the years. Aim of this study is to evaluate MGFA-PIS changes and related predictive factors during the disease course.
Methods: We included 754 ocular and generalized MG patients from 2 Italian Neuromuscular Centers, with MG onset between 2000 and 2018 and at least one year of follow-up. MGFA-PIS was determined by a database algorithm comparing INCB-MG and Mingazzini Scores at each timepoint with the previous one.
Results: Mean age at onset was 48.7±18.6 years and mean disease duration 9.1±5 years. Overall, 348 out of 754 patients had generalised AChR-MG without thymoma (46.2%), 72 MuSK-MG (9.5%), 5 LRP4-MG (0.7%), 103 seronegative MG (13.7%), 123 thymoma-MG (16.3%), 103 ocular-MG (13.7%). Complete stable remission (CSR) was reached in 77/754 (10.2%) patients, including 60 (77.9%) patients achieving and maintaining the CSR until the last follow-up and 17 (22.1%) losing CSR after its achievement, usually in first disease stages. In the latter subgroup 4 out of 17 patients then returned to CSR. Among clinical, immunological and thymus parameters, female sex was the only factor associated with the chance of losing the CSR status.
Conclusion: Chance to achieve the CSR did not vary significantly from literature, but our data showed that its modification over time may change in specific MG-subgroups.
Disclosure: LM has received honoraria for speaking, advisory boards and compensation for congress participations from Sanofi Genzyme, Roche, Alexion, Amicus Therapeutics, Lupin and Biogen, outside the submitted work.

EPO-221

The Burden MG patients Experience in Fatigue, Sleep, and Mental Health Compared to the General Population

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Background and aims: Myasthenia Gravis (MG) is a rare, IgG-driven, neuromuscular disorder marked by a variable combination of weakness of eye, bulbar, respiratory, axial and limb muscles, affecting patients' daily life. This analysis uncovers the problems MG patients experience regarding fatigue, sleep and mental health, compared to the general population.
Methods: The MyRealWorld-MG study enrolled MG patients from 9 countries and collected the following data digitally: demographics, Hospital Anxiety and Depression Survey (HADS), PROMIS-Sleep Disturbance and the FACIT-Fatigue. Comparison of the HADS was based on the POPUP digital observational study, which enrolled a representative sample of the general population in similar countries. The PROMIS-Sleep Disturbance and the FACIT-Fatigue comparisons were based on US standardized population norms.
Results: MyRealWorld-MG included 2,074 MG patients, whereas POPUP enrolled 9,000 respondents. Mean (SD) HADS-Anxiety and HADS-Depression scores for MG patients (11.5 (2.4) and 8.9 (2.0) respectively) were indicative of clinical anxiety and depression. These scores were higher than average scores in POPUP, which revealed fewer problems in depression and anxiety (6.4 (4.6), $p<0.001$ and 5.0 (4.1), $p<0.001$). MG patients had significantly higher mean (SD) PROMIS-Sleep Disturbance scores (53.7 (8.1) vs 50.0 (10.0), $p<0.0001$). Finally, the mean (SD) FACIT-Fatigue score of MG patients was markedly worse than the general population (28.9 (11.5) vs 43.5 (8.3), $p<0.0001$), signaling a large impact of MG on fatigue.

Instrument/Domain	Variable	MyRealWorld-MG	Source	P-value
N		N=324	US General Population	
FACIT Fatigue scale	Mean (std)	28.9 (11.5)	43.5 (8.3)	<.0001
		N=251	US General Population	
PROMIS: Sleep disturbance	Mean (std)	53.7 (8.1)	50 (10)	<.0001
N		N=1159	POPUP, N=9000	
HADS Anxiety	Normal	6.7%	63.6%	<.0001
	Mild	23.6%	16.1%	
	Moderate	47.7%	10.9%	
	Severe	21.9%	9.4%	
	Mean (std)	11.5 (2.4)	6.4 (4.6)	<.0001
N		N=1159	POPUP, N=9000	
HADS Depression	Normal	24.2%	84.0%	<.0001
	Mild	57.3%	9.2%	
	Moderate	16.9%	4.2%	
	Severe	1.6%	2.7%	
	Mean (std)	8.9 (2)	5 (4.1)	<.0001

Table 1. Comparison of fatigue, sleep and mental health between MG patients and the general population

Conclusion: A considerable burden in MG patients was found in this direct comparison of mental health, sleep and fatigue with the general population, using data from two international studies and published population norms.

Disclosure: RM has received speaking honoraria from Biomarin, Alexion and UCB, served on advisory boards for Alexion, argenx BV and UCB and received support for congress participation from Merck, Teva and Biogen FS has received public speaking honoraria from Almirall, Biogen, Mylan, Novartis, Roche, Sanofi and Teva; and served on advisory boards for Almirall, argenx BV, Avexis, Biogen, Forward Pharma, Lexeo, Merk, Novartis, Novatek, Pomona, Roche, Sanofi, and Takeda. SP is an employee of argenx BV, the sponsor of the study SD, NT and MFJ have been commissioned by argenx BV and received honoraria to design the study, analyze data and write the abstract.

EPO-222

Spanish Pompe Registry: New data based on the 130 patients included

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Background and aims: Pompe disease is a rare genetic myopathy with two main clinical phenotyp: Infantile Onset Pompe Disease (IOPD) and Late Onset Pompe Disease (LOPD). Epidemiological studies showed a disease prevalence about 1:40,000 but reliable data in Spain in lacking

Methods: Here we analyzed the data of the 130 patients included in the Spanish Pompe, included between 2019 and 2023. We collected information about demographics, family history, clinical features, ancillary tests, functional outcomes and response to treatments from each individual clinical report.

Results: 118 patients were classified as LOPD while 12 had an IOPD phenotype. 70 patients were males (53.85%). Mean age of our population was of 29.75 years old (SD 42.75). 44 had family history of Pompe, being most common place of birth and parent's origin Andalusia, 100 patients were symptomatic. The most frequent symptom reported was lower limb and axial weakness in 60.7%. Ninety-one patients preserved their ability to walk in their last visit. Forty patients required ventilation support (34 non-invasive). Ninety three patients had high levels of CK with a mean value of 716 UI/L (SD 457.99). The most common mutation reported was IVS1-13T>G (c.-13-32T>G) in 85 patients. 89 were treated with Enzyme Replace Therapy. According to our data the Pompe prevalence is 3/1,000,000 in our country.

Conclusion: The Spanish Pompe Registry give us valuable information about the demographics and clinical features of our population of patients with this rare disease. yielding us a lower prevalence than expected.

Disclosure: The SPR received funding from Sanofi-Genzyme.

EPO-223

Evidence-based expert consensus guidance for ongoing assessment of generalised myasthenia gravis (gMG)

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Background and aims: Regular and consistent disease assessment could provide a clearer picture of burden in gMG and improve patient outcomes; however, there is lack of standardisation on use of assessment tools in practice. This modified Delphi consensus was conducted to review current evidence on assessment tool use in gMG and propose expert-derived guidance for good practice.

Methods: A European expert panel comprising 15 experienced gMG neurologists contributed to development of this guidance, four of whom formed a lead Sub-committee. The PICO (population, intervention, control, outcomes) framework was used to define six clinical questions on gMG assessment tools and a systematic literature review was conducted. Consensus was reached when ≥70% of the experts rated agreement with a statement as ≥8 on a scale of 1–10.

Results: 18 guidance statements were developed based on evidence and expert opinion covering six themes: 1) tools for understanding gMG burden in clinical practice, clinical trials/research, and telemedicine; 2) use of depression, anxiety, and fatigue scales in patient assessment; 3) outcomes/symptoms excluded from existing gMG assessment tools; 4) thresholds for clinically important/meaningful differences; 5) assessment of treatment-related burden; 6) assessments supporting treatment decisions. Expert panel consensus was reached on 16/18 statements after one voting round (Table 1).

Statement	Evidence level and grade	Consensus, % (n)*
Optimal tools and their frequency for understanding gMG disease burden in clinical practice, clinical research and telemedicine		
Clinical practice setting		
Consistent use of the MG-ADL scale should be applied in clinical practice to understand gMG disease burden; if the MG-ADL indicates worsening gMG, the QMG scale can be used to provide greater clinical understanding and support onward decisions	1a† Grade A	93.3 (14/15)
A patient scale, such as the PASS or EQ-5D-VAS, should follow the MG-ADL in clinical practice to determine patient satisfaction with symptom state and treatment and to determine the need for further assessments	2b Grade B	66.7‡ (10/15)
In clinical practice, should patients be dissatisfied with their symptom state or treatment, additional outcomes should be explored, such as quality of life, psychological/emotional burden or fatigue, with appropriate assessments	5 Grade D	100 (15/15)
Timing of gMG assessments should reflect the patient's symptom state (i.e., less frequent for stable vs fluctuating symptoms) and guidance for continuing, stopping retreatment or repeating treatment, should be based on clinical evaluation	5 Grade D	100 (15/15)
Clinical trial/research setting		
The MG-ADL is recommended as the primary endpoint in clinical trials, with the QMG as a co-primary or key secondary endpoint	1a Grade A	93.3 (14/15)
PROs are recommended to be included for the assessment of patient satisfaction with symptom state and treatment in the clinical trial setting	1a Grade A	93.3 (14/15)
The MG-QOL-15r or EQ-5D-5L may be used to measure quality of life in clinical trial settings	2b Grade B	100 (15/15)
Telemedicine setting		
In telemedicine settings, MG-ADL should be used to assess disease severity, and combined with EQ-5D and MG-QOL-15r to assess QoL; the combined results can determine the need and urgency for a face-to-face consultation	2b† Grade B	93.3 (14/15)
Timing of gMG assessments should reflect the patient's symptom state (i.e., less frequent for stable vs fluctuating symptoms) and guidance for continuing, stopping retreatment or repeating treatment, should be based on clinical evaluation	5 Grade D	100 (15/15)
General principles for incorporating depression, anxiety, and fatigue scales in patient assessment for gMG		
No specific scales are validated for measuring depression, anxiety and fatigue in the context of gMG at the current time. However, fatigue and fatigability may be measured effectively using the FSS, MFI-20 or Chalder fatigue scale; and depression and anxiety may be measured effectively using the PHQ, HADS or MDI	2b Grade B	80.0 (12/15)
Comorbidity assessment should include the relevant multidisciplinary team member, such as a psychiatrist for anxiety or depression	5 Grade D	86.7 (13/15)
Patient assessment domains that are not currently included in any existing gMG patient assessment tool		
There is a need for physician- and patient-administered assessment tools to better understand the practical, psychosocial impact of gMG and its treatment on patients, their families and caregivers	5 Grade D	100 (15/15)
Although current evidence does not support the use of a specific scale over others to assess fatigability, measures such as the MFI-20 and Chalder Fatigue scales should be used more consistently to assess the burden and impact of this important symptom in patients with gMG	2b† Grade B	73.3 (11/15)
It is important to ensure full evaluation of ocular symptoms in patients with gMG with the use of ocular-specific symptom scores and scales as they may not be fully assessed by generalised assessment tools	5 Grade D	66.7‡ (10/15)
Thresholds for minimally important/clinically meaningful differences in assessment scores in gMG within clinical practice		
At the current time it is not possible to make recommendations on absolute thresholds for minimally important and clinically meaningful differences in gMG scores as these are heavily dependent on the patient's experience and should be considered relative to baseline assessment scores	5 Grade D	100 (15/15)
Use of a patient satisfaction scale, such as the PASS or a symptom satisfaction questionnaire, can give an indication of whether changes in symptom state as assessed by a clinician, with a scale such as the MG-ADL, correspond to meaningful changes from the patient's perspective	2b Grade B	86.7 (13/15)
Assessment of treatment-related burden in patients with gMG in clinical practice		
There are currently no appropriate scales to measure the adverse event, psychological or practical burden associated with gMG treatment, or to differentiate treatment-related adverse events from gMG-related symptoms; however, treatment-related adverse event burden can be assessed through longitudinal measurement of objective parameters, such as frequency, and the use of toxicity indices in conjunction with MG-specific assessments of MG burden	2b† Grade B	80.0 (12/15)
Support provided by current gMG assessments on decisions around re-treatment or escalation of treatment		
Multiple disease-, patient- and treatment-related factors, including the patient's preferences, need to be considered when defining treatment goals and making therapeutic decisions in gMG; therefore, a general recommendation on how to decide upon re-treatment or treatment escalation is not appropriate	5 Grade D	86.7 (13/15)

*Consensus was reached when >=70% of the experts rated agreement with a statement as >=8 on a scale of 1–10; †Evidence was from patients with MG, and not gMG specifically; ‡Consensus not reached after first voting round; statement to be revised.
EQ-5D, EuroQol-5D; EQ-5D-5L, EuroQol-5d-5L; EQ-5D-VAS, EuroQol-5D Visual Analogue Scale; FSS, Fatigue Severity Scale; (g)MG, generalised myasthenia gravis; HADS, Hospital Anxiety and Depression Scale; MDI, Multiscale Depression Inventory; MFI-20, 20-item Multidimensional Fatigue Inventory; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QOL-15r, 15-item Myasthenia Gravis Quality of Life (revised); PASS, patient-acceptable symptom state; PHQ, Patient Health Questionnaire; PRO, patient-reported outcome; QMG, Quantitative Myasthenia Gravis.

Table 1. Consensus statements following the first round of voting for improving and standardising the assessment of patients with gMG

Conclusion: This process provides evidence- and expert consensus-based guidance for use of objective and subjective assessment tools across gMG care to improve outcomes for patients.

Disclosure: Financial support for this consensus was provided by argenx BV; the Sub-committee retained full control and final approval of the consensus process and outputs.

EPO-224

The ratio of blood circulating miR-206 and miR-409-3p as diagnostic biomarker for idiopathic inflammatory myopathy

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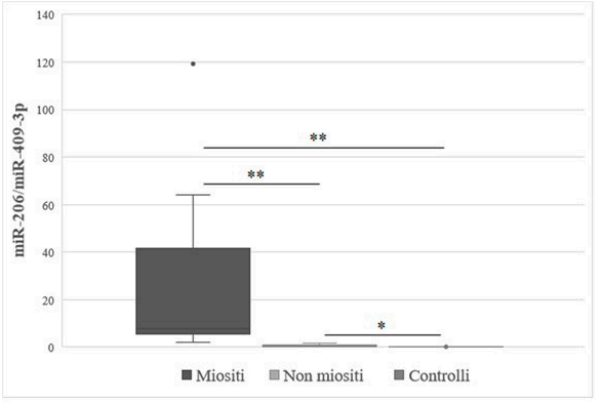
Background and aims: Idiopathic inflammatory myopathies (IIMs) are rare diseases characterised by muscle weakness and muscle inflammation. The diagnostic work-up of a suspected IIM is rather complex and expensive, and usually requires muscle biopsy. Our aim in this study was to identify new biological molecular marker as a non-invasive tool for IIMs to improve diagnostic efficiency.

Methods: We analyzed by quantitative Real Time PCR (qRT-PCR) blood microRNAs (miRs) expression levels of 15 patients with a suspected IIM. We blindly measured the ratio between plasmatic miR-206 and miR409-3p of the subjects. ROC curve analysis was used to determine specificity and sensitivity of the ratio to distinguish between IIMs patients and patients with other muscle disease.

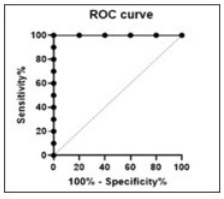
Results: Ratio values above 1.94 were identified as having 100% sensibility (95% CI: 72.25% to 100%) and 100% specificity (95% CI: 56.55–100%) in discriminating IIMs patients from the others. A value above 4.11 defines a patient as part of the IIM group, while under 0.96 identifies a non-myositic subject. Values between 0.96 and 4.11 remain in a "grey area", which warrants further tests.



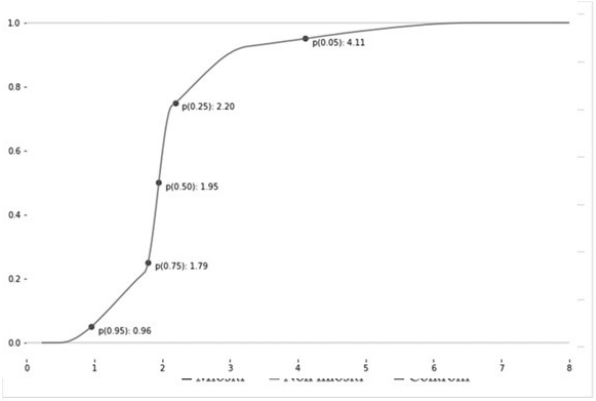
Results

Area sotto la curva ROC	
Area	1
Errore standard	0
95% intervallo di confidenza	1.000 a 1.000
P value	0,002
Dati	
Controlli (ratio non miositici)	5
Pazienti (ratio miositi)	10
Controlli mancanti	0
Pazienti mancanti	0

	Sensibilità%	95% CI	Specificità%	95% CI	rapporto di verosimiglianza
> 0.1400	100	72,25% a 100,0%	20	1,026% a 62,45%	1,25
> 0.3350	100	72,25% a 100,0%	40	7,107% a 76,93%	1,667
> 0.4850	100	72,25% a 100,0%	60	23,07% a 92,89%	2,5
> 1.120	100	72,25% a 100,0%	80	37,55% a 98,97%	5
> 1.940	100	72,25% a 100,0%	100	56,55% a 100,0%	
> 2.695	90	59,58% a 99,49%	100	56,55% a 100,0%	
> 4.875	80	49,02% a 96,45%	100	56,55% a 100,0%	
> 6.730	70	39,68% a 89,22%	100	56,55% a 100,0%	
> 7.210	60	31,27% a 83,18%	100	56,55% a 100,0%	
> 7.730	50	23,66% a 76,34%	100	56,55% a 100,0%	
> 18.93	40	16,82% a 68,73%	100	56,55% a 100,0%	
> 32.08	30	10,78% a 60,32%	100	56,55% a 100,0%	
> 49.15	20	3,554% a 50,98%	100	56,55% a 100,0%	
> 91.72	10	0,5129% a 40,42%	100	56,55% a 100,0%	



ROC and CI



Bootstrapping

Conclusion: Plasmatic miR-206/miR409-3p ratio proved to be an accurate biomarker to identify patients affected by IMM. It has the potential to become a cheap and non-invasive screening tool to guide the diagnostic and therapeutic process. Further studies are needed with higher number of patients to confirm the data and eventually find associations of the biomarker with specific IIMs subgroups.

Disclosure: Nothing to disclose.

EPO-225

Matching-adjusted indirect comparison of ravulizumab/efgartigimod in generalised myasthenia gravis: Timepoint challenges

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Background and aims: Matching-adjusted indirect comparisons (MAICs) may be used to assess the benefits of different treatments for symptom control. In this MAIC, we built on findings from previous comparisons of ravulizumab and efgartigimod and used mean changes from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) scores from the CHAMPION-MG and ADAPT trials to assess the effects of these treatments on symptom control in patients with generalised myasthenia gravis (gMG) at different timepoints.

Methods: Individual patient-level data from CHAMPION-MG were weighted to match summary baseline characteristics from the acetylcholine receptor antibody-positive subset of patients in ADAPT at the trial-arm level, and mean changes in MG-ADL scores from baseline to different timepoints were compared. Anchored comparisons were performed at Weeks 4 and 10, and at Week 8 (efgartigimod) vs Week 26 (ravulizumab).

Results: Baseline characteristics of the patients before and after matching are shown in Table 1. The timepoints chosen to assess the impact of ravulizumab and efgartigimod on MG-ADL were found to affect the results. Improvements in MG-ADL scores appeared to favour efgartigimod vs ravulizumab at Week 4, whereas at Week 10, and Week 8 (efgartigimod) vs Week 26 (ravulizumab), the results trended in favour of ravulizumab (Table 2).

	CHAMPION						ADAPT (AChR-Ab+ patients)		
	Ravulizumab (n=86)		Placebo (n=89)		Total (N=175)		Efgartigimod (n=65)	Placebo (n=64)	Total (N=129)
	Unmatched	Matched	Unmatched	Matched	Unmatched	Matched			
Mean age, years	58.0	44.7	53.3	49.2	55.6	47.0	44.7	49.2	46.9
Female, n (%)	44 (51.2)	61 (70.8)	45 (50.6)	56 (62.5)	89 (50.9)	116 (66.6)	46 (70.8)	40 (62.5)	86 (66.7)
MGFA class II, n (%)	39 (45.3)	37 (43.1)	39 (43.8)	35 (39.1)	78 (44.6)	72 (41.0)	28 (43.1)	25 (39.1)	53 (41.1)
MGFA class III, n (%)	41 (47.7)	46 (53.8)	45 (50.6)	50 (56.3)	86 (49.1)	96 (55.1)	35 (53.8)	36 (56.3)	71 (55.0)
MGFA class IV, n (%)	6 (7.0)	3 (3.1)	5 (5.6)	4 (4.7)	11 (6.3)	7 (3.9)	2 (3.1)	3 (4.7)	5 (3.9)
Mean time since diagnosis, years	9.8	9.7	10.0	8.9	9.9	9.3	9.7	8.9	9.3
Mean MG-ADL score	9.1	9.0	8.9	8.6	9.0	8.8	9.0	8.6	8.8
Steroid use at study entry, n (%)	56 (65.1)	61 (70.8)	65 (73.0)	71 (79.7)	121 (69.1)	132 (75.3)	46 (70.8)	51 (79.7)	97 (75.2)
NSIST use at study entry, n (%)	56 (65.1)	53 (61.5)	63 (70.8)	51 (57.8)	119 (68.0)	104 (59.6)	40 (61.5)	37 (57.8)	77 (59.7)

AChR-Ab+, acetylcholine receptor antibody-positive; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, non-steroidal immunosuppressant therapy.

Table 1. Baseline characteristics before and after matching

Domains **+2 new** (total: 8) *Broadest category of impacts; captures multiple impact elements*	Impact elements **+11 new** (total: 44) *More detailed category than domains; captures multiple impacts*	Impacts **+16 new** (total: 84) *Most detailed category; captures highest levels of nuance*	
		Patient examples	Caregiver examples
Occupation*	Career aspirations, freedom of occupation, unemployment or underemployment, on-the-job disruption, productivity and performance, absenteeism, and educational disruption	Being 'stuck' in a role	Passing up job opportunities
Financial*	Reduced income, financial trade-offs, financial toxicity, out-of-pocket costs, cost of daily living needs and high-cost expenses to support quality of life	Need to hire household support	Taking on dependants
Emotional health	Anger or resentment, fear or anxiety, frustration, sadness or depression, shame or embarrassment, **guilt**, **stress**, **loss of identity**, impaired cognitive function, **disproportionate sense of responsibility**	Shame or embarrassment	Guilt
Physical health†	Neglecting health needs and downstream health impacts	Downstream health impacts	Lack of focus on personal health
Sleep†	Insomnia, quality of sleep and **reliance on sleep aid**	Not sleeping comfortably	Irregular sleep schedule
Social	Strain on or change in intimate, immediate or non-immediate relationships, social isolation, reduced ability or desire to participate in activities across varying sectors, **real or perceived negative public perception and poor public understanding**	Social isolation	Difficulty forming new friendships
Planning and autonomy	Vigilance, disruptions to plans, loss of autonomy, feelings of instability about the future, personal aspirations, necessary life adaptations, illness work	Lack of independence	Altering of personal priorities
Safety	Real or perceived physical safety risks and **medical mistreatment**, and **powerlessness**	Risk of experiencing medical mistreatment	Risk and experience of injuries

Domains and impact elements in bold are newly identified.
*New domain. †Domain split from original 'Physical health and sleep'.

Table 2. Mean (95% confidence interval) MG-ADL changes from baseline to different timepoints

Conclusion: Outcomes from indirect comparisons of the effects of efgartigimod and ravulizumab on symptom control in patients with gMG can vary depending on the chosen timepoints and matching methodology. The consistency of symptom control achievable over a prolonged period should be considered, alongside efficacy and tolerability, when assessing treatment options for patients with gMG.

Disclosure: The study was sponsored by Alexion Pharmaceuticals Inc., with medical writing support provided by Hannah Wedge of OPEN Health Communications.

EPO-226

A single center experience with neuromuscular immune-related adverse events of immune checkpoint inhibitors

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Background and aims: The increasing use of immune checkpoint inhibitors (ICIs) and its immune-related neuromuscular adverse events (NM-iAE) constitutes a challenge due to the lack of guidance in the management of these neurological symptoms. We aimed to describe our experience with NM-iAE, including myositis, myasthenia gravis (MG) or overlap syndromes.
Methods: We retrospectively collected clinical data of patients presenting NM-iAE between 2015-2022 in our center.
Results: Within our 13 patients, 2 (15.4%) presented with myositis, 7 (53.8%) with MG and 4 (30.8%) with myositis-MG overlap. No neurological symptoms were reported before ICI administration. Among ICIs, 84.6% were PD1 inhibitors and 15.4% a combination of PD1+CTLA4. The median (IQR) time of onset since first ICI administration was 49 (30–225) days. The most frequent clinical presentations were bulbar and generalized (69.2% each). 69.2% presented combined symptoms. 6 patients (46.1%) were Ach-receptor antibody positive. 6 (46.1%) showed anti-striated muscle antibodies and 3 (23%) different myositis-related antibodies (Jo1, PL2 and Titin). Regarding treatment, 92.3% received pyridostigmine, 76.9% steroids and 92.3% discontinued ICI. The most severe presentations received intravenous immunoglobulins (46.2%) and plasma exchange (30.8%). 1 (7.7%) received Rituximab. 3 (23%) required mechanical ventilation but ultimately died due to acute respiratory failure (all of them with severe bulbar symptoms at onset). Remaining patients had a favorable neurological response.
Conclusion: Although ICI neurological adverse events are not very frequent, they are potentially fatal. More studies are needed to clarify the management of these complications but probably early recognition and treatment with intensive immunotherapy may be the key.
Disclosure: Nothing to disclose.

EPO-227

KY mutations are a cause of distal neuromyopathies

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Background and aims: Kyphoscoliosis peptidase gene (KY) gene mutations are rare recessive conditions related to myofibrillar myopathy-7 and hereditary spastic paraplegia.
Methods: Study of a patient with a myopathy of childhood onset, follow up in a Neuromuscular Centre, secondary to KY gene mutations, describing the phenotype and the characteristics of the ancillary test performed in order to better characterize this rare condition.
Results: A 58 years old man presented in childhood with gait disturbances and ankle retractions resembling an EDMD. He came to our clinic in adulthood due to progressive muscle weakness with difficulties walking and going up stairs. He had history of multiple fibrous dysplasia and low back pain. He showed weakness affecting mainly distal lower leg, trunk and axial muscles, and also had multiple retractions including rigid spine, scoliosis and foot deformities. CK serum levels were normal. He had a EMG neuromyopathic pattern, without spontaneous activity. Nerve conduction studies showed decreased amplitude of CMAPs in distal stimulation sites of lower legs, and normal sensory NCS . A restrictive respiratory involvement was detected in respiratory assessment. Muscle MRI showed severe involvement of axial and trunk muscles, posterior compartment of lower legs and also affected sartorius and other thigh muscles. A biopsy from tibialis anterior showed myopathic features and myofibrillar disorganization. A homozygous variant p.Arg187Cys in KY was detected in exome analysis.
Conclusion: KY gene should be included as a cause of distal neuromyopathy.
Disclosure: Nothing to disclose.

EPO-228

A comprehensive assessment of the impact of generalised myasthenia gravis (gMG): Insights from patients and caregivers

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Background and aims: The impact of rare diseases is often defined by the effect of symptoms on patients and by treatment expenses. In this study, we take a broader perspective by identifying new and assessing known impacts of gMG on the lives of patients and caregivers.

Methods: This study was performed using qualitative semi structured interviews to assess the impact of gMG on patients and caregivers. Participants included patients with acetylcholine receptor antibody-positive gMG and caregivers who provided unpaid support. The interviews were coded and qualitatively analysed to summarise the key points raised by participants. The impacts identified in interviews were categorised into impact domains and subcategorised into impact elements.

Results: 28 interviews (16 patients and 12 caregivers) were included in the analysis; participant characteristics are shown in Table 1. Of the 84 impacts of gMG identified, 16 were not previously reported in the literature. These impacts were categorised into eight domains (occupation, financial, emotional health, physical health, sleep, social, planning and autonomy, and safety), indicating effects on many aspects of patients' and caregivers' lives (Table 2). There were similarities in the reported impact elements and domains between patients and caregivers, although some of the specific impacts varied (Figure 1).

Characteristic, n (%)		Patients (n=16)	Caregivers (n=12)
Has a caregiver?	Yes	8 (50)	N/A
	No	8 (50)	
Time from diagnosis*	<5 years†	5 (31)	6 (50)
	>5 years†	11 (69)	6 (50)
Race	White	7 (44)	7 (58)
	Black	6 (38)	4 (33)
	Asian	1 (6)	0
	American Indian/ Alaskan Native	1 (6)	0
	Other	1 (6)	1 (8)
Ethnicity	Hispanic/Latinx	0	2 (17)
	Not Hispanic/Latinx	16 (100)	10 (83)
Sex	Male	3 (19)	5 (41)
	Female	13 (83)	7 (58)

*For caregivers, time from diagnosis is reported for the patient they cared for; †Diagnosis timing was noted as of September 2022. Patients diagnosed before or on 31/08/2017 were recorded as >5 years and patients diagnosed from 01/09/2017 were recorded as <5 years.
N/A, not applicable.

Table 1. Participant characteristics

Domains +2 new (total: 8) *Broadest category of impacts; captures multiple impact elements*	Impact elements +11 new (total: 44) *More detailed category than domains; captures multiple impacts*	Impacts +16 new (total: 84) *Most detailed category; captures highest levels of nuance*	
		Patient examples	Caregiver examples
Occupation*	Career aspirations, freedom of occupation, unemployment or underemployment, on-the-job disruption, productivity and performance, absenteeism, and educational disruption	Being 'stuck' in a role	Passing up job opportunities
Financial*	Reduced income, financial trade-offs, financial toxicity, out-of-pocket costs, cost of daily living needs and high-cost expenses to support quality of life	Need to hire household support	Taking on dependants
Emotional health	Anger or resentment, fear or anxiety, frustration, sadness or depression, shame or embarrassment, **guilt**, **stress**, **loss of identity**, impaired cognitive function, **disproportionate sense of responsibility**	Shame or embarrassment	Guilt
Physical health†	Neglecting health needs and downstream health impacts	Downstream health impacts	Lack of focus on personal health
Sleep†	Insomnia, quality of sleep and **reliance on sleep aid**	Not sleeping comfortably	Irregular sleep schedule
Social	Strain on or change in intimate, immediate or non-immediate relationships, social isolation, reduced ability or desire to participate in activities across varying sectors, **real or perceived negative public perception and poor public understanding**	Social isolation	Difficulty forming new friendships
Planning and autonomy	Vigilance, disruptions to plans, loss of autonomy, feelings of instability about the future, personal aspirations, necessary life adaptations, illness work	Lack of independence	Altering of personal priorities
Safety	Real or perceived physical safety risks and **medical mistreatment**, and **powerlessness**	Risk of experiencing medical mistreatment	Risk and experience of injuries

Domains and impact elements in bold are newly identified.
*New domain. †Domain split from original 'Physical health and sleep'.

Table 2. Domains, impact elements and examples of impacts from patient and caregiver interviews

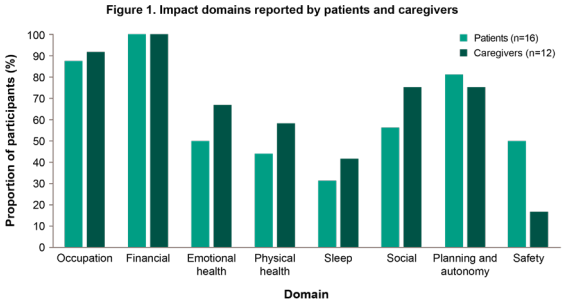

Figure 1. Impact domains reported by patients and caregivers

Conclusion: This study indicates that the impact of gMG on patients and caregivers is broader than previously reported. In the future, it is necessary to consider both patient and caregiver experiences in each of the reported domains when assessing the impact of rare diseases such as gMG.

Disclosure: The study was sponsored by Alexion Pharmaceuticals Inc., with medical writing support provided by Hannah Wedge of OPEN Health Communications.

EPO-229

Generalized myasthenia gravis (gMG) diagnostic journey and treatment: real-world physician and patient perspectives

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Background and aims: Generalized myasthenia gravis (gMG) is a rare, chronic, autoimmune disease that causes debilitating and potentially life-threatening muscle weakness. Patients may endure multiple exams and referrals before diagnosis, delaying treatment. This study characterizes and compares European and US gMG patient journeys from symptom onset to diagnosis and treatment initiation.

Methods: Data was drawn from an Adelphi Disease Specific Programme, a survey of providers and patients with gMG in France, Germany, Italy, Spain, the UK, and US, collected from March to September 2020.

Results: Overall, 557 patients with gMG were included and 36.9% were from the US. Patient demographics are presented in Table 1. The mean time from symptom onset to gMG diagnosis was 9.8 (SD: 13.7) months. Most common symptoms included ocular myasthenia (59.4%), ptosis (58.9%) and general fatigue (58.7%). Patients diagnosed earlier often had more severe gMG (Table 1). Most patients consulted primary care physicians (62.1%) and were then diagnosed by neurologists (79.9%). Providers, on average, used 8.7 (SD: 4.2) tests to aid gMG diagnosis. Among those previously misdiagnosed (26.9%), the most common misdiagnoses were chronic fatigue syndrome (34.7%) and multiple sclerosis (14.7%). Treatment initiation was, on average, 3.2 months (SD: 7.7) following diagnosis. Acetylcholinesterase inhibitors (73.8%) were the most commonly initiated, followed by steroids (42.9%) and immunosuppressive therapies (36.0%). Geographic differences between countries were noted.

Table 1: Patient Demographics by Time to Diagnosis

Time to Diagnosis*	Overall	Less than 6 Months	6 to 12 Months	Greater than 12 Months
Sample Size	**557**	**323**	**113**	**121**
Age (years)				
Mean (SD)	53.2 (15.9)	53.0 (17.0)	58.3 (15.0)	53.2 (13.8)
Sex (n (%))				
Male	277 (49.7%)	168 (52.0%)	57 (50.4%)	52 (42.9%)
Female	280 (50.3%)	155 (47.9%)	56 (49.5%)	69 (57.0%)
Ethnicity (n (%))				
White/Caucasian	466 (83.6%)	271 (83.9%)	98 (86.7%)	97 (80.1%)
African American	27 (4.8%)	15 (4.6%)	4 (86.7%)	8 (6.6%)
Hispanic/Latino	24 (4.3%)	9 (2.7%)	5 (3.5%)	10 (8.2%)
Afro-Caribbean	12 (2.2%)	9 (2.7%)	1 (0.8%)	2 (1.6%)
Mixed Race	8 (1.4%)	3 (0.9%)	1 (0.8%)	2 (1.6%)
Other	20 (3.5%)	16 (4.9%)	4 (3.5%)	2 (1.6%)
Employment (n (%))				
Full-Time	163 (29.4%)	106 (33.02%)	34 (30.0%)	23 (19.0%)
Part-Time	106 (19.1%)	50 (15.5%)	22 (19.4%)	34 (28.1%)
Retired	163 (29.4%)	100 (30.9%)	34 (30.0%)	29 (24.0%)
Other	123 (22.1%)	65 (20.2%)	23 (20.3%)	35 (28.2%)
MGFA Classification at Diagnosis (n (%))				
Class I	91 (16.3%)	44 (13.6%)	25 (22.1%)	22 (18.2%)
Class II	273 (49.0%)	149 (43.1%)	60 (53.1%)	64 (52.9%)
Class III	151 (27.1%)	94 (29.7%)	23 (20.3%)	32 (26.4%)
Class IV	38 (6.8%)	30 (9.2%)	5 (4.4%)	3 (2.5%)
Class V	4 (0.7%)	4 (1.2%)	0 (0%)	0 (0%)

*Time to diagnosis is the number of months from symptom onset to gMG diagnosis.
Abbreviations
gMG: Generalized myasthenia gravis, MGFA: Myasthenia Gravis Foundation of America, SD: Standard deviation

Table 1: Patient Demographics

Conclusion: In this international survey, patients with gMG were diagnosed 10 months following symptom onset and initiated treatment 3 months following diagnosis. Optimizing the diagnosis and treatment pathways may improve health outcomes among patients with gMG.

Disclosure: Research was sponsored by Horizon Therapeutics Jenny Park, Anthony Amatucci, Elizabeth Crane, Cornelia Fuller, Kristina Patterson, and Hari Patel are employees and stockholders of Horizon Therapeutics Gregor Gibson and Emma Chatterton are employees of Adelphi Real World

EPO-230

Clinical and therapeutic long-term follow-up in a large LOPD population: clues from a single centre experience.

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Background and aims: Pompe disease is an inherited metabolic disorder, caused by acid-a-glucosidase (GAA) enzyme deficiency. Late-onset form of Pompe disease (LOPD) presents as a limb-girdle myopathy with variable respiratory involvement. Since 2006, enzyme replacement therapy (ERT) has been available for Pompe disease. However, to date, only a few studies have been conducted on ERT long-term outcomes.
Methods: We describe a 49 LOPD patients' cohort and provide a long-term clinical and laboratory follow-up of patients under ERT, evaluating CK levels, 6MWT, GSGC score and spirometry.
Results: At onset, 43% of patients presented hyperCKemia whereas 57% presented proximal muscle weakness. Interestingly, electromyography showed a myopathic pattern in 61% of cases, of whom 85% had proximal muscle weakness at onset (Chi square=7.912; p<0.005). GAA residual activity was reduced in all 39 muscle samples (median value: 5.5 %; IQR: 7–4.8), correlating with an earlier onset (Spearman rho=0.328; p=0.039). 29/49 patients started ERT and were evaluated at baseline and T last (last evaluation). CK levels decreased after ERT (p=0.021). 6MWT showed a relevant decline at T last (p=0.001), as well as GSGC score (p=0.009). FVC presented an improving trend in the first 2 years, followed by a not statistically significant reduction at T last (p=0.011).
Conclusion: Our study confirms that LOPD is phenotypically heterogeneous. An early diagnosis is crucial to start ERT as soon as possible. Although long-term ERT follow-ups evidence variable responses, these results should be taken as a guide, even suggesting more appropriate therapeutic strategies in light of the emerging proposals.
Disclosure: Nothing to disclose.

EPO-231

Long-term follow up of generalized Myasthenia Gravis patients during 1998-2020 in a Spanish referral Unit.

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Background and aims: Myasthenia Gravis (MG) is a chronaaic, autoimmune, neuromuscular disease that leads to fluctuating muscular weakness. We describe demographic, clinical and therapeutic features of a generalized MG (gMG) patient cohort with long-term follow up.
Methods: Observational retrospective study of gMG patients treated in our referral neuromuscular disease unit in Spain from 1998 to 2020. Demographic, clinical (MGFA class, MGFA-PIS, MG-ADL, clinical exacerbations, myasthenic crisis), and therapeutic data were collected biennially over an 8-year period.
Results: A total of 220 patients newly diagnosed with gMG were included (54.5% women, 58 years of mean age at onset). Ninety percent were seropositive (84% anti-AChR, 6% anti-MusK, one patient was both positive). Overall, 99.5% of patients contributed data to the 2-year assessment and 42.73% to the 8-year assessment. Thymectomy was performed in 26.8% patients. Baseline mean MG-ADL score was 5.04 points (SD 3.23), improving to 0.7 points (SD 1.32) after 8 years follow-up. Exacerbations were more frequent in years 12 (51.1%) than in years 7–8 (20.2%). Myasthenic crisis frequency decreased from 3% in the first two years to 1% in years 7–8 of follow-up. Eighty-nine percent achieved MGFA-PIS minimal manifestations or better at 8 years, 67% of the patients being completely asymptomatic at 8 years from diagnosis. A total of 165 adverse events were reported, leading to drug withdrawal in approximately 20% of cases.
Conclusion: Some patients with gMG experience a high burden of disease despite treatment, due to persistent symptoms, exacerbations and drug side effects that can lead to treatment discontinuation.
Disclosure: This study was funded by UCB Pharma. David Reyes-Leiva, Álvaro Carbayo and Ricard Rojas-Garcia report no disclosures. Luis Querol received research grants from Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS-CIDP Foundation International, Novartis Pharma Spain, Roche, UCB and Grifols, received speaker or expert testimony honoraria from CSL Behring, Novartis, Sanofi-Genzyme, Merck, Annexon, Alnylam, Biogen, Janssen, ArgenX, UCB, LFB, Octapharma and Roche and serves at Clinical Trial Steering Committee for Sanofi Genzyme and Roche, and is Principal Investigator for UCB's CIDP01 trial. Elena Cortés-Vicente has received public speaking honoraria and compensation for advisory boards and/or consultations fees from UCB, Argenx, Janssen and Alexion and is Principal Investigator for UCB, Argenx, Janssen and Alexion.

Neurocritical care; Neuroepidemiology; Neurotraumatology

EPO-232

Prevalence study of Myasthenia Gravis in Lima – Peru

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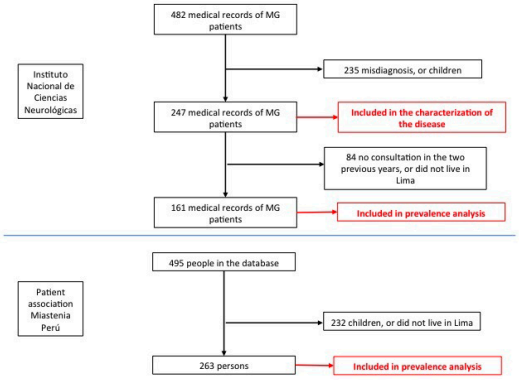
Background and aims: Myasthenia Gravis (MG) is an autoimmune disease that affects the postsynaptic membrane at the neuromuscular junction and is the most common neuromuscular disease. The overall prevalence of MG is 150 to 250 cases per million individuals, with an estimated annual incidence of 8 to 10 cases per million person-years. There are some prevalence studies in Latin America, none of them in Peru. The objective of this study is to estimate the prevalence of MG in Lima – Peru using the capture-recapture method and to describe the clinical characteristics of the disease.
Methods: The data from MG patients were collected from two independent sources, the Instituto Nacional de Ciencias Neurológicas and the patient association Myasthenia Peru. We performed a capture-recapture analysis to estimate the prevalence of MG in Lima – Peru, in 2020. Additionally, we described the epidemiological and clinical characteristics of the patients.
Results: We identified 161 cases in the first source and 263 cases in the second source; 28 cases were common to both sources. We found a point prevalence of 17.28 cases per 100000 inhabitants (95% CI: 11.48–23.08). Early-onset MG represents 51.82% of the cases, with a female predominance (67.97%), and late-onset MG represents 48.18% of the cases, with a male predominance (63.03%).



Flow chart of the study

		Early-onset MG (n: 128)		Late-onset MG (n: 119)		P
Age at diagnosis (Median/IQR)		26	20 -35	64	58 - 69	<0.001*
Sex (n/%)	Male	41	32.03 %	75	63.03 %	<0.001**
	Female	87	67.97 %	44	36.97 %	
Phenotype (n/%)	Ocular	35	27.34 %	56	47.06 %	0.002**
	Generalized	93	72.66 %	63	52.94 %	
Time to diagnosis (months/range)		4.1	1.0 – 13.1	3	1.0 – 10.1	0.092*
Comorbidities (n/%)		33	25.78 %	52	43.7 %	0.367**

(*) Mann-Whitney U test, (**) Fisher's exact test

Clinical characteristics

Conclusion: Lima has a medium MG prevalence and is comparable to other series reported in the literature. The clinical characteristics of our patients are similar to other countries in the region.
Disclosure: Nothing to disclose.

EPO-233

Cerebrospinal fluid galectin-3 as a potential biomarker in severe traumatic brain injury

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Background and aims: There is a limited understanding of the pathophysiology underlying severe traumatic brain injury (TBI). Galectin-3 is an important alarmin in TBI mice. However, its temporal expression in the cerebrospinal fluid (CSF) of severe TBI patients has not been determined. This study measured the temporal CSF expression of galectin-3 and associated cytokines at days 1, 3, 5, and 7 post-severe TBI.
Methods: CSF from severe TBI (n = 35) and non-TBI (n=5) patients were collected. CSF galectin-3 and associated cytokines (IL-1β, IL-6, IL-10, TNF-α, CCL-2, and CCL-20) were studied using the multiplex bead array. Based on the Modified Rankin scale (mRS), patients were separated into 3 groups: mRS 6 (died), mRS 5 (severely disabled), and mRS 1–4 (mild-to-moderately disabled) at 6 months post-injury.
Results: The mRS 5 group had significantly increased galectin-3 at day 1 and 3 and IL-6 at day 3 and 5 compared to mRS 6. Furthermore, galectin-3 at day 1 and 5 post-injury, IL-6 at day 3 and 5 post-injury, IL-10 at day 5 post-injury, and CCL20 at day 1 post-injury were significantly increased in the mRS 5 group compared to patients in the mRS 1-4 group. IL-1β, TNF-α, and CCL-2 showed no significant difference between the mRS groups and time points.
Conclusion: Thus, changes in CSF levels of galectin-3 and associated cytokines correlate with functional outcomes suggesting they are potential biomarkers for diagnosis, prognosis, and a therapeutic target for severe TBI.
Disclosure: Nothing to disclose.

EPO-234

Application of Automated Pupillometry to Improve Outcomes in Patients with Traumatic Brain Injury - Systematic Review

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Background and aims: Assessing changes in pupillary light reflex (PLR) is an important aspect of routine neurological examination in Traumatic Brain Injury (TBI) patients. Research shows that automated pupillometry provides an objective, reliable, non-invasive, and quantifiable method of measuring the PLR. This systematic review aims to explore the application and utility of automated pupillometry to improve outcomes in patients with TBI.
Methods: MEDLINE, Embase, Web of Science, and Scopus databases were searched for relevant studies up to October 9, 2022. PRISMA guidelines were then applied to identify and screen relevant records. 12 observational studies were included in this systematic review.
Results: 12 observational studies met the inclusion and exclusion criteria. All studies reported on the usefulness of automated pupillometry in identifying abnormal pupillary reflexes in the acute hospital stage. 5 studies reported inverse relationship between the Neurological Pupil Index (NPi) and clinical outcomes in TBI patients. 4 studies reported correlation between NPi measured with automated pupillometry and intracranial pressure (ICP). 3 studies reported that NPi score is predictive of surgical interventions in TBI patients.
Conclusion: Automated pupillometry provides an objective, non-invasive and rapid means to assess pupillary function. Current applications of the technology demonstrated diagnostic, prognostic, and therapeutic potential in the management of TBI patients. However further evidence on the application of automated pupillometry in pre-clinical, acute hospital and rehabilitation settings is required to support wider adoption in standard clinical practice.
Disclosure: Nothing to disclose.

EPO-235

Presymptomatic geographical distribution of ALS patients: a population-based cluster analysis

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Background and aims: Environmental factors have been hypothesized to play a role in the etiology of ALS. Clusters in the spatial distributions of patients could underlie the role of environmental factors. However, the degeneration in ALS is thought to start many years before the disease onset and most geoepidemiological studies used the position of patients at the time of their diagnosis. The aim of the study was to investigate the geographical distribution of ALS patients before the disease onset.
Methods: Data from the Piemonte and Valle d'Aosta Register for ALS (PARALS) were used. Patients included were resident in Piemonte at the time of the diagnosis and received an ALS diagnosis during the 2007-2014 period. A cluster analysis was performed using the Kulldorff statistics and considering the residence address of patients at the time of onset and at 1-year intervals until 50 years before the onset. All analyses were sex- and age-adjusted.
Results: A total of 1,124 patients were included. The analysis revealed a higher-incidence cluster in the Western area of Piemonte, 2 to 9 years before the disease onset interval. Four years before the onset, in an area including circa 435,000 inhabitants, 107.99 cases were expected and 153 were observed, resulting in a relative risk (RR) of 1.48 ($p=0.046$).
Conclusion: No univocal factor able to justify our results was found. Multiple hypotheses (industrialization, soil components) have been suggested. More importantly, we showed that analyses focused on the time of diagnosis could miss previous geographical clusters of patients.
Disclosure: No relationships/activities/interests related to the manuscript.

EPO-236

Understanding brain health around the world

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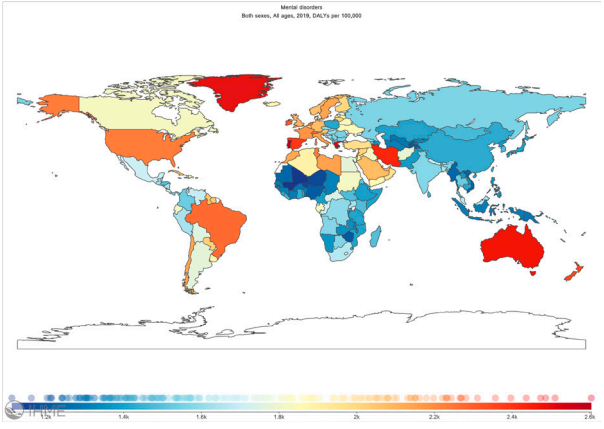
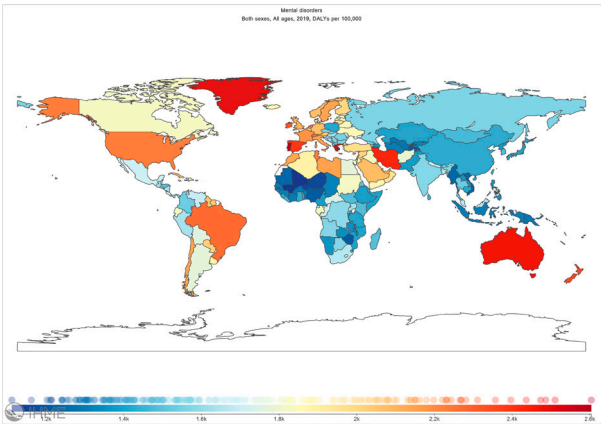
Background and aims: Brain conditions impact people of every age and in every country and have profound effects on our health and well-being.
Methods: The Global Burden of Disease (GBD) study is a systematic, scientific effort coordinated by the Institute for Health Metrics and Evaluation to quantify the magnitude of all major diseases in a highly standardized way, to allow for comparisons over time, across populations, and between health problems. In this secondary analysis of estimates from the most recent iteration of the GBD study, we describe the toll of brain conditions including neurological disorders, mental disorders, cerebrovascular disease, brain cancer, brain injuries, and select infectious conditions by location, age, and sex. We report findings in terms of prevalence, mortality, and total health loss (DALYs).
Results: Globally, more than 16% of all health loss is associated with brain conditions. In 2019, brain conditions led to as much health loss (396 million DALYs) as cardiovascular disease (393 million DALYs) and much more than cancer (251 million DALYs). Depression, among the top causes of health loss worldwide, affects 280 million people, up 64% since 1990. Alzheimer's disease cases increased by 161% since 1990, largely due to population aging, while the number of strokes increased by 95%.



The burden of neurological disorders globally



The burden of mental disorders globally

Conclusion: The burden of brain conditions will increase as populations continue to grow and age, challenging health systems, employers, and families to respond. Data such as that derived from the ongoing Global Burden of Disease study, and associated efforts, are critical to informing evidence-based planning and resource allocation.
Disclosure: Nothing to disclose.

EPO-237

Multiple Sclerosis Mortality in Poland

A. Czarnowska[1], O. Zajkowska[2], W. Brola[3], A. Mirończuk[1], A. Mitrosz[1], J. Kulikowska[1], M. Chorąży[1], J. Kochanowicz[1], A. Kułakowska[1], K. Kapica-Topczewska[1]
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Background and aims: Mortality studies in patients with multiple sclerosis (MS) are scarce. We aimed to investigate the mortality of MS in a large MS cohort from Poland compared w with the general population.
Methods: The yearly mortality data (2010–2018) for all patients with MS who died in Poland (MSD) were obtained from Statistics Poland. Mortality in MS compared with the general population was examined by standardized mortality ratio (SMR).
Results: The overall MSD during 2010–2018 was 3675. The yearly Female/Male (F/M) ratio for MSD ranged from 1.40 (in 2014) to 1.76 (in 2016) but was stable for the observation period (from 1.53 in 2010 to 1.52 in 2018) and varied between cities and the countryside from 1.70 to 1.39, respectively (p=0.0051). In the study period, the median age of death increased from 55–59 years in 2010 to 60–64 years in 2018. We found evidence of a 5-year gain in life expectancy from 2010 to 2018. However, the median life expectancy was 5 years longer in the countryside than in cities. Overall SMR was 0.95 and was decreasing over time (from 1.11 in 2013 to 0.89 in 2018) and was higher for men than women (1.16 versus 0.92).
Conclusion: A rise in survival in patients with multiple sclerosis was observed during the entire observation period. Mortality in men was higher than in women. The duration of life in patients with multiple sclerosis was lower in cities.
Disclosure: Nothing to disclose.

EPO-238

Autoimmune encephalitis and paraneoplastic neurological syndrome: Epidemiology and neuronal antibody testing in Sweden

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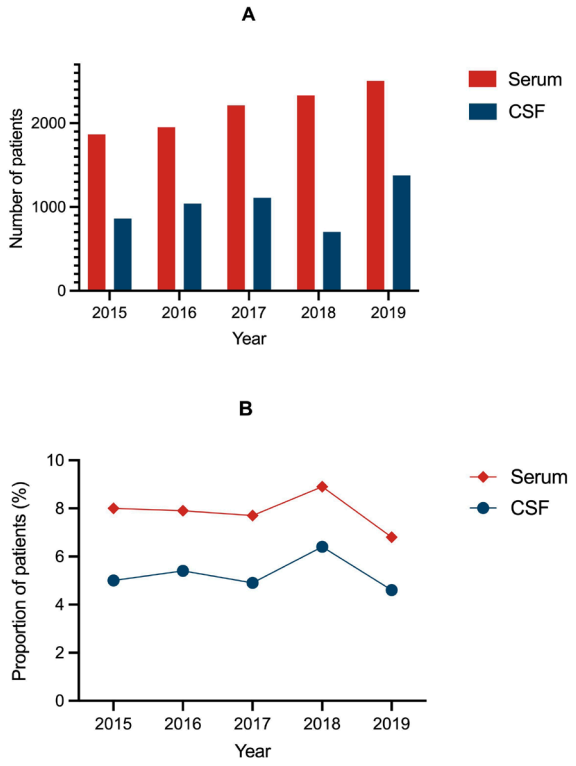
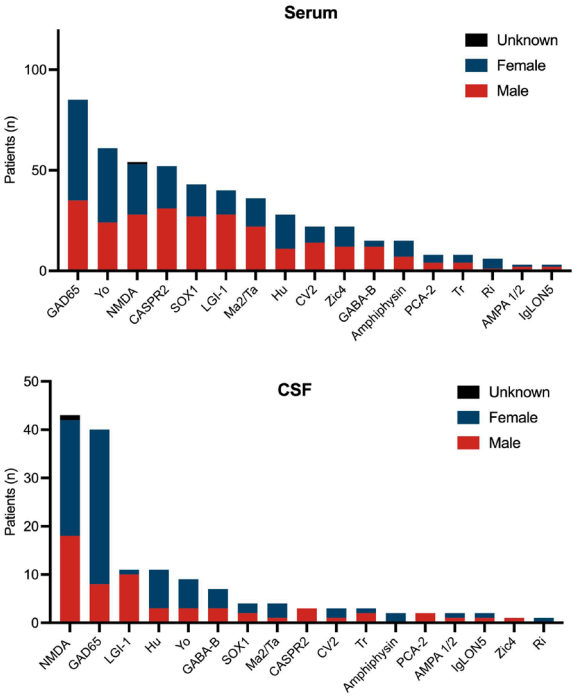
Background and aims: To estimate the 5-year incidence rate of autoimmune encephalitis (AE) and paraneoplastic neurological syndrome (PNS) in Sweden.
Methods: All patients who were tested for a neuronal antibody in Sweden between 2015 and 2019 were included. Patients in Healthcare region Mid Sweden (population 2.1 million) were invited to participate in a case ascertainment sub-study. AE and PNS cases were defined using established diagnostic criteria. Crude and age-adjusted incidence rates of AE and PNS in Healthcare region Mid Sweden were estimated.
Results: The number of tests for neuronal antibodies in Sweden increased between 2015 and 2019 from 1,867 to 2,505 (serum) and 863 to 1,376 (CSF) per annum. The frequencies of positive results were stable over the entire study period and the mean value was 6.1% for serum (CI95% 5.5–6.7), and 4.8% for CSF (CI95% 4.0–5.6). In total 125 patients tested positive for neuronal antibodies in Healthcare region Mid Sweden between 2015 and 2019. Of these, 94 were included and after case ascertainment, thirty-one cases of definite AE or PNS could be identified. The 5-year incidence rate of AE and PNS was 3.0 per million person-years (95%CI 1.9–4.1). The yearly incidence rates increased in the study period, from 1.5 per million person-years in 2015 (95%CI 0.0–3.2) to 4.3 per million person-years in 2019 (95%CI 1.5–7.1).



A) The total number of patients tested for a neuronal antibody in Sweden between 2015 and 2019 B) The proportion of patients (%) tested for a neuronal antibody that had a positive test result.



Antibody subgroups of patients who tested positive for a neuronal antibody in all of Sweden 2015–2019, serum and CSF displayed separately, sex distribution shown.

Table 1 – Crude and age-adjusted incidence rates of AE and PNS in Healthcare region Mid Sweden 2015-2019

Subgroup and time period	Crude incidence (CI95%)†	Age-adjusted incidence (CI95%)‡
AE+PNS 2015-2019	3.0 (1.9-4.1)	2.9 (1.8-3.8)
AE+PNS 2015	1.5 (0.0-3.2)	1.4 (0.0-2.9)
AE+PNS 2016	2.4 (0.30-4.6)	2.2 (0.027-4.2)
AE+PNS 2017	2.9 (0.58-5.2)	2.5 (0.30-4.6)
AE+PNS 2018	3.8 (1.2-6.5)	3.8 (1.2-6.5)
AE+PNS 2019	4.3 (1.5-7.1)	3.8 (1.3-6.3)
AE 2015-2019§	2.4 (1.5-3.4)	2.4 (1.4-3.2)
PNS 2015-2019	1.5 (0.72-2.2)	1.3 (0.66-2.0)
Anti-NMDAR encephalitis 2015-2019	0.58 (0.12-1.1)	0.58 (0.12-1.0)
Anti-LGI1 encephalitis 2015-2019	0.58 (0.12-1.1)	0.53 (0.11-0.95)

†Crude incidence rate per million person-years. ‡Age-adjusted incidence rates per million person-years standardized to the 2013 European Standard population. §AE= definite AE and definite anti-NMDA receptor encephalitis. The population of Healthcare region Mid Sweden contributed with 10 331 778 person-years between 2015–2019. AE= Autoimmune encephalitis; PNS= Paraneoplastic neurological syndrome.

Crude and age-adjusted incidence rates of AE and PNS in Healthcare region Mid Sweden 2015–2019

Conclusion: In this first epidemiological study of AE and PNS in Sweden the number of cases doubled from 2015 to 2019. This likely reflects increased availability of testing and awareness of these conditions.

Disclosure: The authors report no disclosures relevant to this abstract.

EPO-239

Correlation of disease activity and EQ-5D-3L-derived utility in myasthenia gravis patients in a Swedish national cohort

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Background and aims: Myasthenia gravis (MG) is a chronic neuromuscular disease causing motor fatiguability and weakness. The impact of MG on quality of life (QoL) is not well documented. Here, the objective was to explore correlations of either disease severity (MG-ADL) or MG QoL-ratings with the health outcome measure utility.

Methods: Patients were identified in the Swedish nationwide MG registry and included if simultaneous disease activity (MG-ADL) and QoL measures (MG-QoL and EQ-5D-3L) were available. Utility was derived from EQ-5D-3L using the UK Time Trade Off tariff.

Results: We included 121 patients (mean age 63, 45% female, 67% late-onset MG). Average utility was 0.7, compared to 0.83 in an age- and sex-adjusted reference population. Average utility was 0.85 (reference 0.83) in patients with no to minimal disease activity (MG-ADL $\leq$2) compared with 0.66 and 0.59 in patients with moderate and high disease impact (MG-ADL $\geq$3 and $\geq$6, respectively) (both reference 0.82). Negative correlations between either MG-ADL or MG-QoL, and utility were observed (ρ=-0.57 and -0.71, respectively, both $p<0.001$). In a multivariate regression model, adjusting for sex, age, and disease duration, change in utility was associated primarily with change in disease activity. Further stratifying MG-ADL into its items, change in self-care and diplopia were the strongest factors associated to change in utility.

Conclusion: In this real-life dataset of MG patients, we observed considerably impaired health status in patients with active disease. This indicates an unmet medical need, especially in those with high disease activity, in turn warranting further improvements in MG treatment and care.

Disclosure: Malin Petersson has nothing to declare. Fredrik Berggren is an employee and stockholder of UCB Pharma, Copenhagen, Denmark Ingrid Lindberg is an employee of UCB Pharma, Stockholm, Sweden Fredrik Piehl has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis. Susanna Brauner has received grants from UCB Pharma.

EPO-240

Neuro Virtual Hospital: a pilot study for a model of multidisciplinary remote management of neurological patients

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Background and aims: Some neurological diseases are difficult to diagnose and patients are often forced to move from an hospital to another, in search of a "second opinion" or a satisfactory "taking charge". This trend increases public expenditure and overload of the National Healthcare System. Alternative models are being developed to solve these problems, such as telemedicine. We carried out a pilot study to test the feasibility of the development of a virtual multicentric and multidisciplinary care system (Neuro Virtual Hospital) for patients suffering from complex neurological pathologies.

Methods: .We conducted this pilot multicentre study from April 2020 to June 2021, including six Italian centres. Seventy-three experienced specialists gathered into nine multidisciplinary teams which met virtually every month and took care of eighty patients affected by unusual clinical pictures which needed a multidisciplinary approach.

Results: The model reduced the accesses to the hospitals by 47%, resulting in a decrease of 1.78 for each case, and the time to get to a definite diagnosis or indication to treat by 66% compared to the traditional system. Most of the discussed cases were referred to Cerebrovascular Diseases Team (47.50%) and Neurooncology Team (26.25%).

Conclusion: This pilot study evaluated the first stages of the development of the virtual multidisciplinary and multi-centric model of care for neurological patients in Italy. This model will allow physicians from different medical fields and from different hospitals to meet remotely to take care of patients who require second opinion or multidisciplinary management, regardless of their possibility to access to secondary or tertiary-level centres.

Disclosure: Nothing to disclose.

EPO-241

Epidemiology of Antibody-positive Myasthenia Gravis in Sardinia, Italy

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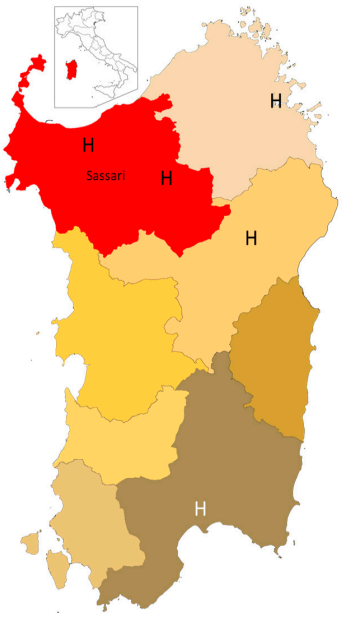
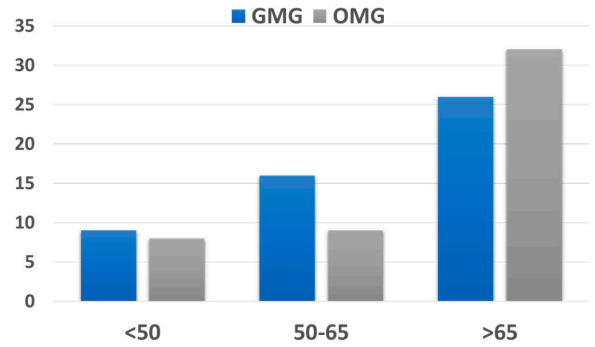
Background and aims: The global mean incidence and prevalence of myasthenia gravis (MG) have been assessed at ≈15 (range, 4-29)/million and 20 (range, 2-37)/100,000, respectively. Sardinia is a recognized area at higher risk for immuno-mediated disorders (e.g., multiple sclerosis). We assessed the incidence and prevalence of MG associated with AchR-IgG and MuSK-IgG in the district of Sassari.



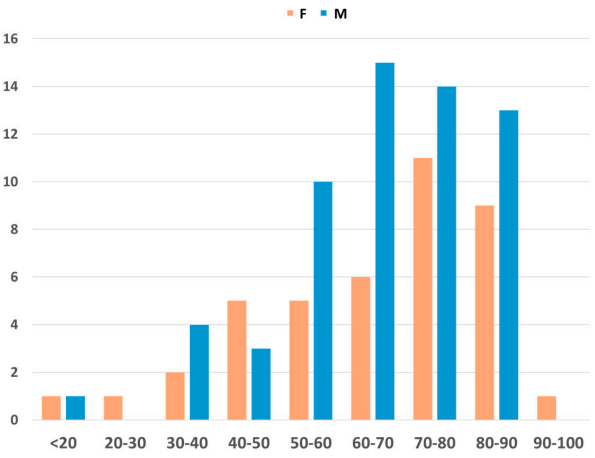
Study area: Sanitary district of Sassari; population: 325,288 (Jan 1, 2020)

Methods: From the Neurochemistry Laboratory of the University-Hospital of Sassari (reference laboratory for AchR-IgG/MuSK-IgG testing in the island since 1998) we retrospectively identified patients with: 1) AchR-IgG (titer ≥0.5 nmol/L) and/or MuSK-IgG (titer ≥100 pg/ml) positivity by radioimmunoprecipitation assay; 2) available medical records; and 3) residence within the district of Sassari. Incidence (January 2010-December 2019) and prevalence (on January 1, 2020; population 325,288) were calculated.

Results: Among 517 antibody-positive patients identified, 183 were included (incident, 97; prevalent, 165). We excluded 334 patients due to: 1) missing clinical information (n=65); 2) residency outside the Sassari district (n=168); 3) not classifiable as incident or prevalent (n=56); and 4) clinical phenotype not consistent with MG (n=45; median AchR-IgG titer, 0.7 [range, 0.5–5.5] nmol/L). The crude MG prevalence was 50.7/100,000 (95% CI, 43.4–58.9), whereas incidence was 29.8/1,000,000 person-years (95% CI, 24.3–36.2). Antibody specificities were AchR in 170 (92.9%; median titer 5.7 [range, 0.5–22]) and MuSK in 13 (7.1%; median titer 1,255 [range, 136-1–730]). Among incidence cases, age at disease onset was distributed as: <18 years (n=2; 2%); 18–50 years (n=14; 14.4%); 51-65 years (n=25; 25.8%); and >65 years (n=56; 57.7%).



Clinical phenotype distribution by age



Age and gender distribution of the patients

Conclusion: We report the highest incidence and prevalence of MG worldwide.

Disclosure: Nothing to disclose.

Headache 2

EPO-242

Persistence of Response With Eptinezumab Over 24 Weeks in Patients With Prior Migraine Preventive Treatment Failures

M. Ashina[1], R.B. Lipton[2], J. Ailani[3], J. Versijpt[4], S. Sacco[5], D.D. Mitsikostas[6], C. Laurberg Christoffersen[7], B. Sperling[7], A. Ettrup[7]

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Background and aims: In DELIVER, eptinezumab treatment showed greater reductions than placebo in monthly migraine days (MMDs). This analysis evaluated persistence of response to eptinezumab at the population and patient level and potential for response in initial non-responders.

Methods: DELIVER (NCT04418765) randomized adults with migraine and 2–4 prior preventive treatment failures to infusion with eptinezumab 100mg, 300mg, or placebo every 12 weeks. Migraine responder rates (MRRs [average percentage change from baseline in MMDs]) of ≥30%, ≥50%, and ≥75% over Weeks (Wks) 1–12 and 13–24, MRRs over 4-week intervals, and percentage of initial non-responders (Wks1–12) achieving response to their second infusion (Wks13–24) were calculated.

Results: Full analysis set: 890 patients (100mg, n=299; 300mg, n=293; placebo, n=298). Between Wks1–12 and Wks13–24, ≥30% MRRs increased from 65.9% to 70.4% (100mg), 71.0% to 74.5% (300mg), versus 36.9% to 43.1% (placebo; p<0. 0001 for both doses/timepoints). Four-week ≥30%, ≥50%, and ≥75% MRRs were generally maintained or increased over the 24-week period, with notable increases after the second eptinezumab infusion (Figure). Of patients with <30% response over Wks1–12, 34.7% (100mg) and 30.4% (300mg) versus 21.1% (placebo) achieved ≥30% response over Wks13-24, and 16.8% (100mg), 15.2% (300mg), vs 6.5% (placebo) achieved ≥50% response. With eptinezumab, ≥30% MRRs over Wks1–12 were maintained over Wks13–24 by >80% of patients, ≥50% MRRs by >70%, and ≥75% MRRs by >60%.

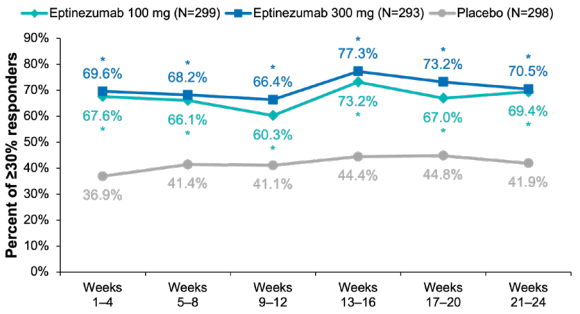

Figure. Percentage of patients achieving a ≥30% migraine response over 4-week intervals. *p<0.0001 vs placebo

Conclusion: Most patients responding to eptinezumab during Wks1-12 maintained response during Wks13-24, with MRRs further increasing with a second infusion. Approximately one-third of initial non-responders became responders after their second infusion.

Disclosure: MA: Consult and honoraria: :Lundbeck. RL-Consultant, ad board,honoraria: Lundbeck Allergan, AAN, AHSAmgen, Biohaven Pharm, BioVision, Boston Scientific, Dr. Reddy's Laboratories, electroCore Medical, Eli Lilly, eNeura Therapeutics, GSK, Merck, Pernix, Pfizer, Supernus, Teva Pharm, Trigemina, Vector, Vedanta. SStock:Biohaven Pharm, Manistee. Compensation: eNeura,Biohaven Pharm.. Research:Amgen, MRF,NHF. JA: IConsultantAlder, Amgen, Allergan, Electrocore, Eli Lilly, Promius, Teva, Impel, Satsuma, Zosano, Revance, Alpha Sites Consulting, Neurodiem, BDSI. CME: Miller Communications, Avent, Peer View, Forefront. SB: : Allergan, Amgen, Electrocore, Eli Lilly, Promius, Teva. JV-Consultant: Teva, Novartis, Lundbeck, Abbvie, Lilly. Honoraria: -Teva and Lilly. Travel support:-Teva, Abbvie. Ad Board: Teva, Novartis, Lundbeck, Abbvie, Lilly. President of BHS. SS- Grants::-Novartis, Uriach. Consultant:: Novartis, Allergan-Abbvie, Teva, Lilly, Lundbeck, Pfizer, NovoNordisk, Abbott, AstraZeneca. Honoraria: -Novartis, Allergan-Abbvie, Teva, Lilly, Lundbeck, Pfizer, NovoNordisk, Abbott, AstraZeneca. Travel support: Lilly, Novartis, Teva, Lundbeck. President ofESO. Second VPEHF DM-Consultant:: Novartis, Eli Lily, Teva, Lundbeck. Honoraria:Allergan, Eli Lily, Novartis, Lundbeck, Teva. Travel support: Allergan, Genesis, Eli Lily, Novartis, Lundbeck, Teva. President,HHS; Co-Chair, Headache Panel EAN. CLC-Employee: H Lundbeck A/S BS-Employee: H Lundbeck A/S AE-Employee: H Lundbeck A/S

EPO-243

Investigating the role of neuropeptides in migraine during anti-CGRP treatment: an exploratory study.

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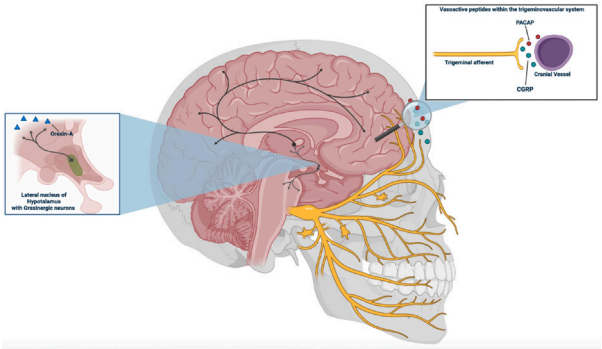
Background and aims: Migraine is a common disabling neurological condition that has been linked to the activity of specific neuropeptides. Of note, anti-Calcitonin Gene Related Peptide (CGRP) targeting therapies opened a new era in migraine prophylaxis.



Putative role of neuropeptides in migraine pathophysiology: a focus on CGRP, OxA and PACAP-38

Methods: In order to investigate the effects of such novel treatment on neuropeptides modulation, sixteen consecutive migraine patients underwent plasmatic dosage of CGRP, Orexin A (OxA) and Pituitary Adenylate Cyclase-Activating Peptide-38 (PACAP-38). Measurements were obtained at baseline (T0) and after six-month treatment (T1) along with the collection of clinical data. Plasmatic levels were then compared with non migrainous controls.
Results: In line with previous studies, results confirmed treatment efficacy. OxA and PACAP-38 levels were significantly higher in patients at baseline ($p<0.05$ and $p<0.001$ respectively) compared to control group. OxA emerged as an inverse independent predictor of clinical response ($p<0.05$). Basal CGRP levels inversely correlated with clinical outcome at T1.
Conclusion: Our pilot study suggests on one hand a possible association between OxA and clinical outcome; on the other hand it questions the role of baseline CGRP as a possible predictor of clinical response to treatment.
Disclosure: Nothing to disclose.

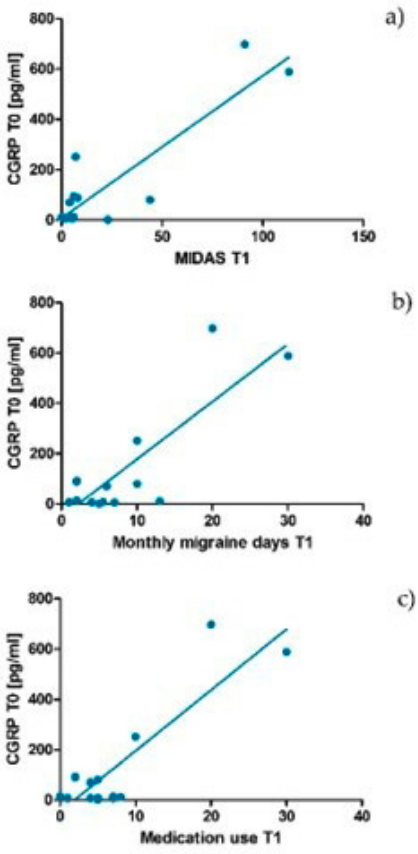
Table 1. Neuropeptides plasmatic concentration at T0. Data is expressed as mean ± standard deviation.

	Patients T0	Controls	p value
CGRP [pg/ml]	121.65 ± 214.10	30.77 ± 60.60	0.120
PACAP [pg/ml]	212.75 ± 41.68	126.83 ± 43.95	<0.001
Orexin A [ng/ml]	0.88 ± 0.24	0.73 ± 0.21	0.055

Table 2. Plasmatic neuropeptides concentration in the anti-CGRP treated patients. Data is expressed as mean ± standard deviation.

		Patients T0	Patients T6	p value
Erenumab (N=5)	**CGRP** [pg/ml]	156.6 ± 244.3	121.8 ± 210.4	0.186
	PACAP [pg/ml]	228.1 ± 50.1	219.1 ± 37.12	0.625
	Orexin A [ng/ml]	0.777 ± 0.294	0.887 ± 0.101	0.313
Fremanezumab (N=5)	**CGRP** [pg/ml]	73.47 ± 105.6	111.4 ± 173.6	0.313
	PACAP [pg/ml]	187.6 ± 14.45	203.7 ± 21.57	0.063
	Orexin A [ng/ml]	0. 934 ± 0.223	0.943 ± 0.167	1.00
Galcanezumab (N=6)	**CGRP** [pg/ml]	133.5 ± 277.9	870.3 ± 19.19	0.031
	PACAP [pg/ml]	220.9 ± 45.71	225.8 ± 61.51	1.00
	Orexin A [ng/ml]	0.927 ± 0.213	1.037 ± 0.210	0.688

Figure 2. Correlations between CGRP at T0 and clinical outcomes at T1



a) Correlation between CGRP at T0 and MIDAS at T1, Pearson correlation r = 0.897 , p<0.0001

b) Correlation between CGRP at T0 and MMD at T1, Pearson correlation r = 0.843 , p<0.0001

c) Correlation between CGRP at T0 and monthly acute medication use at T1, Pearson correlation r = 0.879 , p<0.0001

EPO-244

"Preventive oral treatment in migraine: efficacy and drop-out rates observed at a tertiary headache center."

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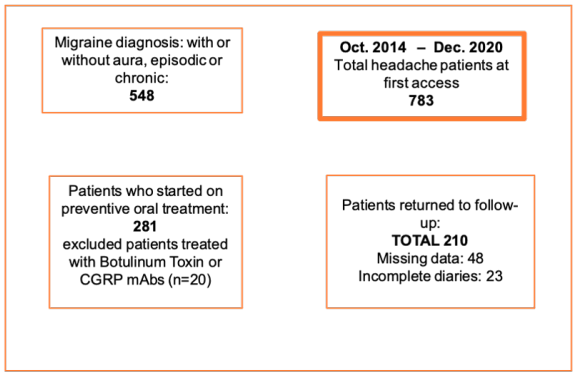
Background and aims: Migraine is a common and disabling neurological condition. Despite advances in the field, some patients remain without symptomatic pain relief. Our analysis aim to study the short and long-term effect of preventive treatment in a cohort of migraine patients, enlightening possible predictive factors for ineffectiveness and also analyzing the preventive's drop-out rates, clarifying the underlying reasons
Methods: This retrospective analysis included 210 patients who received a diagnosis of migraine without aura (MO), migraine with aura (MA) or chronic migraine (CM), according to ICHD-3 diagnostic criteria, with indication for prophylactic treatment. Three groups were defined and studied regarding the efficacy of oral preventives and drop-out rates: group A referred to patients treated with a first preventive, group B with a second and group C a third respectively.
Results: Overall efficacy of our preventive treatment was low with 40% of patients improving with their first preventive. Also, successive prophylactic attempts were associated with progressively lower rates of efficacy. Patients in whom coexisted MOH had lower rates of preventive inefficacy. The preventive's drop-out rates observed were also high (reaching 63.2% in subgroup C patients) with adverse drug reactions such as weight gain and cognitive dysfunction being the main reason for this.

The flowchart depicting patient selection is shown on fig. 1.



Conclusion: The modest effect of the oral preventive drugs as well as the high proportion of patients who dropped out due to drug side events confirm that in a significant proportion of patients, oral preventives can only delay a more focused therapeutic approach such as the new therapies with monoclonal CGRP antibodies.
Disclosure: Nothing to disclose.

EPO-245

Direct switch from onabotulinumtoxin A to erenumab in multidrug-resistant chronic migraine with medication overuse

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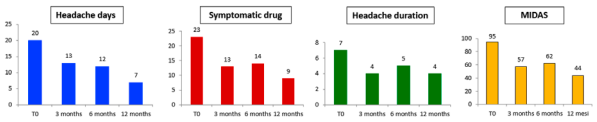
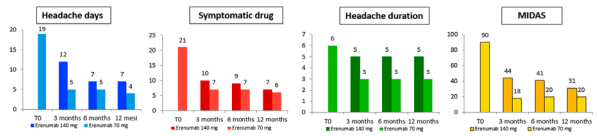
Background and aims: Aim of this study was to evaluate the therapeutic effect of a direct switch from onabotulinumtoxin A (BoNTA) to erenumab in multidrug-resistant chronic migraine with medication overuse.
Methods: After minimum 4 different ineffective prophylaxes tried, all subjects performed 3 unsuccessful sessions of BoNTA 195 U. Three months later they received erenumab 70 mg at time 0 (T0), incrementable to 140 mg after 3 months (T1). Therefore, patients were evaluated after 6 (T2) and 12 months (T3). Subjects had not to use other prophylactic drugs. Demographic and clinical data were analyzed with SPSS 24.0.
Results: 11 patients (3 males, 8 females, mean age 44±11) were enrolled. Subjects had used 7±1 ineffective migraine prophylactic molecules. Symptomatic medications overused were triptans (63.6% of cases), analgesics combinations (18.2%), analgesics in association (9.1%), non-steroidal anti-inflammatory drugs (9.1%). 50%, 75% and 100% responders were 54.6%, 18.2% and 9% of patients respectively. All headache outcomes improved from T0 to T3 (days of headache/month: 20±5 at T0, 7±6 at T3; attacks duration [hours]: 7±1 at T0, 4±2 at T3; symptomatic drugs/month: 23±7 at T0, 9±6 at T3; MIDAS: 95±38 at T0, 44±40 at T3). Out of the six patients responders, 3 switched from erenumab 70 to 140 mg with further improvement (days of headache/month: 12±6 at T1, 7±1 at T3; symptomatic drugs/month: 10±2 at T1, 7±2 at T3; MIDAS: 44±15 at T1, 31±8 at T3).



Improvement of headache parameters in responder patients



Comparison in clinical response between patients receiving erenumab 70 and 140 mg

Conclusion: Innovatively, a direct shift from onabotulinumtoxin A to erenumab is effective in multidrug refractory chronic migraine with medication overuse.
Disclosure: No conflicts of interest to declare.

EPO-246

Clinical and therapeutic characteristics of a series of 106 patients with epicrania fugax

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Background and aims: Epicrania fugax (EF) is a headache included in the research appendix of current edition of International Classification of Headache Disorders. It is defined by brief, recurrent pain attacks, rapidly radiating forwards or backwards across the surface of one hemicranium. We aim to present characteristics of a large series of patients.
Methods: Prospective observational study of patients attended in a headache unit from March-2008 (first description of EF) to January-2023. We collected clinical and therapeutic data.
Results: We included 106 patients (79 females, 27 males). Age at onset was 46.8±17 years (16–84) with time between onset and diagnosis of 21.5±34.2 months (1–240). In 69 cases (65.1%) EF was a classic forward variant, in 34 (32.1%) a backward EF and in 3 (2.8%) paroxysms described both trajectories. In 86 (82.1%) the pain paroxysms occurred on only one side, in 14 (13.2%) on both sides and in 5 (4.7%) trajectory was sagittal. 36 (34%) patients presented an interictal pain in stemming area, generally circumscribed fulfilling diagnostic criteria of nummular headache (25 cases). Pain intensity was 7±1.8 (1–10) in verbal analogical scale (VAS). Quality was mainly electric (70 cases, 66%). In 67 patients (63.2%) it was necessary to prescribe a preventive treatment, being the most used lamotrigine (32). Lack of response requiring additional preventatives was observed in 17 cases (16%).
Conclusion: EF is not an uncommon diagnosis in a headache unit. It may be a disabling headache syndrome requiring frequently preventive therapy.
Disclosure: No potential disclosures related to this work.

EPO-247

Are PROMs passing the message?

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Background and aims: Patient-reported outcome measures (PROMs) are of increasing importance in disease outcome monitoring in headache disorders, yet its implementation in real-life clinical practice is challenging and may influence its reliability.
Methods: We applied two identical PROMs (HALT-90 and MIDAS) simultaneously in every clinical evaluation (each 3 months) over a year to a series of patients treated with monoclonal antibodies for migraine in real life clinics. We calculated intra-individual agreement for each question in each visit, using the intraclass correlation coefficients (ICC) and analysis the missing data over the 4 visits.
Results: Our sample included 92 patients 92.4% females of 44.8 years-old on average. Missing data increased from 14% in the first to 58% in the last visit. Moderate (0.50 to 0.75) and poor (<0.50) ICC were observed all but one item of these PROM in different evaluations. No learning effect was detected.
Conclusion: We observed a reliability variability in patients motivation and responses to PROMs in repeated applications, This information serves as an alert to clinicians to the limitations of PROM use in real-life clinical practice.
Disclosure: Nothing to disclose.

EPO-248

Erenumab discontinuation in migraine patients: final results of the APOLLON study

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Background and aims: The monoclonal antibody erenumab is an anti-CGRP pathway target developed for the prevention of episodic and chronic migraine. A recent update to the EHF guideline on the use of monoclonal antibodies suggests pausing the treatment after 12 to 18 months. There is, however, only limited data on the impact of treatment discontinuation. This study aims to assess the significance of a drug holiday in patients treated with erenumab.
Methods: Patients enrolled in the 128-week open-label APOLLON study, assessing the long-term safety and tolerability of erenumab in migraine in 701 patients in Germany, were allowed to pause the treatment after 12 weeks of continuous treatment with erenumab. Impact of treatment discontinuation on monthly migraine days (MMD) was assessed 4 weeks prior to, during and 12 weeks after the medication-free epoch.
Results: This final analysis includes details on the drug holiday and its impact on the respective patients' MMD. Treatment interruption amounted to about 107 days (median). More than half the patients returned to treatment after drug holiday with the majority thereof returning to their previous dose. At drug holiday initiation, the average MMD was 4.2±2.9 days. After an increase to 7.2±5.7 MMD in the second month of treatment discontinuation, the average MMD decreased again to 4.5±2.7 MMD within the first 2 months after the drug holiday.
Conclusion: Providing insights into the patients´ response after erenumab treatment discontinuation and subsequently after the re-uptake of treatment, the results can further inform current guidelines on the treatment of migraine with the monoclonal antibody erenumab.
Disclosure: H. Göbel received honoraria for consulting and lectures from Allergan, Almirall, Astra Zeneca, Bayer Vital, Berlin-Chemie, Bionorica, Bristol-Myers-Squibb, Elli Lilly, Fujisawa, GlaxoSmithKline, Grünenthal, Hermal, Hormosan, Ipsen-Pharma, Janssen-Cilag, Johnson& Johnson, Krewel-Meuselbach, Klosterfrau, Lichtwer, Menarini Pharma, Merz Pharmaceuticals, Minster Pharmaceuticals, MSD, Novartis Pharma, Pfizer, Pharmacia, Sandoz, Schaper und Brümmer, Schwarz-Pharma, Teva, Weber&Weber, Smith Kline Beecham. M. Koch is an employee of Novartis AG. C. Weiss is an employee of Novartis Pharma GmbH.

EPO-249

Impact of preventive anti-CGRP therapies on Insomnia Severity Index scale in patients with migraine

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Background and aims: Previous studies shown that insomnia is a common complaint among individuals with migraine. However, there is scarce information of the impact of anti-CGRP therapies on insomnia. We aimed to investigate possible sleep changes in patients with migraine treated with anti-CGRP preventive therapies using the validated sleep questionnaire Insomnia Severity Index(ISI).
Methods: We analyzed a cohort of patients with migraine attended at the Headache Unit of a tertiary hospital who completed one year of anti-CGRP treatment and had ISI scale scores at baseline and 12 months. We collected demographic data, headache variables and ISI scale scores during follow-up visits at 3, 6 and 12 months. The primary endpoint was the ISI scale score at 12 months after anti-CGRP preventive treatment compared to baseline.
Results: A total of 17 patients were included. Among them, 88.23%(15/17) were women, mean age 50(13.8), 94.2%(1/17) chronic migraine, mean number of preventive treatments 10(3.5). There was an improvement in the ISI scale score in 60% of patients at 3 months 60% at 6 months and 70.6% at 12 months. We found a statistically significant reduction in the mean ISI score at 12 months compared to baseline [12.12(5.9);8.12(6);p=0.023], changing from sub-threshold insomnia(8–14) to not clinically significant insomnia(0–7).
Conclusion: According to our study, 70% of patients with migraine under anti-CGRP therapies had an improvement on ISI scale score at 12 months with a statistically significant reduction and score scale change, suggesting a potential benefit of anti-CGRP therapies on sleep; further studies with larger sample size are needed.
Disclosure: Alicia González-Martinez Dr. Alicia Gonzalez-Martinez has received education funding from Lilly, Novartis, Roche, TEVA, Abbvie-Allergan, & Daichi. Dr. S. Quintas has received speaker honoraria from Lilly and Novartis. Dr. José Vivancos has served as speaker, consultant, and advisory member for or has received research funding from MSD, Pfizer, Daychii-Sankyo, Bayer, Sandoz, Bristol Myers Skibb, Lilly, Boehringer Ingelheim, Almirall, Sanofi-Aventis and Ferrer Pharma. Dr. Ana Beatriz Gago-Veiga has received honoraria from Lilly, Novartis, TEVA, Abbvie-Allergan, Exeltis & Chiesi.

EPO-250

Commonalities and differences between COVID-related headache and COVID vaccine-related headache

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Background and aims: To compare the clinical phenotype of coronavirus disease (COVID)-related headache and COVID vaccine-related headache.
Methods: Case-control study including adult patients with headache attributed to COVID (cases) and patients with COVID vaccine-related headache (controls), matched for age, sex, and prior history of headache. A standardized questionnaire was administered, assessing demographic variables, prior history of headache, headache phenotype, and associated symptoms.
Results: 238 patients were enrolled, including 143 cases and 95 controls. There were no differences regarding demographic variables and prior history, except for family history of headache. After adjusting for multiple comparisons, patients with COVID-19 related-headache exhibited a higher frequency of arthralgia, diarrhea, dyspnea, chest pain, expectoration, anosmia, myalgia, odynophagia, rhinorrhea, cough, and dysgeusia. Patients with COVID-19 related-headache had a more prolonged daily duration of headache and described the headache as the worst headache ever experienced. Patients with COVID-19 vaccine-related headache, experienced more frequently pain in the parietal region, phonophobia, and worsening of the headache by head or eye movements. Cough (Odds ratio (OR): 21.316; 95% confidence interval (CI): 4,298-105,725) and rhinorrhea (OR: 15.433; 95% CI: 3,104-76,721) were associated with COVID-19 related-headache in the multivariate analysis.
Conclusion: Headache caused by SARS-CoV-2 infection and COVID-19 vaccination related-headache present more similarities than differences, supporting a shared pathophysiology. In both cases, headache may arise from the activation of the innate immune response. The main differences between COVID-19 related-headache and COVID-19 vaccine related-headache were observed regarding frequency of associated symptoms.
Disclosure: The authors have not conflict of interest.

EPO-251

Brain derived neurotrophic factor during migraine attacks

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Background and aims: Migraine is a very common neurologic disorder. The mechanisms involved in the generation of migraine attack are probably multifactorial and are not fully understood. Brain derived neurotropic factor (BDNF) is a neurotrophin that has been implicated in the generation and modulation of pain. The present study aimed to investigate the role and importance of brain neurotrophic factor in the clinical course of migraine.
Methods: This study sponsored by International Headache Society. In our research work, the main contingent of patients were collected in the clinical hospital of Tashkent medical academy, Uzbekistan. 78 patients aged 18 to 44 years (average age 32.8±7.8) with episodic migraine were selected for the study. The control group consists of 30 healthy volunteers (average age 29.9±3.7).
Results: The increase in BDNF was 83.3% in patients with migraine attacks and 16.67% in patients without migraine attacks, while the decrease in BDNF was 16.67% in patients with attacks and 83.3% in patients without migraine attacks. In this case, x^2 was 30.9, r=0.29, the hazard ratio was 25.0. The Odds Ratio was 5.0. The Risk Difference was 66.6. Fisher-Exact index was 0.000001.
Conclusion: It was observed that the concentration of BDNF in the blood serum of patients increased during migraine attacks. This, in turn, leads to a decrease in the quality of life of patients with acute migraine, and a decrease in the effectiveness of treatment.
Disclosure: This research work founded by International headache society.

EPO-252

Post-dural puncture headache in Kuwait: A hospital-based study

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Background and aims: Lumbar puncture (LP) is a common neurological procedure that can be complicated by PDPH after both diagnostic and therapeutic procedures. We aim to identify the incidence, risk factors and clinical characterization of PDPH in the inpatient setting of the main tertiary neurology hospital in Kuwait.
Methods: We conducted a prospective observational cohort study that included patients who were admitted to neurology department at Ibn Sina hospital, Kuwait, over 2-year period, on whom LP was performed for diagnostic and/or therapeutic reasons.
Results: A total of 285 patients were included; 225 females (78.9%), mean age of 32.9±11.7 years. PDPH was reported by 84 patients (29.5%), with mean headache onset of 1.7± 0.8 days, and mean duration of 2.4 ± 2.1 days. The commonest headache type was dull aching in 49 patients (58.3%). Headache severity was mild/moderate in 64 patients (76.2%), with mean NRS of 4.1±0.9. Most PDPH (99.3%) resolved with conservative medical management. In multivariate logistic regression model, there was a statistically significant correlation between development of PDPH and young age (p=0.001), female gender (p=0 .001), low BMI (p<0 .001), pre-LP headache (p=0.001), history of previous PDPH (p=0.001), and number of LP attempts (p<0.001).
Conclusion: Our findings in the main tertiary neurology hospital in Kuwait were in line with literature findings. Younger age, female gender, lower BMI, pre-procedural headache, previous history of PDPH, and number of LP attempts were found to be independent risk factors for developing PDPH. To our knowledge, this study represents the first comprehensive description of PDPH in a population from the Arabian Gulf Region.
Disclosure: The authors report no sources of funding and no conflicts of interest.

EPO-253

Treatment with anti-CGRP monoclonal antibodies in patients with idiopathic intracranial hypertension: a pilot study

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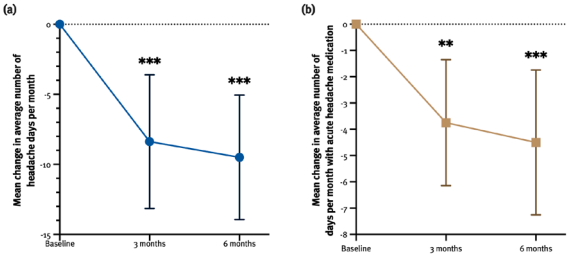
Background and aims: Idiopathic intracranial hypertension (IIH) is a disease mostly occurring in young obese women, often presenting with chronic migraine-like headache. Monoclonal antibodies (mAbs) against calcitonin gene-related peptide (CGRP) or its receptor are a novel effective preventive treatment in migraine patients.
Methods: In this pilot single-centre study, pwIIH with resolved papilledema, yet persisting migraine-like headache, were offered to receive anti-CGRP mAbs. The primary endpoint was mean change in number of headache days/month after three (M3) and six months (M6). Secondary endpoints were defined as follows: (1) reduction of acute headache medication use, (2) improvement of headache days (≥50%) or headache freedom, (3) adverse events (AE).
Results: Eight pwIIH (mean age 30.5 years [SD 10.3], 100% female, median disease duration 1.2 years [IQR 0.4–6.8]) were included (erenumab: 6, fremanezumab: 2). Mean number of headache days/month at baseline was 15.3 (5.3). The latter was reduced by 8.4 (5.7) and 9.5 (5.3) days at M3 and M6, respectively (p<0.001). Mean number of days/month with acute headache medication was reduced at M3 (–3.8 [2.9], p=0.004) and M6 (–4.5 [3.3], p<0.001). Improvement in headache days was seen at M3 (4 [50.0%]) and M6 (5 [62.5%]), whereas headache freedom was achieved in one patient at M3 but none at M6. No serious AE were observed. One patient experienced transient injection-site reaction, and no infections or elevation of liver enzymes were noted. There was no discontinuation of treatment.



Mean number of headache days per month (a) and mean number of days per month with acute headache medication (b) were significantly reduced at M3 and M6.

Conclusion: Anti-CGRP mAbs may be a safe, efficient and well-tolerated treatment option in pwIIH with migraine-like headache persisting after papilledema resolution.
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

EPO-254

Isolated headache in cerebral venous sinus thrombosis due to vaccine-induced immune thrombotic thrombocytopenia

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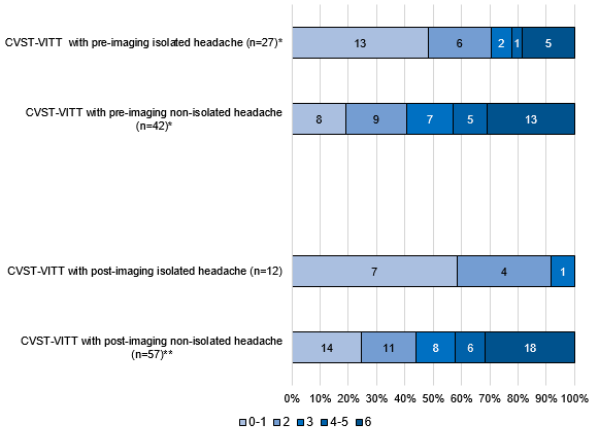
Background and aims: Cerebral venous sinus thrombosis due to vaccine-induced immune thrombotic thrombocytopenia (CVST-VITT) is a rare adverse event occurring after SARS-CoV-2 vaccination. Our aim was to analyse mortality and functional outcomes of CVST-VITT patients presenting with isolated headache.

Methods: Data originated from an international registry of patients with post–SARS-CoV-2 vaccination CVST with cases reported until 10 May 2022. We compared in-hospital mortality and functional outcomes of CVST-VITT patients presenting with isolated and non-isolated headache, assessed pre- and post-imaging. Pre-imaging isolated headache was defined as headache without other neurological signs/symptoms and post-imaging headache as pre-imaging headache without intracerebral lesions on admission neuroimaging.
Results: Of 128 CVST-VITT patients, we included 29 (23%) patients with pre-imaging isolated headache and 44 (34%) with non-isolated headache. Post-imaging, these numbers were 12 (9%) and 61 (48%), respectively. In the pre-imaging isolated headache group (21/29, 72% women and median age 35 years [IQR 25–47]) the in-hospital mortality was 5/29, 17% (vs 13/44, 30% in non-isolated, p=0.277). Post-imaging, none of the isolated headache patients died (0/12, 0%, vs 18/61, 30% in non-isolated, p=0.031). Independency at discharge among pre-imaging isolated headache patients was 19/27, 70% (vs 17/42, 40%, in non-isolated, p=0.026) and among post-imaging isolated headache patients - 11/12, 92% (vs 25/57, 44%, in non-isolated, p=0.003).

Figure 1. Discharge modified Rankin Scale scores of CVST-VITT patients with isolated and non-isolated headache pre- and post-imaging.



CVST = cerebral venous sinus thrombosis; VITT = vaccine-induced immune thrombocytopenia, as defined by Pavord et al. *two missing values; **four missing values

Figure 1. Discharge modified Rankin Scale scores of CVST-VITT patients with isolated and non-isolated headache pre- and post-imaging.

Conclusion: Despite their apparent benign presentation, CVST-VITT patients presenting with isolated headache without other neurological signs/symptoms are still at risk of poor functional outcome. Patients with isolated headache and absence of focal lesions on baseline neuroimaging had no mortality and a good functional outcome.
Disclosure: This research was funded by The Netherlands Organization for Health Research and Development (ZonMw, grant number 10430072110005) and the Dr. C.J. Vaillant Foundation. The funding organizations had no role in gathering, analysing, or interpreting the data.

EPO-255

Design of the ContemporAry ProspecTive Understanding of Migraine Real-world Evidence (CAPTURE) Study

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Background and aims: Insufficient longitudinal evidence is available describing the impact of migraine. This global study will assess how headache/migraine frequency, disability, and treatment patterns change over a 2-year period in individuals being treated for migraine.
Methods: ContemporAry ProspecTive Understanding of Migraine Real-world Evidence Study (CAPTURE) is a 2-year, global, observational, longitudinal, prospective study that will enroll individuals ≥18 years of age being treated for migraine. Participants will be stratified into 3 baseline monthly headache day (MHD) cohorts: 4–7 days; 8–14 days; ≥15 days. Eligibility criteria include men/women diagnosed with migraine for ≥1 year, ≤50 years of age at migraine onset, taking ≥1 migraine medication, and a history of ≥4 MHDs in the 3 months prior to screening, which was confirmed prospectively with headache e-diary data in the 30-day screening period. Key study design elements and endpoints are depicted in the Figure and Table.
Results: The target enrolled sample size is approximately 2000 (cohort 1: 30% [n=600]; cohorts 2–3: 35% [n=700 each]). Patients will be enrolled from approximately 135 sites in 15 countries. The target for first patient enrollment is early 2023 and the last patient completion is anticipated to be late 2025. The study will collect clinical outcomes, patient-reported outcomes, and changes in the number of patients among the migraine cohorts. Only the methodology of this study will be described.
Conclusion: CAPTURE will provide a better understanding of headache/migraine frequency, disability, and treatment patterns in individuals being treated for migraine and will be one of the first global prospective longitudinal studies of its kind.
Disclosure: Study supported by AbbVie.

EPO-256

Work impact and cost-effectiveness of anti-CGRP monoclonal antibodies in patients with migraine

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Background and aims: Migraine is one of the main causes of disability worldwide. Anti-CGRP drugs are effective preventive drugs, but their use is restricted in many countries due to the high cost. Objective: To study the efficacy and cost-effectiviness of anti-CGRP monoclonal antibodies (mAbs) in patients with migraine.
Methods: A prospective cohort study of consecutive migraine patients treated with anti-CGRP mAbs (erenumab, fremanezumab and galcanezumab) in a specialized headache clinic. Migraine characteristics and the work impact scale (WPAI) were compared between baseline (M0) and at 6 months (M6). Using WPAI and the average hourly wage in Catalonia, we calculated indirect savings attributable to the improvement in absenteeism and presenteeism. A cost-effectiveness study was performed considering the different costs and savings of treating with mAbs (Table 1).

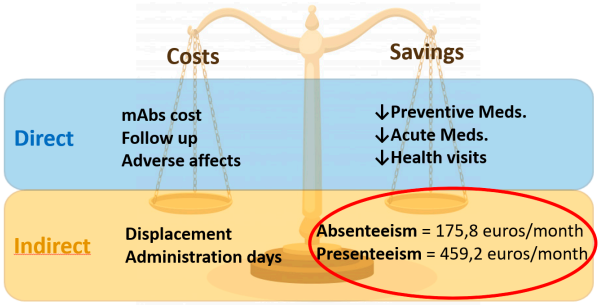

Table 1.- Variables considered in the cost-effectivity. The savings in indirect labor costs (absenteeism and presenteeism) attributable to mAbs are shown in the table.

Results: From 130 treated working age patients, 82 were employed (71 women; mean age 47.5 years, SD=8.6). 56% (46/82) were responders and 44% (36/82) were non-responders, with no significant differences in baseline characteristics. Statistically significant reductions between M0 and M6 were found for the principal clinical variables (Resp, NResp p<0.001), Absenteeism (Resp, p=0.015) and Presenteeism (Resp, NResp p<0.001) (Table 2, Figure 1). The average saving in indirect costs per patient at M6 were: absenteeism 175.8 euros/month and presenteeism 459.2 euros/month. Considering the monthly cost of anti-CGRP mAbs used, the estimated monthly savings significantly exceeded the expenses of these drugs.

	Time M0	Time M6	Difference	Resp.	No Resp.
Days of migraine/month, mean (SD) *P value*	19,2 (7,3)	9,7 (7,6)	-9,5	-14,5 **p<0,001**	-3.2 **p<0,001**
Migraine intensity, mean (SD) *P value*	1,3 (0,6)	0,6 (0,48)	-0,8	-1,04 **p<0,001**	-0,4 **p<0,001**
Acute treatment days, mean (SD) *P value*	12,8 (6,1)	6,8 (4,9)	-6	-8 **p<0,001**	-3,8 **p<0,001**
Absenteeism, hours/week (SD) *P value*	4,8 (9,9)	2,4 (6,8)	-2,4	-3,9 **p=0,015**	-0,5 P=0,66
Presenteeism, % (SD) *P value*	41,1% (31,7)	16,6% (24,9)	-24,5%	-25% **p<0,001**	-23,75% **p<0,001**

Table 2.- Results of the comparisons between M0 and M6 Absenteeism = Lost work hours due to migraine in the last week / (Number of work hours in the las week + Total of lost hours in the last week). Presenteeism = Work productivity due to migraine.

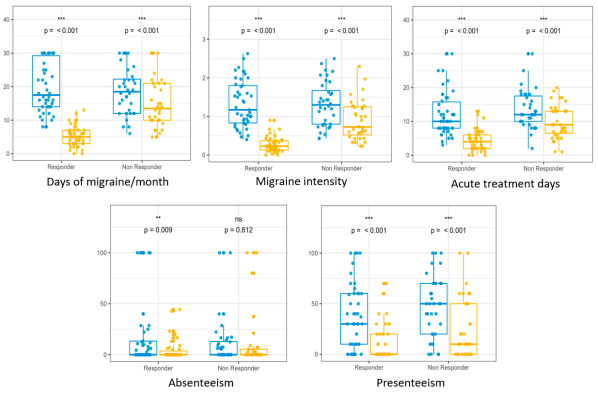

Figure 1.- Graphic representation of the main dependent variables. In blue the results at baseline (M0) and in yellow the results at 6 months (M6); for both responders (>50% reduction in headache days/month) and non-responders (<50% reduction in headache

Conclusion: The use of anti-CGRP mAbs generates a positive impact in the workforce reducing absenteeism and presenteeism. This benefit overcomes the expenses from the use of anti-CGRP mAbs in our cohort.
Disclosure: No conflicts of interest to disclose.

Neuroimmunology 2

EPO-257

Clinic and laboratory predictive factors in different types of encephalitis: the ENCOVID multicentre study

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Background and aims: Encephalitis is defined by the presence of an inflammatory process of the brain in association with clinical evidence of neurologic dysfunction. The diagnosis and treatment are still challenging and prognostic studies are currently lacking. We aimed to investigate the predictive factors associated with poor outcomes in a large spectrum of subjects with different subtypes of encephalitis.

Methods: In this observational multicenter study, 216 patients diagnosed with 4 different types of encephalitis were recruited. The four groups were compared through ANOVA and k2 test, were appropriate. Linear and logistic regression models explored predictors of mortality and worse progression of the disease.

Results: The different types of encephalitis showed several clinical and laboratory differences. Linear regression analysis confirmed lymphocytes at admission (p=0.025) and CSF cells count (p=0.035) as the strongest predictive factors of poor outcomes, independently from demographic, clinical and laboratory characteristics. Logistic regression analysis identified apathy (p=0.018) as the most significant predictor of mortality, adjusting for demographic features and neurologic/systemic symptoms.

Conclusion: In patients with encephalitis, CSF cells count and blood lymphocytes value appear to indicate worse disability at discharge. Apathy, on the other hand, is the strongest predictor of mortality, independently from the diagnosis. Further prospective studies are needed to confirm our findings, to identify patients at high risk of mortality and poor outcomes, and to develop specific strategies for prognostic improvement.

Disclosure: All the authors reported no disclosures.

EPO-258

Clinical profile, and treatment outcomes of autoimmune encephalitis: Experience from a single centre study in South Asia

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Background and aims: Autoimmune encephalitis (AE) encompasses a spectrum of non-infectious, immune mediated neurological disorders, with pathogenic antibodies targeting neuronal surface or synaptic antigens and non-pathogenic antibodies against intracellular, onconeural antigens, in addition to a seronegative group. The present study attempts to focus on clinic-radiological patterns and treatment outcomes of these two subset of AE patients.

Methods: A longitudinal follow-up study was conducted at a tertiary care neurological centre in Kolkata, India, between March 2019 and September 2020. AE was diagnosed as per Grauss et al., after exclusion of mimics. All patients were treated with immunotherapy as per institutional guidelines. Appropriate statistical tests were applied for analysis.

Results: A total of 62 AE patients were selected, of which 41 (66.13%) were sero-positive, of which anti NMDA antibodies were most common (80.45%). Majority of patients were female (59.68%). The median age of onset was significantly higher in the seronegative subset as compared to antibody positive (27 years vs 19 years., p=0.040). Behavioral abnormalities were the most common presentation (77%), followed by seizures (69%) and movement disorders (50%). Outcomes were better in the antibody positive group as compared to seronegative (78.04% vs 52.38%, p=0.02). Odds ratio of developing unfavorable clinical outcomes was more in males (22.53, p=0.036). Delay in initiation of therapy had the most significant likelihood of contributing to unfavourable patient outcomes (p=0.041).

Conclusion: Prompt initiation of immunotherapy in suspected cases AE should be emphasized. Therapeutic decision-making should be individualized, depending on antibody status, patient profile, cost-effectiveness and side-effect profile of drugs.

Disclosure: There is no conflicts of interest amongst the authors. No grants or financial aid was received. Detailed informed consent was obtained from the patients and/or their kin.

EPO-259

Abstract withdrawn

EPO-260

Clinical and real-world pharmacovigilance data of meningococcal infections in eculizumab or ravulizumab-treated patients

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Background and aims: Terminal complement inhibiting therapies (C5ITs) initially approved to treat rare haematological disorders, and more recently rare neurological disorders, are associated with increased Neisseria meningitidis (Nm) infection risk. Robust risk mitigation measures implemented worldwide include vaccination, education materials and patient safety cards. A pharmacovigilance analysis of exposure-adjusted incidence and mortality data for Nm infections in eculizumab- or ravulizumab-treated patients in clinical trial and real-world settings evaluated infection and mortality rates over time as exposure has substantially increased.

Methods: A cumulative search of the Alexion safety database was performed for eculizumab (Mar 2007–Oct 2022) and ravulizumab (Dec 2018–Jun 2022) across all indications, using the MedDRA High Level Term of Neisseria infection. Identified cases were reviewed to include only those associated with Nm.

Results: Cumulative clinical trial Nm infection rates for eculizumab- or ravulizumab-treated patients across four indications are approximately 0.30 and 0.21 cases per 100 patient-years, respectively (Table 1). Cumulative post-marketing reporting rates for Nm infections in eculizumab- or ravulizumab-treated patients are stable at approximately 0.24 and 0.08 cases per 100 patient-years, respectively (Figure and Table 2).

Table 1. *Nm* infection and mortality rates among eculizumab- and ravulizumab-treated patients in the clinical trial setting

Treatment	Cumulative exposure, PY	*Nm* infection, rate per 100 PY	*Nm* mortality, rate per 100 PY	Total *Nm* infections	Total *Nm* fatalities
Eculizumab[1]	2,331	0.30	0	7 cases per 2,331 PY	0
Ravulizumab[2]	2,870	0.21	0.03	6 cases per 2,870 PY	1

[1]Eculizumab first approvals: PNH in 2007, aHUS in 2011, gMG in 2017 and NMOSD in 2019. Data collected between March 2007–October 2022. [2]Ravulizumab first approvals: PNH in 2018, aHUS in 2019 and gMG in 2022. Data collected between Dec 2018–June 2022.
aHUS, atypical haemolytic uraemic syndrome; gMG, generalized myasthenia gravis, *Nm*, *Neisseria meningitidis*; NMOSD, neuromyelitis optica spectrum disorder; PNH, paroxysmal nocturnal haemoglobinuria; PY, patient-years

Table 1: Nm infection and mortality rates among eculizumab- and ravulizumab-treated patients in the clinical setting

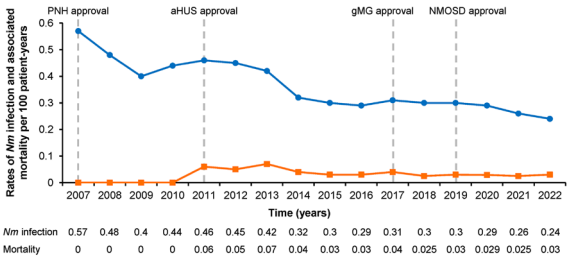
Table 2. *Nm* infection and mortality rates among eculizumab- and ravulizumab-treated patients in the real-world setting

Treatment	Cumulative exposure, PY	*Nm* infection, rate per 100 PY	*Nm* mortality, rate per 100 PY	Total *Nm* infections	Total *Nm* fatalities
Eculizumab[1]	78,416	0.24	0.03	191 cases per 78,416 PY	20
Ravulizumab[2]	7,533	0.08	0.02	6 cases per 7,533 PY	1

[1]Eculizumab first approvals: PNH in 2007, aHUS in 2011, gMG in 2017 and NMOSD in 2019. Data collected between March 2007–October 2022. [2]Ravulizumab first approvals: PNH in 2018, aHUS in 2019 and gMG in 2022. Data collected between Dec 2018–June 2022
aHUS, atypical haemolytic uraemic syndrome; gMG, generalized myasthenia gravis, *Nm*, *Neisseria meningitidis*; NMOSD, neuromyelitis optica spectrum disorder; PNH, paroxysmal nocturnal haemoglobinuria; PY, patient-years

Table 2: Nm infection and mortality rates among eculizumab- and ravulizumab-treated patients in the real-world setting

Figure. Rates of *Nm* infection and associated mortality for eculizumab per 100 patient-years from 2007 to 2022 in the real-world setting



Data are expressed as cumulative rate per 100 patient-years and are inclusive of PNH, aHUS, gMG and NMOSD (indications approved in March 2007, September 2011, December 2017 and June 2019, respectively). Ravulizumab data are not shown owing to low number of cases ($n = 6$) as of data cut-off.
aHUS, atypical haemolytic uraemic syndrome; gMG, generalized myasthenia gravis; *Nm*, *Neisseria meningitidis*; NMOSD, neuromyelitis optica spectrum disorder; PNH, paroxysmal nocturnal haemoglobinuria.

Figure: Rates of Nm infection and associated mortality for eculizumab per 100 patient-years from 2007 to 2022 in the real-world setting

Conclusion: While cumulative exposure to eculizumab has increased, including addition of rare neurological indications, Nm infection rates have steadily decreased and mortality rates have remained stable since 2007. Comparable rates were observed in patients treated with ravulizumab. Raised infection awareness, risk mitigation strategies and availability of additional vaccines effectively reduced the risk of Nm infections in C5IT-treated patients, underlining the importance of adhering to those measures.

Disclosure: All authors are employees of, and hold stock in, Alexion, AstraZeneca Rare Disease.

EPO-261

DACH1 antibodies in immune checkpoint inhibitors-related neurological syndromes

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Background and aims: Dachshund-homolog 1 (DACH1) antibodies (Ab) are recently characterized biomarkers of paraneoplastic neurological syndromes (PNS) . We report two patients with post-ICI DACH1-Ab neurological syndromes identified in the French reference centre for PNS.
Methods: DACH1-Ab were tested by a cell-based assay in 203 patients with suspected PNS for which indirect immunofluorescence assay showed a neuronal nuclear staining pattern without identification of the target antigen (March 2020-September 2022): in 7 patients the staining was selective for Purkinje cells nuclei (Figure 1), and 2 were DACH1-Ab positive.
Results: Both DACH1-Ab patients were men and developed a rapidly progressive cerebellar syndrome 10 months after the first ICI dose (atezolizumab) for small cell lung cancer (patient 1) or limbic encephalitis 3.5 months after the first ICI dose (pembrolizumab) for neuroendocrine bladder cancer (patient 2) with no evidence of cancer dissemination or infectious aetiologies. Brain MRI showed superior cerebellar peduncles T2 hyperintensity and vermian atrophy in patient 1 (Figure), while it was normal in patient 2. There were CSF-unique oligoclonal bands in patient 1 and elevated protein levels in patient 2. Both patients were severely disabled at diagnosis (modified Rankin score of 4 in patient 1, 5 in patient 2) and did not improve at last visit (9 and 4 months after onset, respectively) despite permanent ICI discontinuation and immunosuppression (intravenous steroids and immune globulins in both, cyclophosphamide in patient 2).

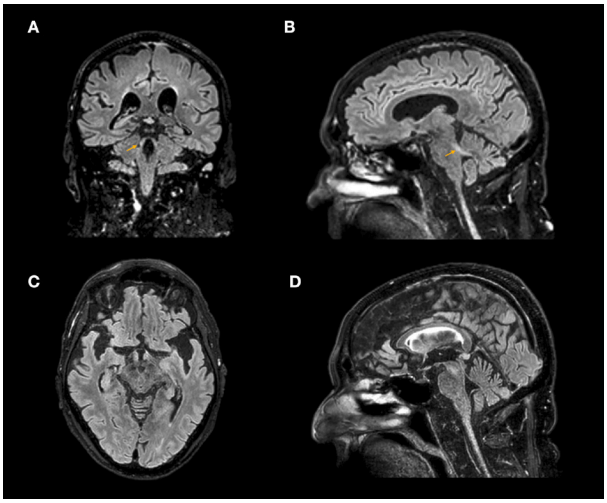

Figure. Brain MRI findings in patient 1. Superior cerebellar peduncles T2/FLAIR hyperintensity (A,B). Vermian atrophy (C,D)

Conclusion: Although exceedingly rare, DACH1-Ab may represent useful biomarkers of post-ICI neurological syndromes clinically resembling PNS.
Disclosure: Macarena Villagrán-García received a research fellowship grant from the Spanish Foundation Alfonso Martín Escudero. Antonio Farina received a research fellowship grant from the European Academy of Neurology in 2022.

EPO-262

Switch to oral cladribine from first line DMD in MS: 2nd Interim Analysis of CLAD CROSS

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Background and aims: CLAD CROSS is a prospective, non-interventional, multicenter, Phase IV study in patients with a confirmed diagnosis of RRMS who switch from first-line disease modifying drugs to treatment with cladribine tablets in routine clinical practice. The primary objective is to evaluate the change in ARR between the 12-month pre-

baseline period and over the 12 months period before end of study follow-up (2 years). Here we report the planned one year interim analysis results.
Methods: The sample size of the study is 250 patients. The second interim analysis was planned at completion of 12-month follow-up for the initial 60% of patients. ARR was compared by the repeated measures Wilcoxon signed-rank test, between the 12-month pre-baseline and first 12 months post-switch to cladribine tablets-period. Treatment satisfaction was measured by treatment satisfaction questionnaire (TSQM) v1.4.
Results: One hundred twenty-four (124) patients were included in the efficacy analysis. ARR decreased from 1.14±0.866 to 0.12±0.451 ($p<0.0001$). Treatment satisfaction was high, with a slight increase of median TSQM score at 12 months to 82%. 60 patients had a treatment emergent adverse event (TEAE) in the total population (n=250, 24.0%), 6 had a serious TEAE (2.4%) and 5 discontinued permanently due to a TEAE (2.0%). The most common TEAEs were infections and infestations (10.4%), lymphopenia (6.4%), and headache (3.2%). No malignancy and no PML were reported.
Conclusion: In the one-year interim analysis of CLAD CROSS, cladribine tablets demonstrated high efficacy with low ARR. Treatment was generally safe and well tolerated. Patient satisfaction was high.
Disclosure: The presenter has received honoraria and travel support from Biogen Idec, Biologix, Novartis, TEVA, Bayer, Merck Serono, Genesis Pharma, Sanofi – Genzyme, ROCHE, has received consultancy fees from Biogen Idec, Novartis, TEVA, BAYER, Bayer, Merck Serono, Genesis Pharma, Sanofi – Genzyme, Cellgene , ELPEN, ROCHE, has received lecture fees from Biogen Idec, Novartis, TEVA, Bayer, Merck Serono, Genesis Pharma, Sanofi – Genzyme, ROCHE and research grants from Biogen Idec, Novartis, TEVA, Merck Serono, Genesis Pharma, Sanofi – Genzyme, ROCHE

EPO-263

Clinical characterization of patients in the post-acute stage of anti-NMDA receptor encephalitis

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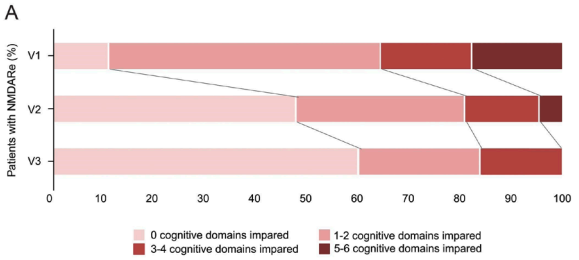
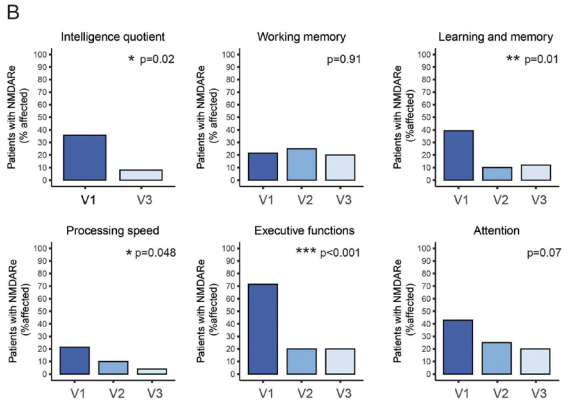
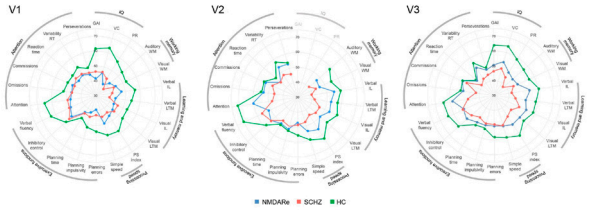
Background and aims: Anti-NMDAR encephalitis (NMDARe) associates with poorly defined protracted symptoms. We characterized the clinical features of post-acute stage NMDARe, similarities with schizophrenia spectrum disorders (SCZ), and predictors of cognitive-psychiatric outcomes.
Methods: In this prospective observational study, patients in the post-acute stage of NMDARe underwent 3 visits (V1, study entry; V2, 6 months; V3, 12 months) including comprehensive neuropsychiatric evaluations at Hospital Clínic, Barcelona. SCZ patients and healthy participants (HC) undertook similar evaluations. Linear mixed-effect models served to assess longitudinal differences.
Results: 28 NMDARe, 27 SCZ, and 27 HC were recruited. Although, by V1 (median 4 months [IQR 3–7] from disease onset), many acute-stage NMDARe symptoms had resolved (acute stage median mRS 5 [IQR 4–5] vs V1 mRS [1–2]; $p<0.0001$), 89% of patients showed deficits in ≥1 cognitive domain (CD). In NMDARe, 15/22 (68%) CD variables were impaired at V1, whereas only 8/22 (36%) were altered at V3 ($p=0.016$). In SCZ, 11/22 (50%) variables (all shared with NMDARe) were impaired at V1, without changes at V3. Two acute-stage NMDARe features (decreased consciousness; no improvement within first 4 weeks of treatment) and a visuospatial task at V1 predicted CD outcomes. At V1, all psychiatric symptom clusters were similarly altered in NMDARe and SCZ, but only NMDARe subsequently recovered ($p=0.031$). The greatest NMDARe cognitive-psychiatric improvement occurred between V1-V2.





Follow-up of cognitive domains in the post-acute stage of NMDARe



Comparison of variables of the 6 cognitive domains among study participants

Conclusion: The cognitive-psychiatric symptoms of post-acute NMDARe resembled those of stabilized schizophrenia, but only NMDARe progressively improved, predominantly during V1-V2. These findings are important for clinical trials on NMDARe and suggest the value of prompt cognitive-psychosocial rehabilitation.

Disclosure: Nothing to disclose.

EPO-264

Paraneoplastic Kelch-like protein 11 antibody-associated cerebellar syndrome caused by metastatic "burned-out" seminoma

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Background and aims: Paraneoplastic neurologic syndromes are remote immune-mediated effects of a cancer. The diagnosis is challenging, and treatment may be delayed when the suspected primary tumor shows complete spontaneous regression (i.e. "burn-out") and masquerades as scar tissue.

Methods: Herein we present the case of a conventional neuronal antibody negative rapidly progressive cerebellar syndrome in a patient with burned out seminoma.

Results: A 45-year-old Caucasian male patient presented with progressive gait and limb ataxia, weight loss and perceptual hearing loss. Initial detailed imaging screening for malignancy as well as testing a diverse set of paraneoplastic and autoimmune neuronal antibodies in both the serum and cerebrospinal fluid (CSF) gave negative results. CSF cytology and flow cytometry, microbiology, genetic testing and serum tumor markers were negative. Serialbrain MRI showed right hippocampal transient contrast enhancing lesion and progressive cerebellar atrophy. Only repeated whole-body FDG-PET CT revealed a hard-to-detect single paraaortic lymphadenopathy – metastasis of a spontaneously regressed testicular seminoma seen as scar tissue on histology. This highly unique clinical presentation suggested, and additional serologic testing in French national reference centre confirmed anti-Kelch-like protein-11 (KLHL11) encephalitis. After 5 cycles of plasma exchange, orchiectomy, metastasis removal and adjuvant chemotherapy the patient's symptoms only stabilized without meaningful clinical improvement: he remained essentially wheelchair-bound.

Conclusion: Our case highlights the importance of continued efforts to find an often burned-out testicular cancer (masquerading as scar tissue) in young male patients with progressive cerebellar ataxia and hearing loss that are highly characteristic of the recently described Kelch-like protein 11 (KLHL11) antibody-associated paraneoplastic encephalitis.

Disclosure: JH is funded by the BETPSY project, which is supported by a public grant overseen by the Agence

Nationale de la Recherche (ANR) as part of the second Investissements d'Avenir program (ANR-18-RHUS-0012), and by the LABEX CORTEX (ANR-11-LABX-0042) of the Université de Lyon operated by the ANR.

EPO-265

Vitamin D promotes the neuroprotective astrocyte phenotype A2 in an animal model of progressive multiple sclerosis

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Background and aims: Vitamin D (VD) is a discussed supplement for multiple sclerosis (MS) patients. Especially the VD effect on the progressive MS form still needs to be better understood. We developed an animal model with a high similarity to human progressive MS pathology. In previous studies, we could observe a positive effect of VD on cellular features of our model with an upregulation of activated astrocytes. Since neuropathology can induce two types of astrocytes that were termed A1 (C3d+; harmful) and A2 (S100A10+; neuroprotective) according to Liddelow et al., 2017; we further investigated the astrocytic phenotypes.
Methods: Male rats received 400 IE VD (Fresenius-Kabi, Graz, Austria) once weekly at age 3 weeks and underwent the standard procedure of our animal model, according to Ücal et al., 2017. Tissue was harvested on peak disease, and GFAP/A1 and GFAP/A2 immunohistochemical double-stainings were performed.
Results: Overall, male (n=10) VD-rats showed a significant upregulation of GFAP/A2+ astrocytes (90/±40 to 151/± 47A2/mm^2; $p<0.009$). An inverse pattern was observed in our preliminary results of GFAP/A1 positive astrocytes.
Conclusion: In summary, our preliminary data show an upregulation of the A2 phenotype and, at the same time, a downregulation of the A1 phenotype in VD-supplemented male rats. Since we already observed gender differences in our animal model, with females having a significant ($p=0.02$) better total antioxidative capacity and less myelin loss, in our ongoing study, we investigate whether a gender difference is detectable in astrocyte phenotypes as well.
Disclosure: This study was partially funded by Fresenius-Kabi (to Hochmeister S). MTH declares no conflict of interest. MÜ declares no conflict of interest. MN declared no conflict of interest. WW declares no conflict of interest. US declares no conflict of interest. CE declares no conflict of interest. SH declares no conflict of interest.

EPO-266

Tumefactive onset of multiple sclerosis treated with anti-CD20 therapy: a case series

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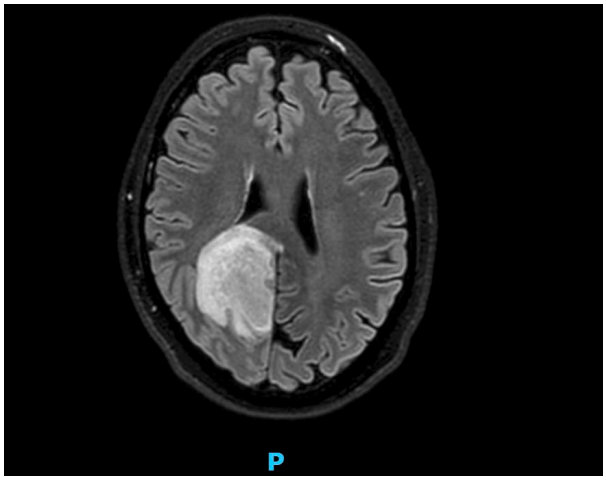
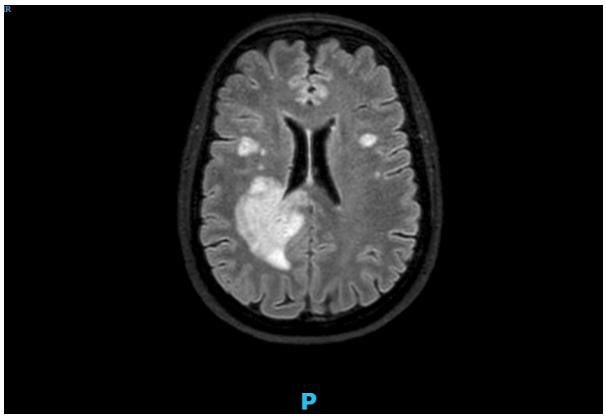
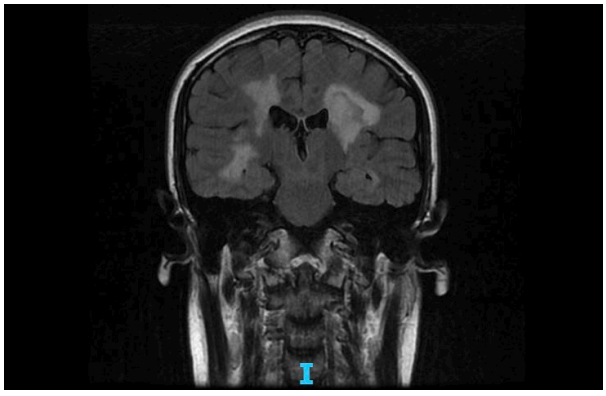
Background and aims: Tumefactive lesions are uncommon manifestations of demyelinating diseases at onset. Some clinical and radiological features may help to suspect this challenging diagnosis.
Methods: We collected three patients at our MS center (two female, mean age 39 years old). They presented differently: case 1 – cognitive impairment and seizures; case 2 – sensitive emisyndrome rapidly evolving to motor impairment and ataxia; case 3 – severe sensory-motor left deficits. Autoimmune and infective screening was negative in all of them. Only –3 had oligoclonal bands.
Results: Magnetic resonance imaging revealed: 1 – a voluminous T1-hypointense and T2/FLAIR hyperintense right parietal lesion with a peripheral enhancement; 2 – multiple hyperintense areas in FLAIR, of whom the largest enhancing in the right frontal-parietal lobe; 3 – multiple pseudotumor-like demyelinating lesions with enhancement. Spectroscopy was performed only in 1 and 3 with an increase in choline peak and a reduction in the N-acetyl-aspartate peak (suggestive for inflammation). Only case 1 underwent neurosurgical exeresis, in the suspicion of a glioma, confirming features of tumefactive demyelination. All patients were treated with high doses of corticosteroid in the acute phase, and they started anti-CD20 therapy (1 rituximab and 2–3 ocrelizumab) with no further relapses at the moment.



Case 1 before exeresis



Case 2



Case 3

Conclusion: Acute or subacute onset with rapid progression of neurological deficits with peculiar MRI/spectroscopy features are suggestive of tumefactive demylinating syndromes. We confirm an effect of B-lymphocyte-depleting agent for typical and atypical MS. Even if the first episod of tumefactive MS is more severe than an usual disease onset, mid-term prognosis could be similar if properly treated.
Disclosure: Nothing to disclose.

EPO-267

Bibliometric analysis of global literature on multiple sclerosis over eight decades (1945–2021)

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Background and aims: Bibliometric studies on the field of multiple sclerosis (MS) research are scarce. The aim of this study is to offer an overarching view of the body of knowledge about MS research over eight decades–from 1945 to 2021–by means of a bibliometric analysis.
Methods: We performed a quantitative analysis of a massive dataset based on Web of Science. The analysis included frequencies, temporal trends, collaboration networks, clusters of research themes, and an in-depth qualitative analysis.
Results: A total of 48,356 articles, with 1,766,086 citations were retrieved. Global MS research showed a steady increase with an annual growth rate of 6.4%, with more than half of the scientific production published in the last decade. Published articles came from 98 different countries by 123,569 authors in 3,267 journals, with the United States ranking first in a number of publications (12,770) and citations (610,334). A co-occurrence network analysis formed four main themes of research, covering the pathophysiological mechanisms, neuropsychological symptoms, diagnostic modalities, and treatment of MS. A noticeable increase in research on cognition, depression, and fatigue was observed, highlighting the increased attention to the quality of life of patients with MS.
Conclusion: This bibliometric analysis provided a comprehensive overview of the status of global MS research over the past eight decades. These results could provide a better understanding of this field and help identify new directions for future research.
Disclosure: The authors report no sources of funding and no conflicts of interest.

EPO-268

IgG as a biomarker of clinical efficacy in generalized myasthenia gravis: Model-based meta-analysis of FcRn inhibitors

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Background and aims: Generalized myasthenia gravis (gMG) is a rare chronic autoimmune neuromuscular disease. Therapeutic anti-FcRn antibodies are being evaluated (e.g nipocalimab) or are approved (efgartigimod) for treatment of gMG. Anti-FcRn's inhibit FcRn-mediated IgG recycling thus lower circulating serum IgG, including anti-AChR pathogenic autoantibodies. Model-based meta-analysis of clinical data from four anti-FcRn treatments were used to explore IgG as a potential biomarker for the clinical endpoint, MG-ADL score.

Methods: The proportion of treatment effect (PTE) method (Li 2001) was used. Specifically, the contribution of a biomarker (e.g IgG) to the overall treatment-related change in clinical endpoint is calculated as the ratio of an estimated surrogate-contribution (if statistically significant) versus an estimated treatment-effect. Clinical data for nipocalimab, efgartigimod, rozanolixizumab and batoclimab were combined from eight studies (Table 1). PTE was calculated using weighted regression on steady-state, aggregate values of placebo-corrected change from baseline MG-ADL (ΔΔMG-ADL) and percent change of IgG from baseline (ΔIgG) from all studies (Figure 1). Due to the limited dataset (18 datapoints) covariates or random effects were not included.

Results: The estimated IgG coefficient was statistically significant (0.03±0.005 [SE]), suggesting 10% ΔIgG translates to ΔΔMG-ADL of ~0.3. The PTE(%CV) from all aggregate-level FcRn data was 0.82(15%) indicating that a majority of the anti-FcRn effect on ΔΔMG-ADL could be explained by ΔIgG.

Compounds	Study name (NCT)	Study phase
nipocalimab	MOM-M281-004 (NCT03772587)	2
batoclimab	ASCEND-MG (NCT03863080)	2
	9161.3 (NCT04346888)	2
efgartigimod	ARGX-113-1602 (NCT02965573)	2
	ADAPT (NCT03669588)	3
	ADAPT SC (NCT04735432)	3
rozanolixizumab	MG0002 (NCT03052751)	2
	MycarinG (NCT03971422)	3

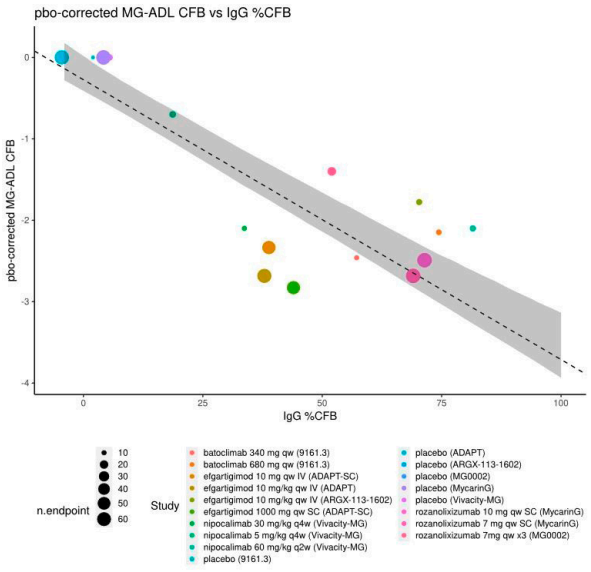

Figure 1: Weighted Linear Regression Model Correlating Placebo-corrected MG-ADL Change From Baseline to IgG Reduction at Steady-State for anti-FcRn's

Conclusion: Since ΔIgG explains a large proportion of anti-FcRn effect on ΔΔMG-ADL, IgG could be used as a potential biomarker for clinical efficacy. This would increase the efficiency of clinical trials (size and duration) to reduce burden for patients in gMG.

Disclosure: All authors except Eugène Cox are J&J employees and might hold J&J stock.

EPO-269

Efficacy of Immunotherapy and Risk Factors for Poor Outcome in LGI1 Antibody Encephalitis Patients: A Meta-analysis

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Background and aims: Anti-leucine-rich glioma inactivated 1 (LGI1) encephalitis is a group of severe antibody-mediated brain diseases presenting with mental symptoms, faciobrachial dystonic seizures, and hyponatremia, etc. Immunotherapy response rate in LGI1 encephalitis patients varied between 67%-92%. We conducted the meta-analysis to assess the efficacy and safety of immunotherapy, and considered the potential predictors of poor outcomes following immunotherapy.
Methods: We systematically searched PubMed and Embase for studies reporting immunotherapy data of LGI1 encephalitis patients. The proportion of poor functional outcome (mRS>2) and ORs with 95% CIs of predictors were pooled using fixed-effects or random-effects model.
Results: 162 articles with 1066 patients were included. The proportion of poor outcome was 14% (95% confidence interval [CI]: 10%–18%) at 12 months, 14% (95%CI: 11%–18%) at last follow-up. We did not find statistically significant association between worst mRS in the acute phase (p=0.449), delayed immunotherapy (p=0.113), second-line treatment (p=0.540), maintenance immunotherapy (p=0.872), follow-up time (p=0.878) and outcome. Adverse effects were recorded in 68 of 225 (30%) patients treated with immunotherapy. Three predictors of poor outcome were identified: elderly age (odds ratio [OR]: 1.03, 95%CI: 1.01–1.05); cognitive impairment (OR: 2.61, 95%CI: 1.15–5.93); CSF antibodies to LGI1 poitive (OR: 1.89, 95%CI: 1.08–3.31).
Conclusion: No association between worst mRS in the acute phase, delayed immunotherapy, follow-up time, second-line treatment, maintenance immunotherapy and outcome in anti-LGI1 encephalitis patients. Patients with elderly age, cognitive impairment, and the presence of CSF antibodies to LGI1 had a high risk for poor outcome. These associations may contribute to improve individualized prognostic assessment.
Disclosure: Nothing to disclose.

EPO-270

Autoimmune encephalitis with antibodies to neuronal surface antigens – the single site experience in Poland.

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Background and aims: Autoimmune encephalitis (AE) are associated with antibodies against neuronal synaptic and cell surface antigens characterized by subacute onset of memory disturbances, seizures, psychiatric changes, and particular neuroradiological findings. We present a retrospective study of cases diagnosed in the Institute of Psychiatry and Neurology in 2013–2021.
Methods: We searched the hospital database for "autoimmune encephalitis" and "limbic encephalitis" and laboratory database for the patients with positive results of antibodies (ab) to surface neuronal antigens. All the patients had their plasma and cerebrospinal fluid (CSF) tested using commercial kits with EU90 transfected cells - Autoimmune Encephalitis Mosaic 1: NMDA, GABA B, AMPA1/2, LGI1, CASPR2 (EUROIMMUN, Germany) and from 2017, AE mosaic 6 with addition of DPPX .
Results: We found 50 cases (23 males, 27 females) diagnosed as autoimmune encephalitis (43 definite and 7 probable): 22 with ab to NMDAR, 10 to LGI1, 8 to CASPR2, 2 to GABA B, 1 to AMPA-1/2 and 7 cases without antibodies but fulfilling criteria for probable AE. Through the laboratory database we found also 12 cases with the antibody presence (8 with ab to NMDA and 4 to CASPR2) without typical AE clinical features, mostly in chronic refractory epilepsy patients.
Conclusion: AE should be taken into consideration in subacute neurological and psychiatric disorders. On the other hand, we do not know clearly what is the role of autoantibodies in patients with no or only minor symptoms and what should be the management in such cases.
Disclosure: Authors have nothing to disclose concerning presented study.

EPO-271

Neuroimaging as a upfront diagnostic tool in childhood GBS

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Background and aims: Guillain-Barre syndrome (GBS) is characterized as an acute, symmetric progressive, inflammatory demyelinating polyneuropathy. Enhancement of cauda equina nerve roots represents the radiological hallmark of GBS. Many clinical symptoms of GBS are non-specific, therefore contrast enhanced neuroimaging of brain and spinal cord is a important tool for diagnosis of GBS and ruling out other differentials. Neuroimaging may allow early detection in patients with inconclusive clinical examination and helps in early treatment plan.
Methods: We included a total of 33 children between 0–18 years who had a final diagnosis of GBS and followed up in pediatric neurology OPD at a tertiary care centre.
Results: The study group comprised 22 (66.6%) boys and 11 (33.3%) girls. The age ranged from 0–17 years. Clinically cranial nerve involvement was present in 17 (51%), while radiological cranial nerve involvement was seen in 14 (51.8%). 16 (48.4%) children required mechanical ventilation. Out of 27 children in whom Lumbar puncture was performed 20 (74%) children had albuminocytological dissociation. In 12 (44.4%) anterior cord involvement was seen, 9 (33.3%) had contrast enhancement or thickening of cauda equina nerve roots. 3 (11.1%) had Anterior>posterior cord involvement and 2 (7.4%) had simultaneous involvement of anterior and posterior nerve roots.
Conclusion: Contrast enhancement brain and spinal MRI is a sensitive and important diagnostic test for diagnosing GBS in children. It can be used as a supplementary diagnostic tool in resourceful settings.
Disclosure: There was no conflict of interest among authors. The project didn't required any funding.

COVID-19; Infectious diseases 2

EPO-272

The Risk of Acute Transverse Myelitis Following COVID-19 Vaccination in Korean Population-based Study

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Background and aims: Acute transverse myelitis (ATM) is a rare neurological condition, but cases of COVID-19-associated ATM have occurred during the pandemic. To address concerns about the causal relationship of reported ATM following COVID-19 vaccination, we assessed the risk of ATM after vaccination with COVID-19.
Methods: We used a large-linked database of claims data from the National Health Insurance Service and COVID-19 vaccine registry from the Korea Disease Control and Prevention Agency from January 1, 2002, to October 31, 2021. We included ATM patients who were newly diagnosed with ATM (ICD-10 code: G37.3). We performed a self-controlled case-series design within 90 days observation period after vaccination date and estimated incidence rate ratio (IRR).
Results: People received the first COVID-19 vaccination was 19,639,721. Among 52 ATM cases, risk and control intervals were 31 and 21cases, respectively. Of 21 were men (52.5%), and half of patients were over 65 (n=26, 50.0%). The risk of ATM increased following COVID-19 vaccination (IRR=2.16; 95% CI: 1.25–3.73). The ATM risk in subgroup analysis was increased for male (IRR=3.07, 95% CI: 1.35–7.00, 50-64 ages (IRR=3.54; 95% CI: 1.07-11.67), CCI score≥5 (IRR=2.82; 95% CI: 1.53–5.21), and AstraZeneca vaccinees (IRR=3.17; 95% CI: 1.50–6.70).
Conclusion: Our analysis revealed an increase in ATM following COVID-19 vaccination. Nevertheless, several concerns should be considered for a causal link between ATM and COVID-19 vaccination: 1) validity of ATM diagnosis without detailed clinical information 2) relative rarity of ATM in general population 3) small number of ATMs in this analysis. Corroborative hospital-based case review can be planned as future work.
Disclosure: There are no financial conflicts of interest to disclose.

EPO-273

Myelitis associated with COVID-19: clinical, radiological, laboratory characteristics (serum and CSF cytokines profiles)

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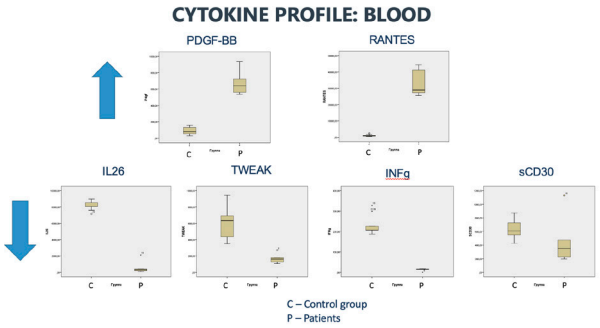
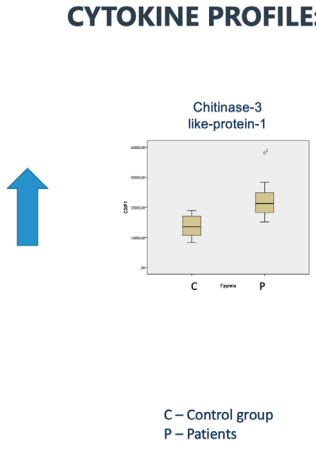
Background and aims: Spinal cord injury is a common complication of a novel coronavirus infection. Current study was aimed to analyze the various types of spinal cord pathology in COVID-19 patients, its clinical, radiological, laboratory characteristics, response to treatment as well as to study cytokine levels in patients' serum and CSF.
Methods: 27 patients with various immune-mediated spinal cord pathologies developed within 3 months after COVID-19 observed at the Research Center of Neurology in Moscow from September 2020 to December 2022 were enrolled in the study. Clinical, radiological data as well as serum and CSF findings of these patients were analyzed. Cytokine profiles were studied using both Bio-Plex Pro Human Cytokine and Bio-Plex Pro Human Inflammation Panel.
Results: Symptoms of myelitis developed in 4,3±2,6 weeks after the infection. Radiological findings were diverse: transverse myelitis (n=8), longitudinal extensive transverse myelitis (n=6), multifocal spinal cord lesions (n=6), myelitis involving dorsal and lateral columns (n=5) and myelitis without MRI abnormalities (n=2). CSF analysis revealed lymphocytic pleocytosis in 3 patients, elevated protein (>0,7 g/l) in one patient. Polyclonal IgG synthesis pattern both in serum and CSF as well as negative CSF PCR for SARS-CoV-2 were found in our group. Significantly higher levels of PDGF-BB, RANTES, lower titers of sCD30, IL26, TWEAK, INF-gamma in the serum and high level of chitinase-3-like-protein-1 in CSF were observed in myelitis patients comparing to healthy controls.



Significantly higher levels of PDGF-BB, RANTES, lower titers of sCD30, IL26, TWEAK, INF-gamma were observed in the serum of patients with myelitis comparing to controls



High level of chitinase-3-like-protein-1 in CSF were observed in CSF of patients with myelitis comparing to controls

Conclusion: This preliminary analysis confirms clinical heterogeneity of COVID-19 associated myelitis and supports the hypothesis of an important role of cytokine changes in its pathogenesis.
Disclosure: No conflict of interest.

EPO-274

Neurological complications after COVID-19 vaccines and SARS-CoV-2 infection in Lombardia (Italy)

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Background and aims: The influence of COVID-19 vaccination on the risk of different neurological diseases has been subject of intense investigation. No large scale results have been published so far in the population of around 10 million people of Lombardia in Italy.
Methods: Linkable administrative health databases from the Lombardia region were used. By using the adapted self controlled case series (SCCS) method for event dependent exposures, we estimated the relative incidence of different neurological diseases following pre-specified windows at risk after vaccination and after COVID-19 infection in the over-12 population of Lombardia. Follow-up time before vaccination (Pre-Vax period) was compared with follow-up time 0–28 days (high-risk period) from the day of vaccination as well as for COVID infection. The SCCS model was fitted using a conditional Poisson regression model to estimate the Relative Incidences (RI) and their 95% Confidence Intervals (CI).
Results: The 28-day post-vaccination period was associated with a significant increase in the occurrence of ischemic stroke, cerebral haemorrhage, TIAs and myelitis (IRR 1.44, 1.50, 1.67 and 2.65 respectively). When the risk conferred by COVID19 infection was assessed in the same cohort, significant IRR were greater in the occurrence of ischemic stroke, cerebral haemorrhage, and TIAs (IRR 5.6, 3.62, 6.83) and includes also Multiple Sclerosis, neuromyelitis, and polymyositis (5.25, 8.81, 5.67).
Conclusion: Our data suggest that the increased risk of non-inflammatory CNS disorders following COVID-19 vaccination is lower than the risk conferred by COVID-19 infection, and that COVID-19 infection increase the risk of some inflammatory neurological disorders.
Disclosure: FMB has received compensations by Roche, Biogen-Idec and Merck-Serono.

EPO-275

Altered motor cortex long intracortical inhibition and intracortical facilitation in Long COVID cognitive impairment

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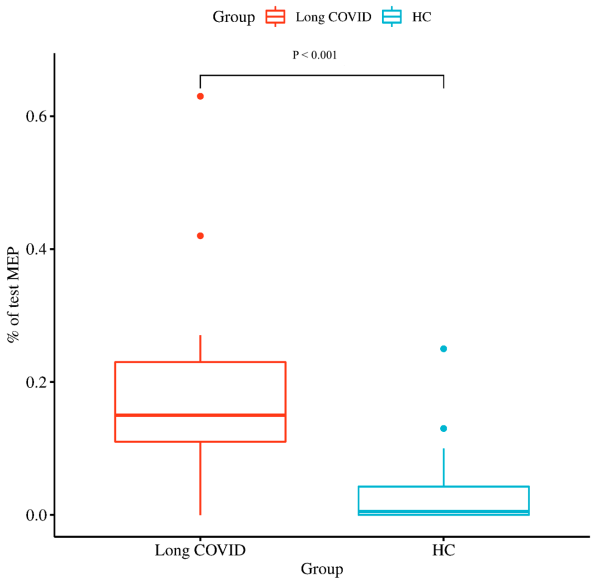
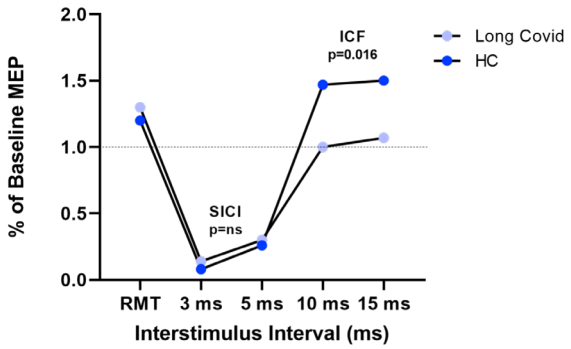
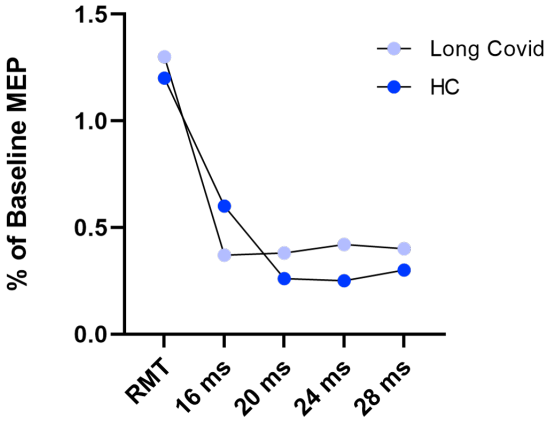
Background and aims: Attention, working memory and executive processing have been reported to be consistently impaired in Neuro-Long COVID. We investigated the functional state of inhibitory and excitatory cortical regulatory circuits by paired-pulse transcranial magnetic stimulation (ppTMS) and Short Afferent Inhibition (SAI).
Methods: We compared clinical and neurophysiological data of 18 Long COVID patients complaining of persistent cognitive impairment with 16 Healthy control (HC) subjects. Cognitive status was evaluated by means of the Montreal Cognitive Assessment (MoCA) and a neuropsychological evaluation of the executive function domain. Resting motor threshold (RMT), the amplitude of the motor evoked potential (MEP), Short Intra-cortical Inhibition (SICI), Intra-cortical Facilitation (ICF), Long Intra-cortical Inhibition (LICI) and Short-afferent inhibition (SAI) were investigated over the motor (M1) cortex.
Results: All the patients' performed sub-optimally in the neuropsychological assessment of the executive functions. RMT, MEPs, SICI and SAI were not significantly different between the two groups. On the other hand, Long COVID patients showed a reduced amount of inhibition in LICI ($p=0.003$) and a significant reduction in ICF ($p<0.001$).



LICI differences in the two groups



SICI-ICF differences in the two groups.



SAI differences in the two groups

Conclusion: Neuro-Long COVID patients performing sub-optimally in the executive functions showed a reduction of LICI related to GABAb inhibition and a reduction of ICF related to glutamatergic regulation. No alteration in cholinergic circuits was found. These findings parallel the pattern of neurophysiological alterations seen in clinical syndromes involving the frontal lobes and allow to frame cognitive deficits in Long COVID as explained by inflammatory states affecting frontal and pre-frontal executive hubs.
Disclosure: The authors declare no competing interests for this study.

EPO-276

Subacute sclerosing panencephalitis: clinical and paraclinical study of Tunisian pediatric cases

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Background and aims: Subacute sclerosing panencephalitis(SSPE) is a rare, fatal and subacute encephalitis secondary to chronic infection with Measles virus. Main signs include cognitive decline, motor disorders and vegetative signs. Our aim is to report clinical, neuroimaging and laboratory feature, treatment and outcome in recent cases with SSPE.
Methods: We conducted a retrospective and descriptive study over the period of 5 years [2019–2023] in our department of Child and Adolescent Neurology. SSPE was diagnosed according to modified Dyken's criteria.
Results: Eight children were included in the study(6 boys and 2 girls). The median age at diagnosis was 43months (38–60). The average age at the time of Measles virus infection was 6months(1-10). One patient was not vaccinated. The mean age of SSPE neurological symptoms onset was at 33months (22–48). Mean latency of 27months(15–40) was noted after primary infection. Neurological exam revealed behavioral changes (n=4), hypotonia (n=8), pyramidal signs(n=4), ataxic gait (n=8), parkinsonism (n=2), movements disorders such as myoclonus (n=7), dystonia(n=3) and swallowing difficulties (n=2). Epilepsy was noted in four patients. Brain imaging showed lesions in the pons and middle cerebellar peduncles realizing pattern of "mustache" (n=3). EEG revealed periodic activity (n=7). CSF analysis showed normal cytology, high levels of anti-measles IgG in the CSF (n=8) and oligoclonal bands (OCBs). Our patients received monthly courses of immun doglobulins(n=7) and antiviral treatment with Isoprinozine (n=7). The evolution was marked by the appearance of akinetic mutism and vegetative signs.
Conclusion: Our study highlights several important points, including the inadequate recognition of measles infection in children. This study alerts the clinicians to consider a possibility of SSPE in children with cognitive decline and myoclonus.
Disclosure: Nothing to disclose.

EPO-277

Serum markers of neuronal and glial damage after full clinical recovery from mild COVID-19 infection.

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Background and aims: Serum neurofilament light chain(sNfL)and glial fibrillar acidic protein(sGFAP)have been demonstrated to increase in patients during the acute phase of COVID-19, regardless of the presence of neurological manifestations. The aim of this study was to evaluate sNfL and sGFAP levels in COVID-19 patients with mild neurological symptoms after full clinical recovery,and compare them with age- and BMI-matched healthy controls in order to assess possible neuronal and glial damage.
Methods: We enrolled a cohort of 147 COVID-19 patients as part of the occupational health surveillance (82 females, 65 males),with an unremarkable past medical history, following a mild COVID-19,and 82 controls(52 females, 30 males). Blood samples were collected within 1 week of clinical recovery following COVID-19 infection and a negative nasopharyngeal swab for SARS-CoV2–PCR test. sNfL and sGFAP levels were assessed in each serum sample of workers and controls using the commercially available immunoassay kits for GFAP and NfL run on the ultrasensitive SR-X™Biomarker Detection System (Quanterix). Cognitive Failures Questionnaire was administered to all the patients and mild cognitive impairment was defined as a score≥43.
Results: Age and BMI-corrected sNfL and sGFAP levels were higher in COVID-19 patients(sNfL median=22.82pg/ml, range 4.18–152.74pg/ml; sGFAP median=146.32pg/ml, range19.17–570.87pg/ml)than in controls(sNfL median=7.21pg/ml, range1.85–29.26pg/ml;sGFAP median=63.53pg/ml, range 8.89–299.34pg/ml; $p<0.001$ for both). Patients with mild cognitive impairment showed higher sNfL levels (median=52.03pg/ml, range 11.41–152.74pg/ml), than those without (median=21.85pg/ml, range 4.18–84.24pg/ml; $p=0.011$),whereas no significant difference between these two groups was observed for sGFAP.
Conclusion: The results of this study show that neuronal and glial injury persists even after full clinical recovery in patients with previous COVID-19 infection.Interestingly, sNfL levels were higher in patients with mild cognitive impairment,suggesting the importance to monitor potential long-term neurological sequelae.
Disclosure: Nothing to report in relation to the study.

EPO-278

Tick-borne encephalitis clinical forms and diagnosis: retrospective study, Belarus, 2018-2021

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Background and aims: Tick-borne encephalitis (TBE) virus is the leading cause of CNS infections in Belarus. Our purpose is to describe the spectrum and characteristics of patients with TBE.
Methods: Retrospective, single-center cohort study with patients admitted due to confirmed TBE infection from 2017 through 2021 (descriptive analysis). For confirmation of TBE serology (IgM and IgG antibody detection) and polymerase chain reaction (PCR) tests of serum and cerebrospinal fluid (CSF) were used.
Results: A total of 90 adults (61.1% males) with a median age of 50.5 years were included. Abortive form was diagnosed in 10.0%, meningitis – in 72.2%, meningoencephalitis – in 15.6%, meningoencephalomyelitis – in 2.2% (2/90) of patients. 74.4% had a biphasic course. None died, but 2 patients with meningoencephalomyelitis had residual sequelae. CSF analysis showed median pleocytosis 69 WBC/uL with lymphocyte predominance (median 85%), protein level 0.52 g/L, glucose level 3.28 mmol/L and lactate level 1.75 mmol/l. TBE IgM and IgG antibodies in patients with TBE CNS invasion were detected in 100% cases but PCR of CSF was positive only in 1 patient with meningitis. RNA of TBE virus by PCR of serum was detected only in 3/8 patients with abortive form of disease.
Conclusion: Meningitis and meningoencephalitis represent the most frequent clinical forms of TBE infection in Belarus. Serology is a highly sensitive test for confirmation of TBE with CNS invasion while PCR of CSF is useless in clinical settings due to low sensitivity. PCR of serum may be useful for early diagnosis of TBE infection before CNS invasion.
Disclosure: Nothing to disclose.

EPO-279

COVID-19 outcomes and vaccination to SARS-CoV-2 in siponimod treated patients: clinical trial and real-world evidence

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Background and aims: Treatment with S1P-modulators such as siponimod may increase the risk of infection. During the SARS-CoV-2 pandemic, and once vaccines became available, the question arose whether or not patients with Multiple Sclerosis (MS) on disease-modifying therapies (DMTs) would mount a sufficient immune response. Therefore we compared infection dynamics of COVID-19 in MS patients treated with siponimod and how SARS-CoV-2 vaccination was coordinated in a clinical study as well as in real-world setting.
Methods: The two german studies, in which siponimod was prescribed as part of clinical routine were analyzed for SARS-CoV-2 vaccinations and COVID-19 infections. AMA-VACC is an open-label prospective clinical study including 41 MS patients currently treated with siponimod or a first-line DMT, analyzing serum neutralizing antibodies and SARS-CoV-2 specific T-cells after vaccination. In the ongoing non-interventional real-world study AMASIA siponimod patients are followed over 3 years.
Results: Most patients treated with siponimod received an mRNA vaccine in both studies. Final data from the AMA-VACC study indicate that patients treated with siponimod were able to mount an immune response after vaccination. The dynamics of COVID-19 breakthrough infections suggest that infections occurred predominantly during the omicron wave (n=29) after vaccination. Most cases were mild and did not require hospitalization, treatment with siponimod was continued throughout the infection.
Conclusion: COVID-19 infection dynamics in siponimod-treated patients seem similiar in the two studies, reflecting frequency and severity of the SARS-CoV-2 pandemic in the general population. This analysis will support clinicians to make an informed decision about coordinating SARS-CoV-2 mRNA vaccination and MS treatment.
Disclosure: HS received research grants and honoraria from Almirall, Bayer Healthcare, Biogen, Merck, Novartis, Roche, and Teva. OH served on scientific advisory boards and/or received speaker honoraria from Bayer Healthcare, Biogen, Bristol Myers Squibb/Celgene, Merck, Novartis, Roche, Sandoz, Sanofi, Teva; received financial support for research activities from Biogen, Novartis, and Sanofi. TZ has received research support, consulting fee and honoraria for lectures from Alexion, Biogen, Celgene, Merck, Novartis, Roche, Sanofi, Teva. TB has received consulting fee and honoraria for lectures from Biogen, Celgene, Merck, Novartis, Pathos Therapeutics, Roche, Teva. CW and VEW are employees of Novartis. Sponsor of this study is the Novartis Pharma GmbH.

EPO-280

Long-term headache after COVID-19 infection: 2 years follow-up

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Background and aims: Headache is part of long-COVID syndrome including worsening of pre-existing or new post-COVID headache. We characterized headache in a cohort of COVID-19 patients two years after infection.
Methods: Prospective cohort of 449 COVID-19 patients consecutively diagnosed between March-June 2020. Follow-up of neurological evaluation was performed face-to-face or by phone. We applied a structured clinical questionnaire to characterize headache before and 24-months after infection.
Results: We included 449 patients with a mean age of 51.5 (s.d.=16.8) years old at COVID-19 diagnosis and 61.0% females. 60.8% (273/449) had acute symptomatic headache, of which 52.0% (142/273) reported headache at 24-months. Previous history of headache was present in 25.8% (116/449). New post-COVID headache occurred in 16.2% (54/333) patients previously headache naïve. The new headache was pressure-like in 70.4%, unilateral in 29.6%, with photophobia in 44.4%, phonophobia in 29.6%, and nausea/vomiting in 29.6%. More than a third (38.9%) had 10 or more monthly episodes, 57.4% with impact on daily life. Moreover, the new headache fulfilled migraine diagnostic criteria in 64.8% (35/54). In patients with previous headache history, 41.4% (48/116) reported changes after infection: a different type (22.9%), more frequent (15.5%), more severe (6.9%), and both (11.2%). The vaccination rate was >95% in all groups.
Conclusion: De novo long-term headache is frequent at 2 years post-COVID. Migraine was the most common type. This is an important finding with a potential impact on healthcare and quality of life, given the number of COVID-19 cases and the known burden of migraine worldwide.
Disclosure: Nothing to disclose.

EPO-281

Role of clinical, radiological and biomarkers of stress in the outcome of cerebral salt wasting syndrome in TBM.

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Background and aims: Hyponatremia and cerebral salt wasting (CSW) have been recognized as important management issues in tuberculous meningitis (TBM). The underlying pathophysiology of CSW has been attributed to stress biomarkers. We report the role of clinical MRI and biomarkers of stress in prediction of 6 months functional outcome of TBM patients with CSW.
Methods: 51 TBM patients with CSW were included. The patients with secondary causes of hyponatremia and polyuria were excluded. The demographic details, MRI finding, clinical symptoms and seizures were noted. Serum antidiuretic hormone (ADH) was measured by ELISA and vasopressin receptors and Endoplasmic stress (CHOP, ATF4, GRP 78) by reverse transcriptase polymerase chain reaction (RT-PCR) and catecholamine (adrenaline, nor-adrenaline and dopamine), Liquid chromatography Mass spectrometry (LCMS). Outcome was assessed by 6 months using modified rankin scale (0-6) and classified as death (mRS 6) or survived and good(mRS 0-2) and poor (mRS 3,4,5)
Results: 15 (34.9%) patients. 17 (39.5%) had poor and 11 (25.5%) had good outcome. On univariate analysis the predictors of death was age, gender, duration of illness, adrenaline, dopamine and V2 receptor. Multivariate analysis dopamine (OR 1.03, 95% CI 1.00–1.06; p=0.017) was independent predictors of death.The independent predictors of poor outcome were dopamine (OR 1.06; 95% CI 1.00–1.12; p=0.04) and CHOP (OR 7.37; 95% CI 1.08–1.82; p= 0.04)
Conclusion: Biomarkers of stress, especially dopamine is independent predictors of death and poor outcome in TB patients with CSW
Disclosure: Nothing to disclose.

EPO-282

The Impact of the first year of COVID-19 pandemic on stroke network performance: experience of a drip-and-ship model

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Background and aims: Regional telestroke networks have been developing recently and can offer advantages during periods of crisis. We aimed to assess the impact of the first year of COVID-19 pandemic on the performance metrics and the outcome in patients with ischemic stroke transferred for endovascular treatment (EVT).
Methods: A multicentric cohort study of a regional telestroke network was performed. We obtained clinical and imaging data from patients evaluated in teleconsultation, recorded time measures and outcome (modified Rankin scale at 3 months) for those transferred for EVT. Data from the first year of the COVID-19 pandemic (19/03/2020 to 18/03/2021) was compared the period between 01/01/2018 and 18/03/2020. Statistical analysis comprised univariate and multivariate analysis adjusted for potential confounding variables. Statistical significance was set at $p<0.05$.
Results: 3,082 Patients were evaluated in teleconsultations with a mean age of 73.3±14.0 years, 50.2% females. The number of consultations per day increased 8.2% during the pandemic (2.7 vs 2.9 consultations/day) and the number of patients transferred per day increased 12.9% (0.59 vs 0.68 patients/day). During the COVID-19 period, there was an increase of 95.8 minutes in the last-known-well-to-door interval (159.5 vs 255.3, $p<0.01$), and of 18.5 minutes in the interval between admission in the primary and the tertiary hospital (1,205.6 vs 224.1, $p=0.04$), while the time between admission in the tertiary hospital and reperfusion decreased 24.2 minutes (101.9 vs 77.7,$p<0.01$). Functional outcome was not affected by the pandemic (OR 0.66 [95%CI 0.7–1.3], $p=0.79$).
Conclusion: During the pandemic, divergent results were observed in different performance measures but without impact in patients functional outcome.
Disclosure: Nothing to disclose.

EPO-283

Impact of COVID-19 pandemic related lifestyle changes on the subjective cognitive performance of hungarian elderly

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Background and aims: Subjective cognitive decline (SCD) can be the earliest red flag of Alzheimer's disease and other dementias appearing about 10 years before diagnosis.
Methods: Our study was conducted within the framework of the World-Wide (WW) FINGERS Network. The aim of the global study was to conduct a survey to monitor the effects of the COVID-19 pandemic on the elderly regarding changes in lifestyle, behaviour and mental well-being. In this study, we analysed the data of 359 elderly Hungarians who filled out the WW-Fingers SARS-CoV2 survey.
Results: A quarter of the respondents (n:88) reported SCD affecting their memory functions that could be related to the pandemic. Participants with SCD showed special characteristics: 1) they were older; 2) they were women; 3) pre-pandemic smoking was more frequent among them; 4) they lived with higher number of chronic disorders; 5) showed more prominent impairment in physical mobility; and 6) used internet more frequently during the pandemic (all p's<0.001). To eliminate the potential interrelation across these group differences, stepwise logistic regression was applied. It highlighted that only two parameters defined the outcome of the responders, the physical mobility and independence (ability to walk 500 meters without difficulties; OR=1.186; $p<0.001$; 95%CI=1.101, 1.270) and changes in time spent with grandchildren (OR=1.04; $p=0.015$; 95%CI= 1.008, 1.073).
Conclusion: As a major finding of this model, impaired pre-pandemic physical mobility and reduced time spent with family during the pandemic were the most characteristic predictors of SCD.
Disclosure: Nothing to disclose.

Movement disorders 2

EPO-284

Social cognition in adult onset primary cervical dystonia

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Background and aims: This study aimed to evaluate the impact of adult-onset focal idiopathic cervical dystonia on general cognition and social cognition. In addition, the correlation between disease severity, duration, mood disturbances, and cognitive impairment was examined.
Methods: 36 cervical dystonia patients and 40 healthy age, gender, and education-matched control were included. Addenbrooke cognitive examination (ACE-R), trail making test (TMT) A and B, Stroop test, reading mind from eyes test, faux pas recognition test, Beck depression scale (BDI), Hamilton anxiety rating scale (HAM-A) were administered to all participants. Cervical dystonia severity was evaluated using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). Both groups were compared statistically on cognitive domains.
Results: Compared to controls, patients displayed significantly decreased performance on executive functions. All participants were shown similar results on the theory of mind test. Except when we matched 13 years or higher graduated participants, cervical dystonia patients had low scores on the faux pas recognition test, unlike controls ($r=1.25$ $p<0.001$). Disease severity and theory of mind scores were negatively correlated. It was not the case for disease severity and general cognition. Functional loss due to torticollis was most severe in patients with higher anxiety and depression scores.
Conclusion: We have found medium-high effect-sized general cognitive impairment in patients with cervical dystonia. For social cognition, education level and verbal comprehension skills were found to be determinative. Theory of mind should be evaluated with tests that have low requirements on working memory and verbal skills in neurological diseases.
Disclosure: Nothing to report.

EPO-285

Rest tremor in essential tremor patients, analysis using typing software.

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Background and aims: Patients with essential tremor (ET) have more risk of developing Parkinson´s disease (PD) compared with controls; some patients with ET can also have rest tremor. Our aim is to evaluate patients with ET and rest tremor measuring keyboard press time and time between taps using software designed for this aim.
Methods: We developed software (Teclasos) which collected data about the time between each tap (TST) and the ressing time of each key (PT). "Teclasos" was used in ET patients with and without rest tremor. We asked patients to alternate taps between "S " and "T" keys. Data regarding gender, age, cardiovascular risk factors and non-motor features were also collected. Bradykinesia and rigidity on physical examination were exclusion criteria.
Results: Thirty-nine patients participated in this study, 16 females (41%) and 23 males (59%); the mean age was 69.18±11.4. We found differences in TST in patients with rest tremor (178.67±137.12ms; $p=0.05$) and in the PT amongst patients with non-motor features (407.24±554ms; $p=0.02$). Patients with rest tremor and non-motor features had higher TST and PT, showing statistical significance ($p=0.01$ and $p=0.08$, respectively). Although differences were also found in patients with cardiovascular risk factors, diabetes mellitus and gender, they were not significant. Patients older than 80 showed higher PT than younger patients (610.15±170ms; $p=0.01$).

AGE	75,66±10,87 years old	
HOEHN&YAHR	2,41±0,4	
LED	582,5±234mg	
		p-value
OFF time PRE	5,93±2,74	0,037
OFF time POST	4,81±2,36	
OFF PRE%	31,75±18,91	0,006
OFF POST%	21,77±12,63	
Cadence PRE	38,5±2,73	0,780
Cadence POST	38,38±2,96	
Step fluidity PRE	6,19±1,3	0,080
Step fluidity POST	6,34±1,32	
FOG PRE	2,2±4,19	0,600
FOG POST	1,88±2,42	
Step lenght PRE	1,25±1,59	0,240
Step lenght POST	1,28±1,64	
Stride speed PRE	0,5±0,07	0,150
Stride speed POST	0,51±0,09	
Acceleration PRE	0,28±0,5	0,140
Acceleration POST	0,27±0,05	

Table 1

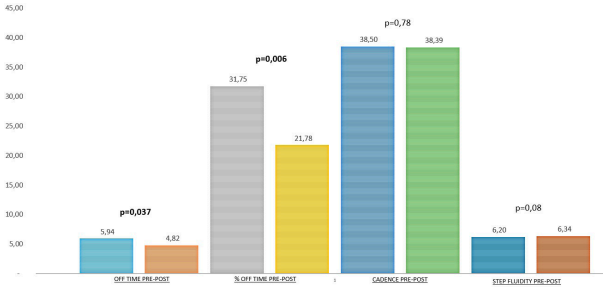

Figure 1

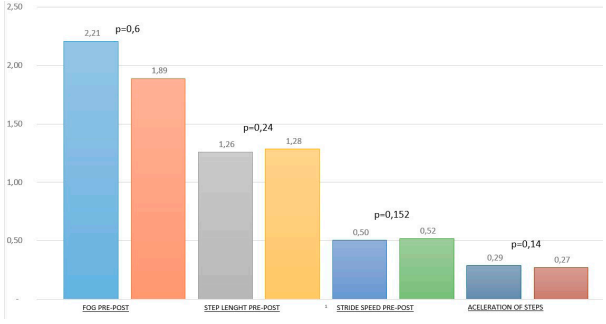

Figure 2

Conclusion: Patients with ET and rest tremor and non-motor features spent more time in TST and PT. These findings could indicate that the pathologic process responsible for rest tremor in ET may have spread into motor systems outside of the cerebellum-cerebellar outflow connections.

Disclosure: Nothing to disclose.

EPO-286

Safinamide improves motor and non-motor symptoms in fluctuating Parkinson's Disease patients.

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Background and aims: The occurrence of motor complications and non-motor symptoms is a crucial problem in the long-term management of Parkinsons' disease (PD). Targeting non-dopaminergic system could be a complementary approach to improve such complications. Safinamide has a unique dopaminergic and non-dopaminergic mode of action that may provide a comprehensive symptomatic relief for PD patients.

Methods: The effects of safinamide on motor and non-motor symptoms were investigated using the data from four Phase III, randomized, double-blind, placebo-controlled pivotal trials, studies 016, 018, SETTLE and XINDI.

Results: Safinamide significantly improved motor fluctuations (OFF time reduced by 1.10 hours, $p<0.0001$), motor symptoms (improvement of 5.15 points in UPDRS III, $p=0.0003$), pain (reduction of concomitant pain-killer treatments of 22%, $p=0.0478$), and mood (improvement of 0.76 points in GRID-HAMD, $p=0.0027$). These improvements were observed after only 2-weeks of treatment, showing a rapid-onset of the efficacy of the drug.

Conclusion: Safinamide, administered as add-on therapy in fluctuating PD patient, improved motor symptoms and motor complications without increasing troublesome dyskinesia, irrespective of whether other drugs were added to the baseline levodopa treatment. Moreover, safinamide improved pain and mood, two important non-motor symptoms often underestimated and undertreated. These favorable effects may be explained by its modulation of glutamatergic hyperactivity.

Disclosure: Carlo Cattaneo, and Constanza Oliveros are Zambon SpA employees; Ivan Marjanovic and Erminio Bonizzoni are Zambon SpA consultants.

EPO-287

Influence of RBD onset on the clinical characteristics of Parkinson's disease patients: a retrospective study.

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Background and aims: In Parkinson's Disease (PD), Rapid Eye Movement (REM) Sleep Behavior Disorder (RBD) might either precede the appearance of motor symptoms, or develop during the disease course. PD patients with RBD are characterized by a higher burden of cognitive impairment and hallucinations. However, few studies have analyzed the clinical characteristics of PD patients according to the timeline of RBD onset.
Methods: PD patients have been retrospectively enrolled. Presence and onset of probable RBD (pRBD) has been evaluated using RBD Screening Questionnaire (score ≥6). Presence of Mild Cognitive Impairment (MCI) at baseline has been evaluated using the MDS criteria level II. Presence of motor complications and hallucinations has been evaluated at a 5-year follow-up.
Results: At total of 115 PD patients (65 men, 56.5%; mean age 62.5±9.7 years; mean disease duration 3.7±3.9 years) have been enrolled. Out of these, 63 fulfilled the diagnosis of pRBD (54.8%) with 21 (33.3%) reporting the RBD onset before the onset of the motor symptoms (PD-RBDpre), and 42 (66.7%) after the motor symptoms (PD-RBDpost). At enrolment presence of MCI was associated with PD-RBDpre patients (OR 5.04; 95%CI 1.33–19.05; p-value=0.02). At follow-up, a higher risk of developing hallucinations was also associated with PD-RBDpre (OR 4.82;95%CI 1.30–17.85; p=0.018).
Conclusion: PD patients with RBD occurring before the onset of motor symptoms represent a subgroup of patients with a more severe cognitive phenotype and with a higher risk of developing hallucinations along the disease course, with significant implications in terms of prognostic stratification and therapeutic approach.
Disclosure: Nothing to disclose.

EPO-288

Neurological spectra of neurofibromatosis type 1 in adults: a case series

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Background and aims: Neurofibromatosis type 1 (NF-1) is an autosomal dominant multisystem disorder, with predominant neurological involvement. Aim: To perform a clinical, imagological, and genetic analysis of a NF-1 adults' cohort.
Methods: Patients were identified from an institutional database. Files review was performed according to a structured protocol.
Results: Eleven patients (from nine non-consanguineous families) were identified, 5 females, with age 39±12 years. Ten had family history in first-degree relatives. All had disease onset in childhood, the most frequent presentation being café-au-lait (CAL) spots (9). All subjects had one or more neurological symptoms/signs: pyramidal signs (8), headache (5), learning disabilities (4), movement disorders (4), delayed milestones (2) and epilepsy (1). Two patients developed optic pathway gliomas. Cutaneous involvement was present in all: CAL spots (11), freckling (9) and cutaneous neurofibromas (7). Eight had ophtalmological manifestations, the most frequent being Lisch nodules (5). In 8 patients, brain MRI revealed T2-weighted hyperintensities, consistent with myelin vacuolization, at the cerebellum (4), hippocampus (3) and/or basal ganglia (3). All had heterozygous pathogenic variants on NF1.
Conclusion: Adults with NF-1 have a wide range of neurological phenotypes, with the most frequent being pyramidal signs, probably in relation with white matter lesions. We highlight the frequency of movement disorders in our patients, which may be underdiagnosed in previous cohorts.
Disclosure: All authors declare that they have no conflicts of interest related to the manuscript.

EPO-289

Atypical immunochemistry staining in rapidly progressive cerebellar syndrome in woman with breast cancer

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Background and aims: Rapidly progressive cerebellar syndrome (RPCS) is frequently paraneoplastic in postmenopausal women with breast and ovarian cancer, associated with so-called high-risk for cancer antibodies. The syndrome is a treatable condition but often with no full recovery.
Methods: A 67-years old woman was admitted for a ten days onset of nausea, vomit, sickness, weight loss, gait instability, dysarthria, hypophonia, diplopia, dysphagia and limb and trunk ataxia (mRS 4).
Results: The patient underwent several brain MRI scans, always negative. The lumbar puncture showed an inflammatory cerebrospinal fluid (CSF): 27 cells/mm^3, glucose 71 mg/dl, proteins 48 mg/dl; coltural, virological exams and most common anti-cerebellar antibodies were negative. PET total body and mammography detected a mammary lesion (BI-RADS 6) with axillary lymphatic metastasis. Immunochemistry and biological profile found out estrogen receptor positive breast cancer. Using indirect immunofluorescent tissue based assay exploiting lightly fixed rat brain tissue, we detected on CSF an uncharacterized nuropilar staining involving the molecular layer of the cerebellum. In the suspicion of RPCS, the patient underwent five days of intravenous immunoglobulins treatment, then replaced by steroid with slow tapering. Surgery was excluded by Breast Unit team. At 6 months follow-up, there was a little neurological improvement with persistence of dysarthria, and ataxic features (mRS 3).
Conclusion: The features of staining resemble anti-Tr/Delta/Notch-like Epidermal growth factor-related Receptor (DNER) antibodies. Our patient presented several clinical features in common with RPCS associated with these antibodies, usually lymphoma and solid tumors related, instead no breast cancer cases were still reported.
Disclosure: Nothing to disclose.

EPO-290

Reasons for exclusion from Deep Brain Stimulation (DBS) for Parkinson's Disease

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Background and aims: Understanding the reasons for exclusion from DBS for Parkinson's disease (PD) might optimize referral. Nevertheless, few studies have addressed it. We aimed to evaluate the reasons for exclusion from DBS for PD in our centre.
Methods: A retrospective observational study evaluated all patients referred to and excluded from DBS between January 2006 and May 2019. We searched our DBS database and reviewed the clinical files of patients consulted at least once for DBS, and a data extraction spreadsheet was developed.
Results: Of 320 patients consulted for DBS, 72 (22.5%) were excluded (52.4% male; average age 65.2 [±6,6] years, range 40–79 years; average disease duration 12,3 [±6.0] years). There were on average 3.3 [±2.4] consultations and 6.7 [±7.3] months until exclusion. 25.4% of patients were excluded in the first consultation. An average of 1.89 reasons were identified, although 44.4% had only one reason for exclusion. 3 patients were excluded due to atypical parkinsonism. 68.3% were referred by Movements Disorders (MD) specialists. The main reasons for exclusion were an MDS-UPDRS motor part score during Best On in items "gait", "freezing" and "postural instability" above the cutoff (23.8%); dementia (2.8%); and age >70 years (22.2%). 20.6% give up from su3rgery after an explanation of the procedure. Reasons for exclusion were similar between patients referred by MD and non-MD specialists.

Conclusion: One-fifth of the patients were excluded from DBS. Levodopa-resistant axial symptoms, dementia, and age were the main reasons, although several give up from surgery after a detailed explanation of the procedure.
Disclosure: Nothing to disclose.

EPO-291

Opicapone versus entacapone: Head-to-head comparison of HCRU in COMT-I naïve People with Parkinson's

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Background and aims: The appearance of motor fluctuations (MF) is a crucial milestone in people with Parkinson's (PwP) as they are associated with increased disability and considerable healthcare resource utilisation (HCRU). Management of MF may require add-on of enzymatic inhibitors such as Catechol-O-methyl transferase (COMT) inhibitors. To date there has been a lack of head-to-head data comparing opicapone and entacapone, the two most commonly used COMT inhibitors in real-world settings.
Methods: In this retrospective cohort study, we assessed HCRU outcomes in PwP naïve to COMT inhibition via UK electronic healthcare records (Clinical Practice Research Datalink and Hospital Episodes Statistics databases, June 2016 to December 2019). HCRU outcomes were assessed before (baseline) and after COMT inhibition at 0-6 months, 7–12 months, and 13–18 months. Opicapone treated PwP (n=173) were 1:4 algorithm-matched to entacapone-treated PwP (n=433).
Results: A significantly higher percentage of PwP in the entacapone-treated group had ≥1 neurology outpatient visits at 6-month follow-up compared to the opicapone-treated group (63% vs 44%, respectively, $p<0.001$). Head-to-head regression analyses (including age, sex, disease duration, baseline HCRU, and baseline medications as covariates) showed that PwP who received opicapone as their first line COMT inhibitor had 18.5% fewer neurology outpatient visits within 6 months of initiation compared to the entacapone-treated group.
Conclusion: This head-to-head study is the first to demonstrate using 'real-world' data that initiating COMT inhibition with opicapone is likely to decrease the need for post-treatment HCRU versus initiation of COMT inhibition with entacapone.

Disclosure: Funded by BIAL. FM: Speaking honoraria from Abbvie, Medtronic, Boston Scientific, Bial, Merz; Travel grants from the International Parkinson's disease, Movement Disorder Society; Advisory board fees from Abbvie, Merz, Boston Scientific; Consultancies fees from Boston Scientific, Merz, Bial; Research support from NIHR, UKRI, Boston Scientific, Merz, Global Kynetic; Royalties for the book "Disorders of Movement" from Springer; member of the editorial board of Movement Disorders, Movement Disorders Clinical Practice, European Journal of Neurology. KRC: Speaking honoraria from AbbVie, UCB, GKC, Bial, Cynapsus, Lobsor, Stada, Zambon, Profile Pharma, Synovion, Roche, Therevance, Scion, Britannia, Acadia, 4D Pharma, Medtronic; Travel grants from AbbVie, UCB, GKC, Bial, Cynapsus, Lobsor, Stada, Zambon, Profile Pharma, Synovion, Roche, Therevance, Scion, Britannia, Acadia, 4D Pharma and Medtronic; Consultancies and Advisory Board fees from AbbVie, UCB, GKC, Bial, Cynapsus, Lobsor, Stada, Zambon, Profile Pharma, Synovion, Roche, Therevance, Scion, Britannia, Acadia, 4D Pharma and Medtronic; Research grants from Bial, Britannia Pharmaceuticals, AbbVie, UCB, GKC; Academic grants EU Horizon 2020, Parkinson's UK, NIHR, Parkinson's Foundation, Wellcome Trust; Kirby Laing Foundation, MRC; Royalties for Oxford (book), Cambridge publishers (book), MAPI institute (KPPS, PDSS 2); Payment for expert testimony from GMC; Committee Chair Movement Disorders Society, European Journal of Neurology.

EPO-292

Is fatigue in Parkinson's disease a disorder of movement preparation? A neurophysiological study

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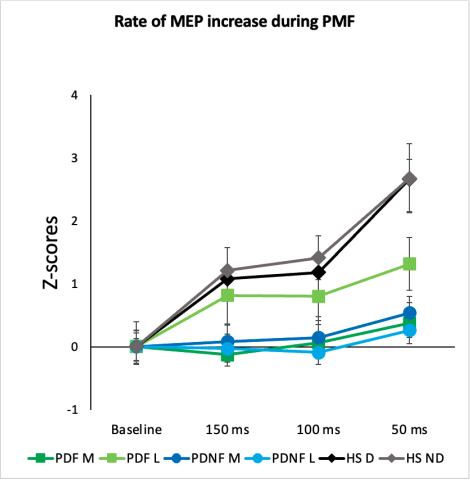
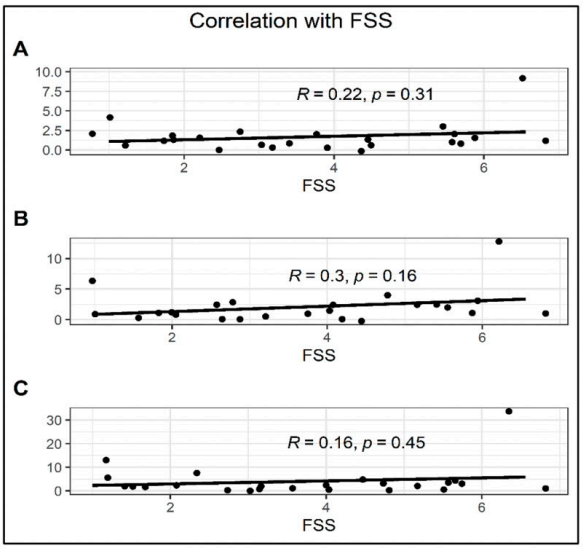
Background and aims: Fatigue is common in Parkinson's disease (PD) and it has been linked to the impairment of motor planning. In Multiple Sclerosis fatigued patients showed reduced pre-movement facilitation (PMF). We aimed at investigating whether PMF is abnormal in PD and is related to fatigue.
Methods: We enrolled 15 PD patients with fatigue (PD-F, Fatigue Severity Scale ≥4), 16 PD patients without (PD-NF) and 16 Healthy Controls (HC). We assessed PMF with transcranial magnetic stimulation (TMS) during a simple reaction time (RT) paradigm. Subjects were asked to briskly abduct their thumb after a go signal and TMS was delivered at 50 ms, 100ms and 150ms before the mean calculated movement onset. 15 PD-F patients (mean age 63.27±9.8 years).
Results: The rmANOVA corrected for age did not show significant interactions group x side x time (F= 0.26, p= 0.9) of amplitude of MEP and at three intervals during PMF (MEPPMF) compared to MEPREST. When computing the rate of MEP increase during PMF (MEPPMF/MEPREST), all groups had a significantly higher rate of PMF at 50 ms (F=4.3, p=0.014*), but HC significantly differ from patients while PD-F and PD-NF did not differ from each other (p> 0.05). No correlation was found between fatigue scores and MEP increase.



Rate of Motor evoked potentials (MEP) increase during pre-movement facilitation (PMF) in Parkinson's disease (PD) patients' most and least affected sides and in dominant and non-dominant hand of healthy controls (HC).



Analysis of correlations between Motor evoked potentials (MEP) increase during pre-movement facilitation (PMF) in Parkinson's disease (PD) patients and Fatigue Severity Scale (FSS)

Conclusion: Our results provide preliminary evidence that PMF is abnormally reduced in PD patients compared to HC and independent from fatigue. Reduced PMF could represents a hallmark of PD patients. Future works are necessary to disentangle the mechanisms of fatigue in PD.
Disclosure: The Authors have no relevant disclosure.

EPO-293

Gender differences in non-motor fluctuations in Parkinson's disease

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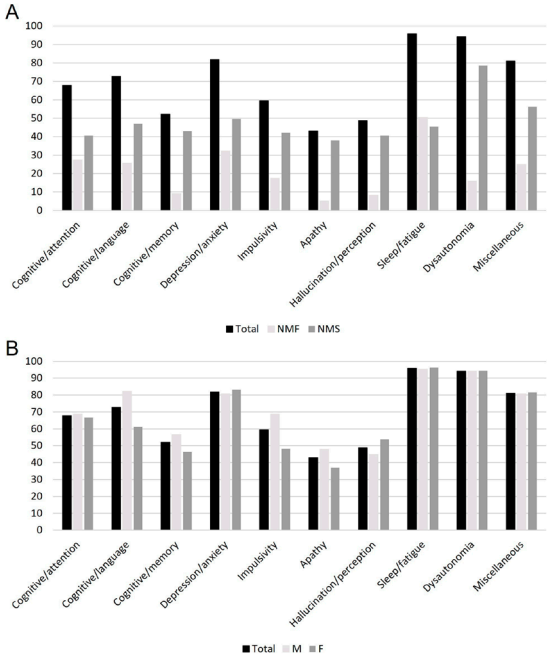
Background and aims: Non-motor symptoms (NMS) and Non-motor fluctuations (NMF) in Parkinson's Disease (PD) are common, involving several domains and affecting quality of life. Aim of the study is to estimate the burden of NMF in PD patients and to evaluate the possible gender effect.

Methods: PD patients fulfilling the MDS-PD diagnostic criteria attending the "Parkinson's Disease and Movement Disorders Centre" of the University of Catania were evaluated using the Non-Motor Fluctuations Assessment (NoMoFA) Questionnaire. NoMoFA items were also grouped into the following domains: cognitive, mood, sleep/fatigue, dysautonomia, hallucination/perception and miscellaneous domains were identified.

Results: One-hundred and twenty-one patients with PD (67 men, 55.4%; mean age 70.2±8.9 years, disease duration 8.3±4.6 years) were evaluated. All PD patients reported at least one NMS, whereas 87 (71.9%) also reported NMF. "Feel sluggish or had low energy levels" (47.2%) along with "Feel excessively sleepy during the day" (40.0%) were the most common NMF reported in the whole sample. The majority of PD patients reported presence NMF during the OFF state (79, 65.3%). At multivariate analysis, NMF were positively associated with the female gender (adjusted OR 3.41; 95%CI 1.28–9.09; p-value=0.01). Women with PD had higher NMF scores especially in depression/anxiety, sleep/fatigue and dysautonomia domains.



Frequency of reported domains in PD sample. A, differences in reported non-motor symptoms in the whole PD sample considering non-motor fluctuation and static non-motor symptoms. B, differences in reported domains between PD male and female

Conclusion: Our study reported the presence of a gender-related pattern in the frequency of NMS and NMF in PD patients, with female gender associated with a higher risk of developing NMF, highlighting the need for personalized treatment strategies when addressing NMF.

Disclosure: Authors declare no disclosures for this work.

EPO-294

Safety of safinamide in routine clinical practice in a Spanish population with Parkinson's disease

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Background and aims: Safinamide is a levodopa add-on therapy with a dual dopaminergic and non-dopaminergic mechanism of action that improves the management of Parkinson's disease (PD). This post-hoc analysis of the European SYNAPSES trial aimed to provide new evidence on the safety profile of safinamide among Spanish study participants in routine clinical practice.
Methods: Once safinamide treatment began, patients with PD were followed for 12 months. The occurrence of adverse events (AEs) was analysed overall and in preselected subgroups that included patients older than 75 or with relevant comorbidities or psychiatric conditions.
Results: Of 511 participants, 131 (25.6%) were older than 75, 373 (73.0%) had relevant comorbidities, and 249 (48.7%) had psychiatric conditions. At least one AE was reported by 280 (54.8%) patients, while 168 (32.9%) had at least one adverse drug reaction (ADR). At least one serious adverse event (SAE) was registered in 38 (7.4%) patients, and 8 (2.0%) had at least one serious ADR. The majority of AEs were mild (69.3%) or moderate (23.5%), and ultimately all resolved completely. Few AEs (2.0%) and no SAEs had a definite relationship with safinamide. No relevant differences for AE and SAE frequencies were detected in elderly patients nor in patients with psychiatric conditions, and slightly higher percentages were observed in patients with comorbidities.
Conclusion: Safinamide proved to be a safe option for different groups of PD patients in routine clinical practice.
Disclosure: The SYNAPSES trial and this post-hoc analysis were funded by Zambon S.p.A.

EPO-295

Dysphagia assessment in Parkinson's disease and risk of aspiration pneumonia

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Background and aims: Dysphagia is a complication that is common in latter stages of Parkinson's disease (PD) influencing quality of life of patients and caregivers. The prevalence of dysphagia and risk of secondary complications such as aspiration pneumonia in dysphagic PD patients is variable, being highly dependent on the methods used for the evaluation. Aim of the study: to assess the prevalence of dysphagia and aspiration pneumonia in patients with PD.
Methods: Cross-sectional study that included patients with PD evaluated in the outpatient clinic or admitted in the Department of Neurology, County Clinic Hospital Brasov. We evaluated the patients using a standardized protocol that included the Hoehn-Yahr scale, Gugging Swallowing Screen (GUSS), fibro-endoscopic evaluation of swallowing (FEES), FEDSS scale and Munich Dysphagia Test (MDT-PD).
Results: There were 35 patients included in the study (43.75% males) with a mean age of 68.2±5.7 years. The mean Hoehn-Yahr stage was 2.8. Swallowing disturbances was frequently encountered in patients with higher H-Y stage (12 patients H-Y 3-5) were 58.33% presented some degree of dysphagia in comparison with 13.04 % in stages 1–2 ($p<0.05$). Pneumonia was encountered in 16.6% of the dysphagic patients with higher H-Y stage, with no cases of pneumonia in patients with lower stages of disease. A higher MDT-PD was corelated with the risk of aspiration and corresponded with the changes observed on the FEES evaluation.
Conclusion: Dysphagia has a high impact on the quality of life of PD patients, being a risk factor for aspiration pneumonia.
Disclosure: Nothing to disclose.

EPO-296

Characterisation of OFF-Time in Levodopa-Treated Parkinson's Patients: A Post-hoc Analysis of an Exploratory Trial

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Background and aims: Optimising levodopa (LD) treatment regimens through catechol-O-methyltransferase (COMT) inhibition is an effective strategy in the management of motor fluctuations (MF) in patients with Parkinson's disease (PD). Study 203 demonstrated that adding the COMT inhibitor opicapone (OPC) to LD therapy increases LD systemic exposure and decreases OFF-time in patients with PD and MF. This post-hoc analysis evaluated the OFF/ON patterns in LD-treated patients included in Study 203 before OPC was added.

Methods: Study 203 was an exploratory, open-label, modified cross-over trial. All participants received LD/carbidopa (CD) 500/125 mg, administered as 5 daily intakes of 100/25 mg every 3 hours for 2 weeks and were then randomly (1:1) assigned to LD/CD 400/100 mg given in 4 or 5 daily intakes plus OPC 50 mg for 2 additional weeks. LD 12-hour pharmacokinetics (PK) was the primary outcome (last daily intake excluded from PK analysis); 12-hour patient ON/OFF monitoring was a key secondary outcome. This study evaluated ON/OFF patterns in patients treated with the LD/CD 500/125 mg regimen before randomisation.

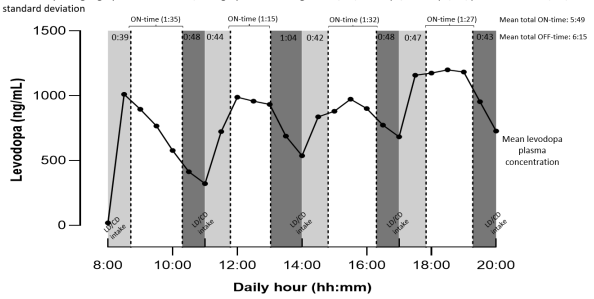
Results: Overall, 24 patients were recruited and received the LD/CD 500/125 mg regimen (Table). For all daily intakes, the mean total ON-time was 5h 49mins and the mean total OFF-time was 6h 15mins (Figure). The total OFF-time was divided into time-to-ON (2h 52mins) and 'wearing-off' (3h 23mins), which represented 45.9% and 54.1% of the total OFF-time, respectively.

Table. Baseline characteristics

	Overall N=24
Male gender, n (%)	13.0 (54.2)
Mean age, years (SD)	62.2 (7.1)
Mean weight, kg (SD)	81.9 (16.0)
Mean height, cm (SD)	167.3 (9.5)
Mean PD duration, years (SD)	6.6 (3.2)
Mean daily OFF-time, hours (SD)	7.3 (1.6)
LD/CD monotherapy or plus other PD drugs excluding DA and MAO-Bi, n (%)	10 (41.7)
Levodopa/carbidopa monotherapy (no other PD drugs), n (%)	7 (29.2)
Patients receiving DA and MAO-Bi* in addition to Levodopa/carbidopa, n (%)	
Levodopa/carbidopa plus DA only	9 (37.5)
Levodopa/carbidopa plus MAO-Bi only	4 (16.7)
Levodopa/carbidopa plus DA & MAO-Bi	1 (4.2)
PD medications given in addition to levodopa/carbidopa, n (%)	17 (70.8)
Pramipexole	6 (35.3)
Selegiline	5 (29.4)
Ropinirole	4 (23.5)
Trihexyphenidyl	3 (17.6)
Amantadine	3 (17.6)

*Some patients were receiving additional PD drugs that were not DA or MAO-Bi
CD, carbidopa; DA, dopamine agonists; LD, levodopa; MAO-Bi, monoamine oxidase inhibitors; PD, Parkinson's disease; SD, standard deviation

Figure. 12-hour ON-/OFF-time data reported on PK* days in relation to the mean LD plasma concentration versus daily hour in patients receiving the 5-intake (every 3 hours) daily oral administrations of LD/CD 500/125mg. *Last daily intake was excluded from the PK analysis. Light grey bars: time-to-ON; dark grey bars: 'wearing off'. LD/CD, levodopa/carbidopa; PK, pharmacokinetics; SD, standard deviation



Conclusion: The current analysis suggests that in LD-treated patients with 'wearing-off' MF time-to-ON following a dose of LD is responsible for nearly half of total daily OFF-time.

Disclosure: Supported by Bial.

EPO-297

Movement disorders as initial manifestation of autoimmune encephalities: A case series.

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Background and aims: Autoimmune encephalitis (AE) and paraneoplastic neurological syndromes (PNS) are a growing field in recent years. Movement disorders are one of the most consistent features of these disorders. Early diagnosis is essential since immunomodulatory treatment can considerably change the prognosis.
Methods: We describe a case series of AE in which the movement disorder was the initial manifestation (The main characteristics of the reported patients are highlighted on table-1).
Results: Patient-1, a 78-year-old man, presented acutely faciobrachial dystonic seizures of seconds of duration. LGI1 antibodies were found in serum. After starting immunotherapy, significant improvement was observed, persisting dystonia with a task-specific component. Patient-2, a 73-year-old man, presented symptoms of gait disturbance and rapidly progressive akinetic-rigid parkinsonism, with early falls, cognitive impairment and insomnia, worsening 3 months until cause serious disability. Anti-IgLON5 antibodies were found on CSF and serum. Patient-3, a 65-year-old woman, developed oral occlusion dystonia, and later on ataxia and ophtalmoplegia, with a rapid progressive course. MRI showed hyperintensity in the superior cerebellar peduncle and pons (Figure-1). Anti-Ri antibodies were detected in CSF and serum and small cell lung carcinoma was found afterwards (being the encephalitis its first symptom).
Conclusion: EAs can debut with different movement disorders. Therefore, it is important to take into account the red flags that can lead us to suspect this type of disease, highlighting acute onset, early disability and early development of other neurological symptoms, as it is a potentially curable cause of encephalitis, with a fatal course in the absence of treatment.
Disclosure: Nothing to disclose.

EPO-298

Evaluation of the effectiveness of safinamide in a Spanish population with Parkinson's disease

E. Freire-Álvarez[1], A. Esquivel[2], J. Gomez-Esteban[3], J. Kulisevsky-Bojarski[4], I. Legarda-Ramírez[5], M. Mata Álvarez-Santullo[6]
[1]Service of Neurology, Elche University Hospital, Elche, Spain/Service of Neurology, IMED Elche Hospital, Elche, Spain, [2]Section of Neurology, Infanta Leonor University Hospital, Madrid, Spain, [3]Service of Neurology, Cruces University Hospital, Barakaldo, Spain, [4]Movement Disorders Unit, Hospital of Santa Creu i Sant Pau, Autonomous University of Barcelona, Barcelona, Spain/CIBERNED, Madrid, Spain, [5]Service of Neurology, Son Espases Hospital, Palma de Mallorca, Spain, [6]Service of Neurology, Infanta Sofia University Hospital, Madrid, Spain

Background and aims: The use of safinamide as a levodopa add-on therapy has proven efficacy in the management of Parkinson's disease (PD) in controlled trials. This post-hoc analysis of the SYNAPSES trial provides new evidence on the use of safinamide in a Spanish cohort in routine clinical practice.
Methods: Once safinamide treatment began, patients with idiopathic PD were followed for 12 months and evaluated through the Unified Parkinson's Disease Rating Scale total score (UPDRS) and UPDRS part III score during ON time.
Results: Compared with the European study population, there was a higher prevalence of psychiatric symptoms and non-compliant use of safinamide (30.9% vs. 16.9%) in the Spanish cohort. A higher percentage of the Spanish participants showed clinically relevant improvement when receiving add-on safinamide only (reduction in UPDRS total score >4.3=57.4%; reduction in UPDRS part III score >2.5=53.7%) compared to treatment with additional adjunct therapies (reduction in UPDRS total score >4.3=44.1%; reduction in UPDRS part III score >2.5=42.8%). Switching from rasagiline to safinamide showed an improvement in 55.1% of patients (UPDRS total score). Safinamide reduced the proportion of patients with motor complications independent of levodopa doses, showing a stronger effect in the absence of other adjunct therapies.
Conclusion: Despite higher off-label use of safinamide within the Spanish study population, a stronger clinical benefit was observed when using safinamide as the unique add-on therapy to levodopa, including in patients with comorbidities.
Disclosure: The SYNAPSES trial and this post-hoc analysis were funded by Zambon S.p.A.

Epilepsy 2

EPO-299

Resting-state brain connectivity differences between epileptic and non-epileptic first events

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Background and aims: Epilepsy is a brain network disorder affecting different regions across the brain. Clinical diagnosis often relies on different "markers" such as brain lesions or signs in the electroencephalography (EEG) tracing. However, in clinical routine these markers are not always clear or present at all, making it difficult to provide a certain diagnosis, especially because different pathologies can underlie the same epileptic symptoms. Here we investigated if measures of functional connectivity applied to resting-state EEG recordings differed between five patients groups (n=15 per each group): epileptic, acute symptomatic seizure (ASS), psychogenic non-epileptic seizures, syncope, and patients who suffered from a single unprovoked seizures.
Methods: We retrospectively recruited untreated first-seizure patients for whom the EEG tracing did not show interictal epileptic discharges, and who presented no epileptogenic brain lesions (besides the hemorrhagic stroke group). We calculated a weighted phase lag index as a measure of connectivity in several regions of interest (ROIs) and for different frequency bands.
Results: We found a significant interaction ($p=0.034$) across groups for clustering coefficient (network segregation), which was increased in epileptic and ASS patients versus controls ($p<0.001$ and $p<0.01$ respectively), specifically in delta frequency.
Conclusion: Given the often difficult diagnosis of epilepsy in the absence of clear signs on the EEG tracing, connectivity measures across patient groups could provide support for the identification of a possible underlying epileptic disorder. Future prospective studies will determine its usefulness as a biomarker for epilepsy.
Disclosure: MS has shares in Epilog.

EPO-300

Better effect of early vs delayed treatment after the first seizure: a brain connectivity study

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Background and aims: Treatment may be delayed after the first seizure in new onset epilepsy (NOE) patients, often as a result of unorganized work-up. Our own observation suggests that antiseizure medication (ASM) <48h is related to a higher rate of patients with seizure control, as compared to later treatment. In this study, we investigated EEG markers of early/late drug therapy through connectivity analysis.
Methods: 36 epileptic patients were retrospectively enrolled (mean age: 53.14; SD: 16.37; 36 females). All received an EEG while in the emergency department (ED). Follow-up EEGs were obtained 1 to 12 months after the first event. 23 patients were treated <48h and 13 were treated later. Connectivity was compared between both groups for all established frequency bands.
Results: Patient groups did not differ in age, gender, presence of a brain lesion or delay of follow-up EEG. The interaction between frequency bands and delay of ASM was significant ($p<0.001$). In the follow-up EEG, patients treated later showed reduced theta connectivity ($p=0.006$) and increased alpha connectivity ($p<0.001$).

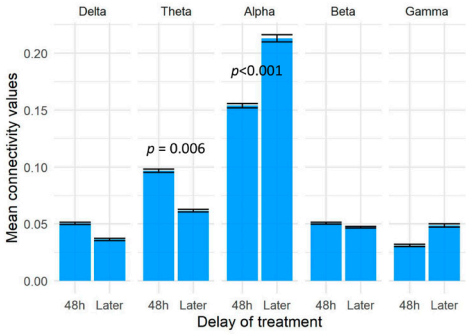

Figure: differences in brain connectivity across all brain regions per frequency band for follow-up EEG. Significant differences are noted and error bars represent standard error of mean.

Conclusion: Our results suggest that swift ASM introduction affects significantly theta and alpha frequencies, up to 1 year after the index event. Larger prospective studies are required to determine if these changes in the EEG connectivity are a useful marker for future treatment success or if it reflects a neurobiological effect of early ASM on possible excitatory and inflammatory processes at the first event.
Disclosure: MS has shares in Epilog.

EPO-301

Predicting risk of relapse by functional connectivity in patients with new onset epilepsy

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Background and aims: After a diagnosis of epilepsy, 20–30% of patients will relapse regardless of treatment. To date, markers able to predict future success in drug response are still lacking. Here, we investigated brain connectivity recorded by means of electroencephalography (EEG) between patients who respond to treatment (responders) and patients who respond poorly (non-responders), to link potential differences to treatment response.
Methods: We retrospectively recruited 65 patients with new onset epilepsy (at least 2-year follow-ups) for whom an EEG was performed before treatment directly upon arrival at the hospital, following a first epileptic seizure. We computed connectivity analyses (weighted phase-lag-index) on all brain regions for delta, theta, alpha, beta, and gamma frequencies. By performing a mixed-model analysis, we tested connectivity differences across frequency bands between responders and non-responders.
Results: After treatment, 50 patients remained seizure-free (mean age: 57; SD: 18) while 15 relapsed (23%; mean age: 54.6; SD: 18.9). No significant differences in age (p=0.11) and sex (p=0.13) were found between groups. In terms of EEG, we observed an interaction between frequency bands and groups (p<0.001). Post-hoc tests showed a delta decrease (p=0.022) and an alpha increase (p=0.022) for patients who relapsed despite treatment as compared to patients who did not. No significant differences were observed for the other frequency bands.

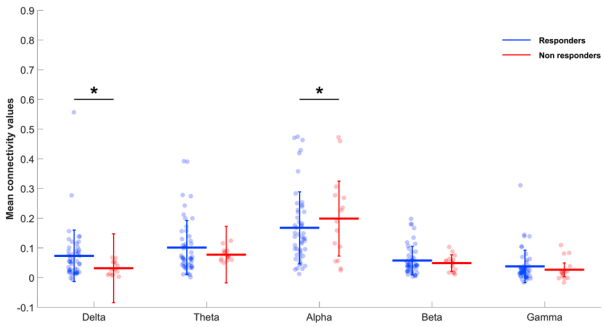

Figure: Brain connectivity values per frequency band between responders and non-responders. Differences between groups marked with a black asterisk are statistically significant (p<0.05). Error bars represent standard deviation.

Conclusion: EEG connectivity in delta and alpha frequencies after a first epileptic seizure appears to be a promising marker for future poor drug treatment response.
Disclosure: MS has shares in Epilog.

EPO-302

Serum microRNA levels can predict ketogenic diet efficacy in adult refractory epilepsy

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Background and aims: Ketogenic diet (KD), is being increasingly used in adult patients with good efficacy and tolerability. Although KD mechanisms of action are yet to be identified, microRNAs (miRs), are thought to be key players in this process. We aimed to address if epilepsy-associated miRs can predict the response to KD in adult refractory patients.
Methods: Circulating miR-146a, miR-155, miR-22, miR21, and miR-134 were quantified in 40 adult refractory epileptic patients (16 M; 33.1±11 years) before and at 3 months of Atkins modified KD regimen.
Results: Three months after treatment onset, 20 out of 40 patients presented seizure reduction, 14 patients were non-responders and 6 reported only a qualitative benefit. At baseline, miR-146a levels were higher in responder patients compared to non-responders (25.95 vs. 23.62, p=0.029). Although no significant differences were observed for the other individual miRs, we combined miR-146a – miR-155 – miR-22 – miR-21 – miR-134 and observed that this panel had a good prognostic value differentiating responders and non-responders with 77% specificity and 70% sensitivity (AUC=0.791[0.624–0.958], p=0.007). In responder patients KD induces changes in miRs levels with the upregulation of miR-134 (M0 vs. M3: 20.96 vs. 21.90, p=0020) and the downmodulation of miR-155 (M0 vs. M3: 23,99 vs. 22,73, p=0,018) and miR-22 (M0 vs. M3: 22.87 vs. 19.79, p=0.020).
Conclusion: The panel miR-146a – miR-155 – miR-22 – miR-21 – miR-134 may be a suitable biomarker for KD response, which could help select epilepsy patients that would most benefit from this treatment. Our results support an epigenetic-reprogramming action of KD, affecting namely inflammation-associated microRNAs.
Disclosure: Work funded by LPCE and CHUPorto bursaries.

EPO-303
Abstract withdrawn

EPO-304
The Long Term Prognosis of IGE: a comparison between syndromes

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Background and aims: Idiopathic Generalized Epilepsies (IGE) are usually drug responsive, but patients with a diagnosis of Juvenile Absence Epilepsy (JAE), Epilepsy with Generalized Tonic-Clonic seizure alone (GTCA) and Juvenile Myoclonic Epilepsy (JME) often require a life-lasting anti-seizure medication (ASM). We tested if syndromic diagnosis is relevant to prognosis.
Methods: Patients with JAE, GTCA or JME and a follow-up of 1) 5 or 2)15 years after the first seizure were included. By Kruskall-Wallis ANOVA , we have compared the a) total number of Generalized Tonic Clonic seizures (GTCs) occured b) the longest GTCs-free period c) time spent to reach this period d) the number of adequate ASM regimen tried to reach this period d) "drug resistant" patients considering any seizure type.
Results: We included 34 and 22 JAE, 44 and 17 JME, 23 and 10 GTCA, for the 5 and 15 years follow up , respectively. The total number of GTCs was higher for GTCA compared to JAE and JME in the 5 years follow up period ($p \leq 0.01$) and to JAE in the 15 follow up period. The longest GTCs-free period and the time spent to reach this period were not different among groups. A higher number of ASM-trials were required and drug resistance was more common in JME in the longer follow-up (1% in JAE, 27% in JME, 0% in GTCA, $p<0.01$).
Conclusion: JAE carried the more benign prognosis. JME required the highest number of adequate ASM trials and were more prone to be classified as drug resistant in the longer follow-up.
Disclosure: The authors declare no conflict of interest.

EPO-305
Social cognition in the spectrum of mesial temporal lobe epilepsy

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Background and aims: Increasing evidence suggests that social cognition is impaired in mesial temporal lobe epilepsy (MTLE). Refractory MTLE (rMTLE) has been found to affect: i) Theory of Mind (ToM), which is the ability recognize and comprehend others' mental states and ii) facial emotion recognition. Milder forms of MTLE (mMTLE), by definition characterized by response to antiseizure medication and seizure-freedom, were not evaluated. The aim of this study was to analyze social cognition in the spectrum of MTLE.
Methods: Forty-five patients with MTLE (25 mMTLE, 20 rMTLE) were compared to 25 healthy controls (HC). ToM was explored with Faux Pas Test (FP) and Reading the Mind in the Eyes Test (RMET). Facial emotion recognition was studied with Ekman Faces Test (EFT). In addition, a specific battery of tests was performed as screening for cognitive and mood disturbances.
Results: With respect to HC, both mMTLE ($p=0.017$) and rMTLE ($p<0.001$) patients had lower scores in the RMET, whereas no differences were identified between the two subgroups of patients. Moreover, only rMTLE patients had lower performances in the FP recognition when compared to HC ($p=0.004$). In EFT mMTLE had lower scores in fear and anger recognition, while rMTLE underperformed also in happiness, sadness, disgust, and surprise recognition.
Conclusion: MTLE affects circuitries of ToM and emotion recognition even in subjects with mMTLE, albeit with a more limited extension compared to rMTLE. This supports the idea that epilepsy itself, even when seizure control is achieved, could damage key areas involved in the complex neural circuits of social cognition.
Disclosure: The authors have nothing to disclose.

EPO-306

Progression of electroclinical features in Lennox-Gastaut syndrome from childhood to adulthood

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Background and aims: Lennox-Gastaut syndrome (LGS) comprises a triad of multiple, medically-refractory seizure types, cognitive impairment, and electroencephalogram (EEG) features including diffuse slow-spike-and-wave (DSSW) and background slowing during wakefulness, and diffuse fast rhythms (DFR) in sleep. However, not all of these EEG features may be present in adulthood. Our study aims to identify how EEG patterns and seizure types evolve as an LGS patient ages.

Methods: Retrospective, single-centre study, including 24 adult patients. Information was collected on types of seizures at onset and at last follow-up, and interictal and ictal findings from paediatric and adult EEG telemetry reports.

Results: Tonic seizures were the commonest in both populations; atypical absences were more common childhood, and generalised tonic-clonic in adulthood. 84.20% childhood interictal EEGs showed DSSW, 100% background slowing, and 100% had DFR in sleep. 72.73% childhood ictal EEGs showed electrodecrement (ED) with fast activity (FA) with tonic seizures, and 27.28% showed only FA. In contrast, 35% of adult interictal EEGs showed DSSW; 60% background slowing, but DFR during sleep were present all adults. DSSW was most commonly replaced by independent multifocal spike discharges (76.92%) in adults. 56.25% adulthood ictal EEGs showed only ED with tonic seizures, 31.25% ED with FA, and 12.5% only FA.

Conclusion: Our study highlights that in LGS, both interictal and ictal EEG features change significantly over the lifespan, and stresses the importance of sleep EEGs in adulthood, due to its implications for LGS diagnosis, and subsequent medical management, especially with medicinal cannabis in the UK.

Disclosure: The authors have no conflicts of interest with regards to this research study.

EPO-307

A retrospective cohort study on the management of early and established status epilepticus

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Background and aims: Status epilepticus (SE) is a time-sensitive medical emergency with high mortality and morbidity. We investigated the management of early and established status epilepticus including timing, dosing and selection of benzodiazepines and efficacy of second line treatments.

Methods: Single-centre, retrospective observational cohort study.

Results: 252 patients. Seizures terminated spontaneously in 54% cases. 46% were given benzodiazepines, of which 25% were given at least one benzodiazepine by family/carers, and 62.1% received benzodiazepines by ambulance services. Benzodiazepines terminated seizures in 71.6% cases. The commonest benzodiazepine was buccal midazolam (35.5%). Median time to first benzodiazepine was 14.5 (6–27) minutes. We found a positive correlation between time to first benzodiazepine and time to seizure cessation, progression to second- and third-line treatment, and respiratory complications ($p<0.05$). 62.9% cases received a correct benzodiazepine dose. Underdosing was commonest, and associated with longer seizure duration and progression to second-line treatment ($p<0.05$). 28.4% cases progressed to second-line treatment; mean time to treatment was 59.4 minutes (±32.3 minutes). The commonest second-line ASM was Levetiracetam (53.8%), followed by Phenytoin (43.6%). Second-line treatment terminated seizures in 57.5% cases. 12.1% cases progressed to third-line treatment; mean time to treatment was 60.6 minutes (±22.24 minutes). Anaesthetic agents included propofol and fentanyl. Respiratory complications occurred in 6.75% cases; none due to benzodiazepines. There were two deaths in refractory SE.

Conclusion: These data confirm that delays in benzodiazepine administration and incorrect dosing lead to worse outcomes. Efforts to increase awareness of SE as a time-sensitive emergency with high mortality and morbidity are needed.

Disclosure: The authors note no conflicts of interest with regards to this research.

EPO-308

Safe and effective implantation of VNS in super-refractory post-anoxic myoclonic status epilepticus in early pregnancy

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Background and aims: The management of super-refractory post-anoxic myoclonic status epilepticus (PAMSE) in pregnancy may be complicated by anti-seizure medication (ASM) polytherapy-associated teratogenicity. We aim to demonstrate the safety and efficacy of vagal nerve stimulation (VNS) in a pregnant patient presenting with super-refractory PAMSE.

Methods: This is a retrospective case-study. Information was obtained from the patient's electronic medical records at her local hospital and our centre.

Results: A 30-year old female, at 5-weeks gestation presented with drug-refractory myoclonic status epilepticus, unresponsive to anaesthetic agents, due to drug overdose. The severity of seizures did not allow extubation, and the patient remained ventilated and sedated. VNS was implanted 26 days after seizure onset. The immediate post-operative output was 0.25mA, which was rapidly titrated up to 0.5mA the next morning, and to 0.75 mA that afternoon. This was further increased to 1.0mA on 3rd day post-operation, and to 1.25mA 7 days post-op. Myoclonic jerks diminished significantly 5 days post-op, and the patient was extubated. 20 days after VNS implantation, no myoclonic jerks were observed. There was increased alertness and mobility, and ability to obey commands. An early pregnancy assessment 17 days after VNS implantation showed normal fetal heart activity, and crown-rump length. A gestational age of 12-weeks + 3-days and a normally-sited pregnancy were confirmed.

Conclusion: This is the first case-study to report the safe implantation and use of VNS during the first trimester of pregnancy for the management of PAMSE. No maternal or foetal complications occurred, and a normal pregnancy was confirmed 17 days after VNS implantation.

Disclosure: The authors note no conflicts of interest with regards to this case-report.

EPO-309

Identifying seizure onset localization using spatial activation: Applying a novel tool into practice.

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Background and aims: The precise localization of the seizure onset zone is crucial for epilepsy surgery planning. The visual analysis is the most used method for reporting seizure type, location and classification. However, in many cases, the ictal onset zone remains unclear due to fast propagation and the mixture of different frequencies. Using quantitative methods could help provide a more precise analysis.

Methods: We used a novel data-driven method, named "Brainfocus" in 10 patients evaluated with SEEG in our Epilepsy Surgery Program. This method quantifies the magnitude of seizure-related spectral changes with respect to a predefined baseline (Global activation) and the spread of these activations across recording sites. Seizures were analyzed using visual inspection and Brainfocus quantitative analysis, respectively. We compared the number of contacts involved in the first 5 seconds of seizure onset and determined the degree of spatial concordance using both methods.

Results: Patient's average age was 40,9 years and the most frequent type of epilepsy was temporal lobe epilepsy (60%). 13 was the average number of implanted electrodes. 72 representative seizures were selected for analysis. The degree of agreement between qualitative visual inspection and Brainfocus´s global activation was substantial; Lin's Concordance Correlation coefficient was 0.97. The sensitivity of Brainfocus for seizure onset localization was 0.93±0.13 (mean±std across patients).

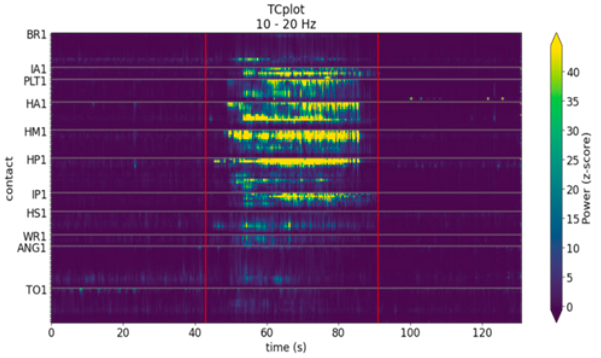
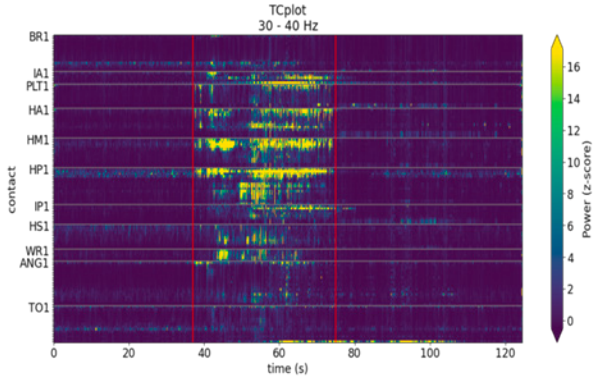


FIG1. Case1. A 37 y/o, male patient, diagnosed with refractory temporal lobe epilepsy. The seizures originated from the posterior hippocampus (HP). As we can see, in seizure (A) the maximum activation is between 10–20 Hz.



In that same case but in other seizure (B), it is between 30–40 Hz, associated with evident preictal activations

Conclusion: Brainfocus is a useful quantitative tool that helps to determine the characteristic spatio-temporal patterns at seizure onset and the visualization of the epileptic activity propagation at different frequency bands, which facilitates the precise interpretation of the SEEG results.
Disclosure: Nothing to disclose.

EPO-310

An EpiCARE survey on dissemination and implementation of guidelines for rare and complex epilepsies

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Background and aims: Clinical practice guidelines (CPGs) are systematically developed statements to standardize patient care and enhance health outcomes. The EU-funded EpiCARE network aims to develop guidelines for rare and complex epilepsies. The purpose of this study was to investigate dissemination and implementation strategies of epilepsy guidelines across EpiCARE centers and to identify main barriers influencing the implementation of guidelines.
Methods: The study was conducted in two phases: (1) the pilot-phase, conducted during the EpiCARE annual meeting among workshop participants, and (2) a network-wide survey. In the second phase, a standardized questionnaire was distributed to 56 participants (physicians and specialized epilepsy nurses) across EpiCARE network. The questionnaire consisted of three sections: demographics, dissemination and implementation, and challenges.
Results: Complete responses were received from 41 participants (71%; 34 physicians and 7 nurses). 20 participants reported previous experience in guideline development. The majority (68%) reported that guidelines were disseminated regularly at their institution. Most frequent actions taken after dissemination of new guidelines were training seminars (65%) and adaptation of guidelines (56%). Major barriers for implementation of new guidelines at a national level were lack of funding (70%); while at an institutional level time constraints (65%), were frequently cited. Moreover, 26% of participants indicated that CPGs are considered useless, because established standard of care already ensures high quality treatment.
Conclusion: Our findings provide a comprehensive overview of the dissemination and implementation strategies used for existing epilepsy CPGs. We identified several barriers to guideline implementation that may help improve application and adherence to CPGs developed by the network.
Disclosure: There are no conflicts of interst.

EPO-311

Abstract withdrawn

EPO-312

Value of neuroglial apoptosis and neuroinflammation in epileptic foci of the brain and blood in drug-resistant epilepsy

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Background and aims: The aim of this study is to evaluate neuronal and glial apoptosis in association with neuroinflammation in brain epileptic focus and inflammatory changes in blood in patients with focal drug-resistant epilepsy (DRE).

Methods: The study follows a case-control design. Biopsies of 32 patients with focal DRE (24–55 years old) were studied. Pathological changes in the temporal lobe in epilepsy (histology, transmission electron microscopy) were studied. Levels of apoptotic and neuroinflammatory proteins: active caspase-3 (immunohistochemistry), full-length form caspase-3, caspase-9, FAS, FAS-L, NF-kB, TNF-α, p53 (Western blot), and cytokine levels in blood: IL-1β, IL-2, IL-4, IL-7, TNF-α, etc. (multiplex analysis) were studied too.

Results: In the present work, ultrastructural and immunohistochemical apoptotic signs were found in neurons and oligodendrocytes in the temporal lobe of DRE patients. Levels of proinflammatory cytokines that play a role in apoptosis (TNF-α, FAS, NF-kB) were increased. The blood concentration of IL-4, IL-7, TNF-α is increased and IL-2 is reduced. Oligodendroglial apoptosis has been shown to play an important role in DRE pathogenesis and to explain demyelination.

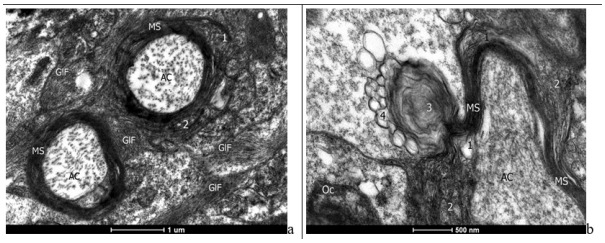

Figure: Structural changes in the epileptic focus. TEM: a - destruction of myelin sheaths; bar, 1 μm; 16500x; b - destruction of myelin sheaths; bar, 500 nm; 26500x. 1 - areas of lamella rupture, 2 – delamination of sheath, 3 – myelin dissociation

Conclusion: Thus, a comprehensive analysis of revealed changes in the blood and brain in DRE patients showed the neuroinflammation in the epileptic focus, which was combined with the development of apoptosis of glial cells and neurons. This creates conditions for the development of drug resistance and the epilepsy progression. Further study of the identified changes may contribute to the search for new methods of DRE treatment.

Disclosure: The project was implemented within the framework of the state task No. 121031000359-3 of the Almazov National Medical Research Center, St. Petersburg, Russian Federation.

EPO-313

The long-term seizure outcome patterns of epilepsy surgery in adult patients with temporal lobe epilepsy

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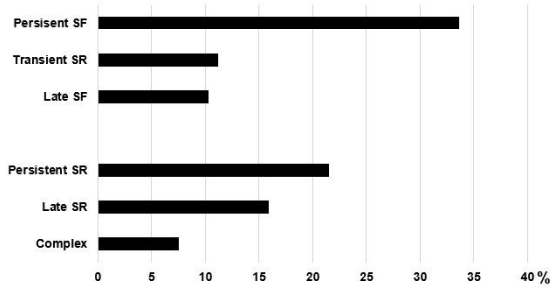
Background and aims: We investigated patterns of seizure remission and relapse after epilepsy surgery in patients with drug-resistant temporal lobe epilepsy (TLE).

Methods: We evaluated long-term (>5 years) outcome postoperatively in 107 TLE adults. Annual outcomes were determined using the ILAE outcome scale. Seizure freedom was defined as ILAE outcome class 1 and 2.

Results: The follow-up period after surgery ranged 60 to 238 months. Hippocampal sclerosis was the most common pathology (69.2%). Persistent seizure freedom was in 36 patients (33.6%), late seizure freedom after at least 1-year of initial seizure recurrence in 11 patients (10.3%), and transient seizure relapse (initial seizure-free with transient relapse, then finally remission) in 12 patients (11.2%). These patterns were grouped into 'seizure-free' (n=59; 55.1%). Persistent seizure recurrence was in 23 patients (21.5%), late seizure relapse after at least 1-year of initial seizure freedom in 17 patients (15.9%), and complex pattern of remissions and relapses in 8 patients (7.5%). These patterns were grouped into 'seizure-relapse' (n=48; 44.9%). Stepwise logistic regression showed that seizure-relapse group was more likely associated with interictal epileptiform discharges <90% concordance with the laterality of surgery (odds ratio [OR] 4.597, p=0.002) and focal to bilateral tonic-clonic seizures during presurgical monitoring (OR 2.459, p=0.047) than a seizure-free group. Older age at surgery and younger age at seizure onset were also associated with a seizure-relapse group, but they did not reach statistical significance (p values<0.1).



The percentage of seizure outcome patterns after epilepsy surgery in patients with temporal lobe epilepsy. SF, seizure freedom; SR, seizure relapse

Conclusion: Our data support the previous findings that epilepsy surgery is a good treatment option for selected patients with drug-resistant TLE.
Disclosure: Nothing to disclose.

MS and related disorders 3

EPO-314

Pediatric Multiple Sclerosis treatment: an ongoing observational study of Natalizumab and comparison with Fingolimod

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Background and aims: Natalizumab is currently prescribed off-label for Pediatric-onset Multiple Sclerosis (POMS), despite its well-known efficacy. Fingolimod is indeed the only second-line treatment approved. The aim of our study is to compare the efficacy of Natalizumab versus Fingolimod in POMS.

Methods: This is an ongoing retrospective/prospective longitudinal multicentric study. We enrolled retrospectively natalizumab (N-PMS) and prospectively N-PMS and fingolimod (F-PMS) treated PMS. We collected Annual Relapse Rate (ARR), Expanded Disability Status Scale (EDSS), and T1 gadolinium-enhancing lesions, T2 lesion load or new T2 lesions on brain MRI at baseline (T0), after 12-18 months (T1) at last observation (T2).

Results: We enrolled 37 N-PMS and 19 F-PMS. N-PMS showed baseline higher ARR vs F-PMS (2[0-5.2] vs 1[0.1–4], p=0.02). Four N-PMS switched to another DMT after a mean time of 12.4±4.2 months [1 for inefficacy (3%) and 3 for safety due to JCV positivity] vs 1 F-PMS switching after 6 months (inefficacy, 6%). Four N-PMS (11%) and 4 F-PMS (25%) experienced one relapse between T0 and T1 (p=0.18). EDSS did not change between T0 and T1. Nine out of 26 N-PMS with follow up longer than 18 months switched to another DMT (at a mean time point of 89±58 months) (1 for inefficacy and 8 for safety concerns).

Conclusion: Preliminary data suggest a comparable efficacy between natalizumab and fingolimod in POMS. However, since baseline characteristics showed higher activity in N-PMS, a comparison is difficult. Ongoing enlargement of the samples might allow to support the high efficacy of Natalizumab in highly active POMS.

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EPO-315

Psychiatric disorder in neuro-Behçet's disease

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Background and aims: Behçet's disease (BD) is a multisystem relapsing infl ammatory disorder of unknown cause. Psychiatric disorder is one of the most serious causes of long-term morbidity and mortality in neuro-BD (NB).
Methods: A retrospective study including 150 patients followed for BD was conducted in the department of neurology and internal medicine of the Military Hospital of Tunis from 2000 to 2022. The diagnosis of psychiatric disorders was established following a specialized psychiatric consultation.
Results: We collected 35 cases of NB. Psychiatric disorders were present in 5 patients. All patients were male. The average revelling age for NB was 34. The average age of revelation of psychiatric disorders was 30 years. These were acute delirium according to DSM-IV criteria with delusions and auditory and visual hallucinations in 2 patients. These disorders were concomitant with relapse with a good evolution under corticosteroid treatment in combination with neuroleptics. Mood disorders of the hypomania state type were objectified in two cases and of the recurrent depression type in one case.
Conclusion: Psychiatric disorders in NB are various and serious this is why the importance of knowing them even in the absence of other symptoms of NB.
Disclosure: Nothing to disclose.

EPO-316

The role of treatment strategy in reducing the disability risk in multiple sclerosis

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Background and aims: The paradigm of multiple sclerosis (MS) treatment has been changing with a recent tendency to start early intensive treatment (EIT) in selected cases. We aimed to identify which treatment strategy was associated with lower disability.
Methods: A single-center retrospective study was conducted, including all patients in our MS center diagnosed as relapse remitting MS (RRMS) that started treatment between 2012 and 2022. The treatment regimen applied was analyzed - escalation or EIT, defined as starting a moderate to high efficacy treatment in the first two years after diagnosis. Reaching an Expanded Disability Scale Score (EDSS) of 3 was the primary outcome. A comparative analysis was conducted between patients with different treatment regimens through a multivariate cox regression.
Results: We included 303 patients, with a mean age at diagnosis 36.3±11.2 years and with a female predominance (67.7%). Most patients (71.0%) were treated with an escalation regimen. Fifty-four patients reached an EDSS of 3 (18.8%). In a mean follow-up of 3.6±2.7 years, there was a lower risk of reaching an EDSS of 3 in patients under EIT in the univariate analysis (HR 0.42, CI 95% 0.22-0.80 p=0.008), that remained significant adjusted to the delay in diagnosis.
Conclusion: EIT was associated with a better prognosis in MS in this analysis, with a significant reduction in the risk of reaching an EDSS of 3 in our cohort, highlighting the importance of a prompt diagnosis and reinforcing the need to consider an early start of moderate-high efficacy treatment.
Disclosure: The authors have nothing to disclose.

EPO-317

Natalizumab extended interval dosing: efficacy and safety profile analysis from a Portuguese Multiple Sclerosis Center

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Background and aims: Standard-interval-dosing (SID) (4-week interval) is the mainstay of natalizumab treatment in multiple sclerosis (MS). A 6-week extended-interval dosing (EID) proved to largely reduce the progressive multifocal leukoencephalopathy (PML) risk but its efficacy is less well studied.
Methods: Retrospective study of MS patients treated with natalizumab between 2007–2022, descriptive and comparative analysis between SID and EID.
Results: From 870 MS-patients in our center, 104 were treated with natalizumab. Time between MS-diagnosis and natalizumab treatment was 6,5 years (SD±6,5) with an average age of 34 years-old (SD±10). Fifteen were positive for JCV prior to treatment. Nine suffered moderate/severe adverse events. 39 (36,8%) were on EID regimen (34 switched from SID and 5 EID ad initio). There were no statistically significant differences between schemes regarding new T2 lesions, relapses, EDSS variation, adverse events and suspension motive. There were no cases of symptomatic and asymptomatic PML nor deaths. EID was associated with lesser suspension of treatment[OR: 0.164 (CI95%: 0.067–0.405), $p<0.01$]. Regarding the EID group, none exhibited new T2 lesions. Five exhibited relapses, one each. Treatment was suspended in 9 patients, after a median time of EID treatment of 26 months (SD±17) due to JCV seroconversion (n=4), suggestive course of secondary progressive MS (n=2), relapses (n=2) and possible adverse event (n=1).
Conclusion: In our MS-cohort, there were no significant differences regarding efficacy and safety under SID or EID natalizumab treatment. Interestingly, EID regimen was associated with lesser treatment suspension.
Disclosure: The authors have nothing to disclose.

EPO-318

MRI, Efficacy, and Safety of Tolebrutinib in Highly Active Disease: 2-Year Data from Phase 2b Long-term Safety Study

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Background and aims: In the phase 2b trial (NCT03889639), brain-penetrant Bruton's tyrosine kinase inhibitor tolebrutinib was well-tolerated with dose-dependent reductions in new/enlarging MRI-lesions. Here, we report MRI, efficacy, and safety outcomes at Week (W) 96 of phase 2b long-term safety (LTS) extension (NCT03996291) in participants with relapsing multiple sclerosis and highly active disease (HAD).
Methods: In double-blind LTS Part-A, participants continued receiving tolebrutinib 5/15/30/60mg daily; in open-label Part-B, all received 60mg/day. Outcomes included gadolinium-enhancing T1- and new/enlarging T2-lesions, annualized relapse rate (ARR), and Expanded Disability Status Scale (EDSS) score.
Results: 61 participants met HAD criteria at baseline; 60 continued in Part-A and 59 transitioned to Part-B. As of March 7th, 2022, 55 participants remained on study. New gadolinium-enhancing T1-lesions remained low in 60/60-mg arm through W96 and were reduced in other arms W48-W96, except for 5/60 (W96 mean±SD: 2.00±3.83, 0.56±1.04, 0.47±1.13, 0.23±0.44 in 5/60-, 15/60-, 30/60-, 60/60-mg arms, respectively). New/enlarging T2-lesions remained low for 15/60-, 30/60-, and 60/60-mg. T2-lesion volume remained unchanged for 60/60-mg. Most common treatment-emergent adverse events (TEAEs) were COVID-19 (20%), nasopharyngitis (16.7%), headache (13.3%), and upper respiratory tract infection (8.3%). There was no dose-relationship for TEAE/serious AE (Part-A) and no new safety findings upon switching to 60mg (Part-B). In participants receiving tolebrutinib 60mg/day for ≥8 weeks, ARR was 0.10 (95% CI: 0.02–0.66) and 92.9% remained relapse-free. Mean EDSS scores were stable through W96.
Conclusion: Through LTS W96, in HAD cohort, tolebrutinib 60mg demonstrated favourable safety, tolerability, and low ARR. MRI-lesion counts remained low for 60/60-mg arm. FUNDING: Sanofi.
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EPO-319

A multidimensional self-reported evaluation of frailty in people with multiple sclerosis.

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Background and aims: Multiple Sclerosis (MS) is a neurodegenerative disease of central nervous system. People with MS have a high risk of frailty that could be measured by different tools. We aim to evaluate frailty using the Tilburg frailty indicator (TFI), a multidimensional self-reported questionnaire, and to explore its relationship with disability.
Methods: People with MS were enrolled and complete by himself TFI (frail with a TFI score ≥ 5 points). The following features were collected: disability using the Expanded Disability Status Scale (EDSS), age and gender. Data were treated through descriptive analyses and hierarchical multiple regression.
Results: A total of 208 adults with MS (mean age 44 years, SD=11; 75% of women; 89.4% relapsing-remitting) were enrolled. The mean TFI total score was 5.7 points (SD=3.0; range 0–14), with the 62.5% resulted frail. Controlling for age and gender, the EDSS influenced the total (β=0.469; R2=0.255; $p<0.001$) and the physical (β=0.571; R2=0.349; $p<0.001$) frailty score, with an explained variance of 25.5% and 34.9%, respectively. No effects on psychological and social frailty domains were detected. 91.7%, 83.3% and 66.0% of people with high EDSS ≥ 6.0, EDSS ranged from 3.5 to 5.5, and EDSS ≤ 3.0 resulted frail, respectively.
Conclusion: Our study shows a high frequency of frail patients. Frailty is more common in patients with higher disability, but it affects also those with low EDSS. Thus, in people with MS frailty could be influenced by factors different than disability.
Disclosure: The authors have not to disclose about this work.

EPO-320

Longitudinal Robustness of Emergent MS Phenotypes from Multiprotein Serum Data

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Background and aims: Novel machine learning techniques for measurement of disease activity (DA) and disease progression (DP) through serum proteomics have shown promise in multiple sclerosis (MS) management. Identifying emergent biomarker profiles (pheno-clusters) can enable proteomic-based MS subtyping and support clinical interpretability of a novel MS DA (MSDA) test, developed by Octave Bioscience. Previous research has demonstrated the feasibility and potential clinical utility of proteomic pheno-clustering in MS.
Methods: Our objective was to characterize the longitudinal stability of pheno-clusters in stable MS patients identified using unsupervised clustering of serum protein concentration data. 137 patient samples were assayed using the MSDA test. The proteomics data was balanced on medication and grouped into pheno-clusters associated with over or under-expression of 18 proteins, using k-means clustering. We applied the learned grouping to 38 longitudinal samples from an independent cohort (15 patients with ≥2 samples ≤30 days apart).
Results: We found 6 protein signatures in the training dataset. In the longitudinal dataset, 67% of patients and 87% [update] of datapoints had no cluster change. We examined protein signatures of the 5 patients who had a cluster change: Proteins with varying concentrations between samples in these patients included GFAP, CD20, CD6, and CXCLl9.
Conclusion: The stability of pheno-clusters in a high proportion of patients demonstrates the clinical relevance of this methodology. Furthermore, cluster changes in 3 patients could indicate a subclinical signal, otherwise undetectable. Neuroinflammation and progression related protein changes in the patients with changing clusters could indeed be indicative of underlying subclinical DA and DP.
Disclosure: A. Ghoreyshi and F. Qureshi are employees of Octave Bioscience. T. Hoyt has nothing to disclose. J. Foley has received research support from Biogen, Octave, and Genentech. He received speakers' honoraria from Biogen. He has participated in advisory boards for Biogen, Horizon, Sandoz, and TG Therapeutics. He has equity interest in Octave. He is the founder of InterPro Biosciences.

EPO-321

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EPO-323

Clinical features of patients with Late Onset Multiple Sclerosis in a large Centre of Central Italy

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Background and aims: Multiple Sclerosis (MS) commonly affects young people. However, people with more than 50 years old may be affected, configuring the Late Onset MS (LOMS). LOMS are supposed to have a different immunological behaviour comparing to early onset MS, with possible different responses to disease modifying therapies (DMTs). Here we describe the main features of LOMS in charge at our Centre in Pisa, Italy.
Methods: Data were achieved from our MS-patients database We included those patients who underwent at least 2 years of clinical and radiological follow-up.
Results: -38 patients (23 female, 15 male) with mean age at onset of 56.7 years -13 patients had primary progressive MS, 19 Relapsing remittent MS, and 6 secondary progressive MS -Mean temporal hiatus between disease onset and diagnosis: 20.7 months -4 patients had supratentorial lesions, 11 had supratentorial plus spinal lesions, 3 had whole-brain lesions, 20 had whole-brain plus spinal lesions -17 patients had motor impairment at disease onset -13 patients did not start any DMTs, 5 started a second line therapy and 20 started a first line treatment -11 of the 16 patients that developed new MRI lesions during follow-up were not under treatment. 5 patients had clinical relapses during follow-up. - 32 among 35 CSF exams were positive for oligoclonal bands -The mean EDSS after 2 years of follow-up remained stable
Conclusion: Since LOMS might have a different immunological behaviour, a precise categorization of this patients' category might help both in choosing a patient-tailored therapeutic approach and in avoiding possible misdiagnosing, preventing diagnostic delay.
Disclosure: The authors have no disclosures.

EPO-324

Serum neurofilament light chain levels during natalizumab treatment with every-4-week and every-6-week dosing in NOVA

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Background and aims: Results from the phase 3b NOVA trial (NCT03689972) suggest that patients with relapsing-remitting multiple sclerosis (MS) who are stable on natalizumab (TYSABRI®) every-4-week (Q4W) dosing can switch to every-6-week (Q6W) dosing without meaningful loss of efficacy. This analysis compares levels of serum neurofilament light chain (sNfL), a marker of neuronal damage in MS, between patients in Q6W and Q4W groups in NOVA.
Methods: NOVA participants who were stable on Q4W dosing for ≥1 year at baseline, had sNfL data at baseline and had ≥1 postbaseline sNfL measurement were included. sNfL levels are presented as geometric mean (GM) values by study visit. GM ratios (GMRs) were calculated using sNfL values at visit versus baseline. The Q6W GMR versus Q4W GMR ratio was determined using a mixed model for repeated measures with natural log-transformed data.
Results: sNfL GM values at baseline were 8.34 pg/mL (n=220; Q6W) and 8.13 pg/mL (n=220; Q4W) and remained stable (<9 pg/mL) through week 72 (Figure 1). GMRs for week 72 versus baseline sNfL values were 1.0 (95% confidence interval [CI], 0.97–1.11) for Q6W (n=191) and 1.0 (95% CI, 0.94–1.07) for Q4W (n=178); the ratio of Q6W to Q4W GMRs was 1.0 (95% CI, 0.96–1.11; p=0.4065).
Conclusion: sNfL levels remained stable in the Q6W and Q4W treatment groups throughout the NOVA study with no significant differences between groups at week 72. Stabilization of sNfL levels in both treatment groups suggests effective control of MS disease activity by both Q6W and Q4W dosing.

Disclosure: Study: Biogen GG: AbbVie, Aslan, Atara Bio, Biogen, BMS-Celgene, GSK, GW, Janssen/Actelion, Japanese Tobacco, Jazz, LifNano, Merck/Serono, Novartis, Roche/Genentech, Sanofi Genzyme, Teva JFF: Biogen, Genentech, Novartis, Octave GD: Biogen, BMS, Merck/Serono, Novartis, Sanofi Genzyme, Teva LZR: Biogen, Celgene, Genentech, Novartis JAC: Biogen, Convelo, EMD Serono, Gossamer Bio, Mylan, PSI; MSJ editor DLA: Biogen, Celgene, Frequency Ther, Genentech, Immunotec, Merck, NeuroRx, Novartis, Race to Erase MS, Roche, Sanofi-Aventis, Shionogi, Xfacto Comm HB: Biogen, Merck, Novartis, Oxford Health Policy Forum, Roche, UCB GC: AI Ther, Alexion, AMO, Antisense Ther, AstraZeneca, AveXis, Biogen, BioLineRx, BMS/Celgene, Brainstorm Cell Ther, Clinical Trial Solutions, CSL Behring, Galmed, Genentech, Genzyme, Green Valley, GW, Horizon, Immunic, Klein-Buendel, Mapi, Merck/Serono, Mitsubishi Tanabe, Novartis, Ntl Heart, Lung, and Blood Inst, Opko Bio, Osmotica, Perception Neuro, Protalix Bio, Prothena Bio, Pythagoras, Reata, Recursion/CereXis, Regeneron, Roche, SAB Bio, Sanofi-Aventis, UA-Birmingham, UPenn, UT-Southwestern, Visioneering Tech JK: Biogen, Genzyme, Merck/Serono, Novartis, Roche, Teva HW: AbbVie, Actelion, Alexion, argenx, Biogen, Biologix, BMS, Cognomed, EMD Serono, Evgen, Gemeinnützige Hertie-Stiftung, GSK, Idorsia, IGES, Immunic, Immunovant, Janssen, J&J, MedDay, Merck/Serono, Novartis, Roche, Sanofi Genzyme, Swiss MS Society, Teva, UCB, WebMD SS, JS, LD, MM, JS, EF, TL: Biogen

EPO-325

Monoclonal antibodies in pregnancy in patients with multiple sclerosis: an updated clinical guide

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Background and aims: The use of high-efficacy disease-modifying therapies (DMTs) early in the course of the disease has been shown to lead to improved clinical outcomes in the long term and has become a popular treatment strategy among neurologists over the past years. Therefore, monoclonal antibodies including natalizumab, ocrelizumab, ofatumumab and alemtuzumab are increasingly used for the treatment of multiple sclerosis in women of childbearing age.

Methods: A review of the published literature was conducted in January 2023 in Embase, MEDLINE and Cochrane Library.

Results: Natalizumab can be administered at approximately 34 weeks and restarted soon after birth to avoid rebound disease activity. Women who are being treated with ocrelizumab or ofatumumab should avoid infusions/injections during pregnancy, however, the last dose can be administered 3 months prior to conception. Alemtuzumab's last infusion should be given 4 months before conception.

	Natalizumab	Ocrelizumab	Ofatumumab	Alemtuzumab
Use in pregnancy	Can be used	No	No	No
Last dose	Last infusion no later than 34 weeks	Last infusion 3 months before conception.	Last injection 3 months before conception.	Last infusion no later than 4 months before conception
Risk of miscarriage	No	No	No	No
Breastfeeding	Yes	Yes	Yes	No. Wait 4 months after last infusion

Table. Monoclonal Antibodies in Pregnancy in Women with Multiple Sclerosis

Conclusion: Discussion with women of childbearing age is crucial to make the most suitable treatment option. Outcomes should be monitored in registries to provide more data.

Disclosure: Nothing to disclose.

EPO-326

Menopause in women with multiple sclerosis: clinical symptoms and possible impact on the course of the disease

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Background and aims: Menopause signals a major shift in hormonal levels in women and causes a variety of symptoms that can overlap and/or interact with those related to multiple sclerosis (MS). These symptoms can have a considerable impact on the quality of life for many women living with MS. Menopause remains a largely unexplored period for women with MS and there are only a few studies that have attempted to investigate the potential effect that menopause may have on the clinical course of MS including inflammatory activity and disability progression.
Methods: We conducted a review of the literature to investigate whether menopause affects the clinical course of the disease and disability outcomes.
Results: Two studies showed that the Expanded Disability Status Scale (EDSS) progression rate was not affected by menopause while the other two showed that EDSS progression rate might have increased after menopause. Similarly, half of the studies showed that the annualized relapse rate (ARR) remained stable after menopause while the rest showed that there was a reduction in ARR.

Study	Design	Sample Size	Results	Limitations
Ladeira et al.	Retrospective	37 women	ARR reduction No changes in EDSS progression rate	Small sample size, no control group
Otero et al.	Prospective	73 (54 after controlling for aging and disease duration)	No changes in EDSS progression rate	Small sample size
Baroncini et al.	Retrospective	108	ARR reduction, EDSS progression rate increased	Small sample size, lack of control group
Bove et al.	Prospective	124	EDSS progression rate increased	Results highly impacted by a significant worsening in one participant's EDSS

Table 1. Studies investigating the effect of menopause on the clinical course of MS

Symptoms	Behavioural/lifestyle interventions	Pharmacological treatment (non-hormonal)
Hot flushes	Air conditioning, cold drinks Avoidance of hot/spicy foods Swimming Vests or cooling collars Weight loss Smoking cessation Acupuncture Hypnosis	Antiepileptic and antidepressant drugs: gabapentin/pregabalin, citalopram, escitalopram, fluoxetine, paroxetine, sertraline, duloxetine, venlafaxine, desvenlafaxine
Affective disorders	Neuropsychotherapy Support groups Optimization of sleep and fatigue Social management of work stressors	Antidepressant drugs: fluoxetine, sertraline, escitalopram, citalopram, venlafaxine, bupropion Antimuscarinics
Urinary disorders	Bladder training: Frequent voluntary emptying (e.g. start with every 2 hours) to keep the bladder volume low. Pelvic muscle exercises (Kegel). Biofeedback. Decreased	Antimuscarinics (oxybutynin, tolterodine, fesoterodine). Antispasmodics (baclofen, tizanidine). Tricyclic antidepressants (amitriptyline). Local oestrogen, or antibiotic prophylaxis, may be required in more disabled patients.
Sexual dysfunction	Decreased sensation: vibrators and other devices may increase stimulation. Patient education and guided counselling, such as body mapping techniques or pelvic floor exercises, can increase arousal, orgasmic response, intimacy and couple communication. Vaginal dryness: lubricants. Counselling focused on sexual feelings, communication and attitudes that interfere with sexual enjoyment. Couples' education/counselling: focused on mutual support, communication, stress and anger management.	Paresthesia. Antiepileptic drugs: carbamazepine, gabapentin.
Cognitive impairment	Cognitive rehabilitation to develop organizational strategies (e.g. making lists, simplifying daily organization). Addressing sleep problems, fatigue, mood and pain	

Table 2. Overlapping MS and menopausal symptoms and therapeutic options

Conclusion: Menopausal symptoms can frequently overlap with MS symptoms. Clinicians should be able to recognize and address them on time before they increase the burden of disease and affect the quality of life. Limited studies with inconsistent results have been conducted to date, and most of them have important limitations, hence not allowing for safe conclusions to be drawn. Larger, longitudinal studies with improved methodology and controlling for aging and disease duration are needed to establish the link between menopause and MS.
Disclosure: Nothing to disclose.

EPO-327

Seroprevalence and seroconversion of anti-JCV antibodies in a cohort of multiple sclerosis patients

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Background and aims: The main goal was to analyse the incidence of JCVpositivity after the first test in a cohort of MS patients and the time to seroconversion during follow-up in the natalizumab-treated MS patients.
Methods: Retrospective observational cohort study including patients screened for anti-JCV antibodies using the STRATIFY JCV™test. Several variables were analyzed to find an association with the risk of seroconversion.
Results: 383 patients have been tested of JCV in the last 6 years. 66.48% were woman. 60.21% were JCV positive with a mean index .18 (0.21–4.91), 69.53% were female with a median age 43 (22–75and). JCV negative patients were 39.80 (16–64) years old. We found a significant correlation between age and JCVpositive antibodies (p=0.0003, r=0.185) and sex and JCV antibodies (p= 0.008). Positive JVC value were more persistent in males (69.5%) than in females (55.5%). However, we did not find correlation between age and index of VJC (p=0.562). 80 patients were in treatment with natalizumab. 70% are female. 24 patients were VJC positive in this cohort, of whom 12 were VJCpositive from baseline and 12 seroconverted. The mean time to seroconversion was 27.8 months (10-71). We didn't find a stadistically significant correlation between age and the time to seroconversion (p=0.176), sex (p=0.646), number of previous treatments (p=0.979) or time from diagnosis to initiation of natalizumab treatment (p=0.405)
Conclusion: We found older age and male sex is associated with the risk of JCV positive. We found no association with other variables such as number of previous treatments.
Disclosure: Nothing to disclose.

EPO-328

Phase 2b trial of NG-01-MS - Autologous bone marrow derived human mesenchymal stem cells in secondary progressive MS

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Background and aims: Over the past 15 years, there have been clinical research efforts around the possibility of bone marrow-derived MSC treatment for MS led by Karussis, et al. at the Hebrew University-Hadassah Medical Center ("Hadassah"). A recent double blind, randomized, placebo-controlled phase 2 study reported by the Hadassah team yielded data to support safety and efficacy of the approach, particularly the use of repeated intrathecal (IT) administration as proposed for this trial. NeuroGenesis Ltd. acquired the technology, now called NG-01-MS, which involves the proprietary manufacturing process of autologous MSCs derived from each patient's bone marrow.
Methods: Aim 1: To test the hypothesis that repeated IT administration of NG-01-MS at 3 months intervals has superior efficacy compared to sham administration (placebo) in SPMS assessed both clinically and by biomarkers of neuroprotection. Aim 2: To assess the safety, tolerability, and relative efficacy of 2 dose levels of intrathecal administration of NG-01 MS (either 50 million or 100 million cells per injection) versus sham administration using sterile saline medium as a placebo. Aim 3: To assess the feasibility (shipping methods, cell stability and viability, etc.) of performing a multi-center clinical trial utilizing NG-01 MS in anticipation of a future phase 3 trial.
Results: Study design considerations including the clinical and imaging endpoints and the exploratory use of neurofilament light chain (NfL) measurements as a biomarker will be discussed.
Conclusion: The proposed trial will attempt to use cell-based therapy to demonstrate neuroprotection and repair in secondary progressive multiple sclerosis (SPMS).
Disclosure: This trial is sponsored by NeuroGenesis Ltd.

EPO-688

Efficacy and Safety of Fenebrutinib, a Noncovalent, Reversible BTK inhibitor, in MS: Primary Results of a Phase 2 Trial

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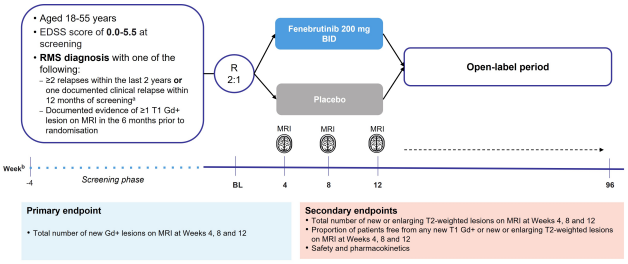
Background and aims: Bruton's tyrosine kinase (BTK) is implicated in peripheral and central nervous system inflammation in multiple sclerosis (MS) and is a therapeutic target for relapsing and progressive disease. Fenebrutinib (FEN) is a potent, highly selective, noncovalent, reversible BTK inhibitor under investigation for MS.

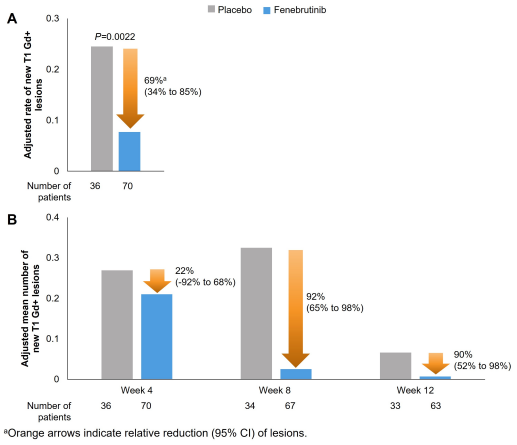
Methods: FENopta, a randomised, double-blind, placebo-controlled, Phase 2 trial (NCT05119569), evaluated efficacy and safety of FEN in relapsing MS (RMS; Fig 1). The primary endpoint was total new gadolinium-enhancing (Gd +) T1 MRI lesions at Wks 4, 8 and 12. Key secondary endpoints were total new or enlarging T2-weighted lesions and safety. Relative reductions in lesions by visit were also analysed.

Results: At Wks 4, 8 and 12 (combined), FEN patients (pts) with evaluable postbaseline MRI data (n=70) had a 69% reduction in total new Gd+ lesions (Fig 2) and a 74% reduction in total new or enlarging T2-weighted lesions (Fig 3) vs placebo (PBO) pts (n=36). Relative reductions in Gd+ and T2 lesions were observed at Wk 8 (92% and 90%) and Wk 12 (90% and 95%, respectively). FEN pts were 4x more likely to be free from new Gd+ and T2 lesions at Wks 4, 8 and 12 vs PBO pts. Overall, 38% of FEN pts (n=73) and 33% of PBO pts (n=36) had an adverse event (AE). No serious AEs or deaths were reported.

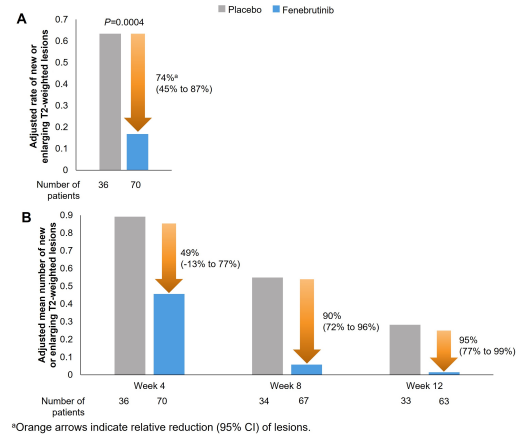
Conclusion: These first data highlight the potential of FEN for treating RMS. The FENopta open-label extension and Phase 3 studies in RMS and primary progressive MS are ongoing.

Disclosure: LHH: personal fees for speaking, consulting, and advisory board activities from Alexion, Bristol Myers Squibb, EMD Serono, Genentech, Genzyme, Greenwich Biosciences, Horizon and Novartis; research salary support paid to her institution from Biogen. ABO: consulting fees from Gossamer, Janssen/Actelion, Atara Biotherapeutics, Biogen, BMS/Celgene/Receptos, F. Hoffmann-La Roche Ltd., Genentech, Inc., MAPI, MedImmune, Merck/EMD Serono, Novartis, Sanofi Genzyme and GSK; contracted research for Genentech, Inc., Novartis and Biogen; salary from the University of Pennsylvania Perelman School of Medicine. MSW: research support from the Deutsche Forschungsgemeinschaft (DFG; WE3547/5-1), Novartis, TEVA, Biogen-Idec, Roche, Merck and the ProFutura Programme of the Universitätsmedizin Göttingen; Editor for PLoS One; travel funding and/or speaker honoraria from Biogen-Idec, Merck Serono, Novartis, Roche, TEVA, Bayer and Genzyme. MH: speaker/consultant fees from Biogen, Merck, Novartis, Pliva/Teva, Roche and Sanofi Genzyme. HB: nothing to disclose. PT, JN, JNR, QQ and AG: employees of Genentech, Inc., and shareholders of F. Hoffmann-La Roche Ltd. MS: employee and shareholder of F. Hoffmann-La Roche Ltd. JD: research support from Merck and Roche; personal honoraria for speaking or serving on advisory boards from Amicus, Bayer Schering Pharma, Biogen Idec, Hemofarm, Janssen, Medis, Merck-Serono, Novartis, Roche, Sanofi Genzyme and TEVA.





[a]Orange arrows indicate relative reduction (95% CI) of lesions.



[a]Orange arrows indicate relative reduction (95% CI) of lesions.

MS and related disorders 4

EPO-329

Promotor Polymorphisms in susceptibility and progression to Multiple Sclerosis

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Background and aims: The aim of this study is to investigate the synergistic effects of MMP-2 C-735T, MMP-9 C-1562T, and MMP-7 A-181G functional polymorphisms in the susceptibility to Multiple sclerosis (MS).
Methods: In this cross-sectional study, 149 patients who were diagnosed with Multiple Sclerosis between January 2017-December 2018 in the department of Neurology, Medical Faculty, Trakya University (Edirne, Turkey) and 152 healthy controls were included. Following DNA isolation from patient and control peripheral blood, allelic discrimination of MMP-7a-181G (rs11568818) polymorphisms was performed with real-time PCR using TaqMan® SNP Genotyping Assay kit for MMP-2 C-735T (rs2285053), MMP-9 C-1562T (rs3918242) and MMP-7A-181G (rs11568818).
Results: A statistically significant difference was found between CC, CT, and CC genotypes in the Expanded Disability Status Scale (EDSS) score. MMP-9 C-1562T functional polymorphism was found in MS patients in terms of transition of C to T (p=0.021). A statistically significant difference was found between men and women in terms of transition of C to T in the MMP-9 C -1562T functional polymorphism (p=0.014).
Conclusion: MMP-9 C-1562 T polymorphism is predicted to be a predictor of disability in MS and its progression, especially in male patients. MMP-2 C-735T functional polymorphism is also a value predictor of susceptibility to MS through the TT genotype and C allele. The presence of both MMP-9 C and MMP-2 C alleles has an even greater risk of MS.
Disclosure: There is no conflict of interest.

EPO-330

AMASIA: real world insight into the impact of siponimod treatment on disease progression of SPMS patients in Germany

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Background and aims: The non-interventional AMASIA study aims to investigate the long-term effectiveness and safety of siponimod for the treatment of patients suffering from active SPMS in a real-world setting and provides insight into the impact on disease progression and quality of life.
Methods: Approximately 700 siponimod-treated SPMS patients at about 120 sites in Germany are followed over 3 years. Every 6 months, disability progression and cognitive changes are evaluated by EDSS and SDMT. Questionnaires from the perspective of patients and physicians on disability progression, cognitive worsening and quality of life are documented.
Results: Extended subgroup analyses of disease progression (EDSS, SDMT) depending on patient age, time since MS diagnosis, disease progression at time of study start and last pre-treatment show the impact of 6, 12 and 18 months of siponimod treatment, by slowing down disease progression in all cases (average EDSS at study start for patients up to 50 years/older than 50 years: 5.4±1.4/5.3±1.4; after 18 months: 5.9±1.4/5.4±1.4). The analysis is an extension to previously presented preliminary data that indicated a trend towards a stable EDSS score over 12 months on siponimod treatment regardless of age or time since diagnosis. Additional data from patient and physician questionnaires will give further insights into the effectiveness of siponimod and the impact on quality of life.
Conclusion: The presented results on the effectiveness of siponimod treatment depending on patient characteristics such as age, time since diagnosis and pre-treatment underline the benefits of early treatment initiation of siponimod in patients with active SPMS.
Disclosure: O. Hoffmann served on scientific advisory boards, received speaker honoraria from Bayer Healthcare, Biogen, Bristol Myers Squibb/Celgene, Merck, Novartis, Roche, Sandoz, Sanofi, Teva; received financial support for research activities from Biogen, Novartis, and Sanofi. H. Schreiber received research grants and honoraria from

Almirall, Bayer Healthcare, Biogen, Merck, Novartis, Roche, and Teva. L. Klotz received compensation for serving on scientific advisory boards, speaker honoraria, travel support, research support from Alexion, Janssen, Novartis, Merck Serono, Sanofi Genzyme, Roche, Biogen, TEVA. She receives research funding from the Deutsche Forschungsgemeinschaft (DFG), the German Ministry for Education and Research, the Interdisciplinary Center for Clinical Studies (IZKF) Muenster, and the Innovative Medical research Muenster. M. S. Weber received research support from the DFG (DFG; WE 3547/5-1), Novartis, TEVA, Biogen-Idec, Roche, Merck, and the ProFutura Programm of Uni Göttingen; editor for PLoS One; received travel funding and/or speaker honoraria from Biogen, Merck Serono, Novartis, Roche, TEVA, Bayer, and Genzyme. C. Weiss is an employee of Novartis Pharma GmbH, Germany. T. Ziemssen received speaking honoraria and financial support for research activities from Almirall, Biogen, Celgene, Novartis, Roche, Teva, and Sanofi. This study is financed by Novartis Pharma GmbH, Nuremberg, Germany.

EPO-331

Real world insight into the characteristics of siponimod treated SPMS patients in Germany from the AMASIA study

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Background and aims: The non-interventional AMASIA study aims to investigate the long-term effectiveness and safety of siponimod for the treatment of patients with active SPMS in a real-world setting. The study also provides insight into siponimod patient profiles and clinical routines in Germany.

Methods: Siponimod-treated SPMS patients are followed over 3 years. Every 6 months, disability progression and cognitive changes are evaluated by EDSS and SDMT. Questionnaires from the perspective of patients and physicians on disability progression, cognitive worsening and quality of life are documented.

Results: According to previous interim analyses of the AMASIA population, patients on average were 54.5 years old and had been diagnosed with MS for 17.4 years when starting siponimod treatment. The largest group of patients (more than 45%) were switched to siponimod from moderately effective therapies, while about 10% were treatment-naïve. Here, we expand these previous analyses by analyzing the complete patient population, following the end of the recruitment period in January 2023. In addition to patient characteristics, details on MS activity, FSMC, SDMT and UKNDS scores and medical history are reported. Results are compared to data from the pivotal clinical trial EXPAND to obtain further insight.

Conclusion: Data and characteristics of the AMASIA study population enable a comparison of clinical trial data to the average siponimod patient treated in routine clinical practice, thus potentially facilitating translation into real-life therapeutic strategies by underlining the importance of a timely SPMS diagnosis and treatment intervention.

Disclosure: O. Hoffmann served on scientific advisory boards, received speaker honoraria from Bayer Healthcare, Biogen, Bristol Myers Squibb/Celgene, Merck, Novartis, Roche, Sandoz, Sanofi, Teva; received financial support for research activities from Biogen, Novartis, and Sanofi. H. Schreiber received research grants and honoraria from Almirall, Bayer Healthcare, Biogen, Merck, Novartis, Roche, and Teva. L. Klotz received compensation for serving on scientific advisory boards, speaker honoraria, travel support, research support from Alexion, Janssen, Novartis, Merck Serono, Sanofi Genzyme, Roche, Biogen, TEVA. She receives research funding from the Deutsche Forschungsgemeinschaft (DFG), the German Ministry for Education and Research, the Interdisciplinary Center for Clinical Studies (IZKF) Muenster, and the Innovative Medical research Muenster. M. S. Weber received research support from the DFG (DFG; WE 3547/5-1), Novartis, TEVA, Biogen-Idec, Roche, Merck, and the ProFutura Programm of Uni Göttingen; editor for PLoS One; received travel funding and/or speaker honoraria from Biogen, Merck Serono, Novartis, Roche, TEVA, Bayer, and Genzyme. C. Weiss is an employee of Novartis Pharma GmbH, Germany. T. Ziemssen received speaking honoraria and financial support for research activities from Almirall, Biogen, Celgene, Novartis, Roche, Teva, and Sanofi. This study is financed by Novartis Pharma GmbH, Nuremberg, Germany.

EPO-332

B cell tailored ocrelizumab in relapsing multiple sclerosis: protocol of a randomized controlled trial

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Background and aims: Ocrelizumab, an anti-CD20 monoclonal antibody (mAb) resulting in B-cell depletion, is highly effective in relapsing-remitting multiple sclerosis (RRMS). Individual B-cell repopulation varies extensively (27–175 weeks), therefore a fixed infusion interval is likely suboptimal. A personalised approach based on individual biological parameters could offer various advantages: decrease of infusion visits in the majority of patients, reducing infusion relating events, and possibly reduction of infection risk and hypogammaglobulinemia. Moreover, exceeding healthcare costs in Europe demand appropriate use of costly mAbs.
Methods: This is a national multicentre randomized controlled trial with two year follow-up. A total of 300 patients will be included. Patients will be randomized 1:1 to the standard interval group or the personalized interval group in which the infusions will be extended as long as the CD19 B-cell count remains below 10 CD19 cells/μL (Figure 1). Inclusion criteria include the diagnosis of RRMS and one year ocrelizumab treatment. All patients will be subjected to visits every six months (Figure 2). All visits include a relapse and adverse event assessment, and clinical testing. An MRI-scan will be performed and blood will be drawn for neurofilament light and IgG levels yearly. By using two validated apps (MS Sherpa/Neurokeys) cognition, hand function and walking speed will be frequently monitored at home.

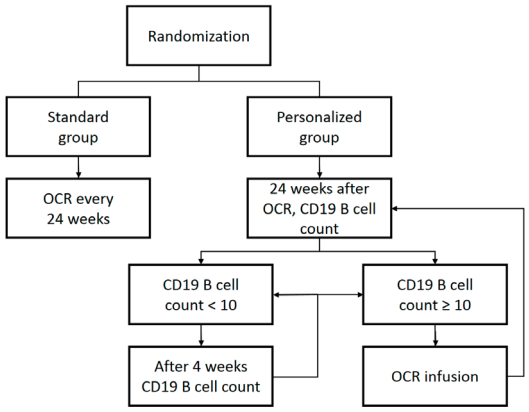

Fig. 1. Randomization procedure for the BLOOMS trial. OCR = ocrelizumab. CD19+ B cells in cells/μL.

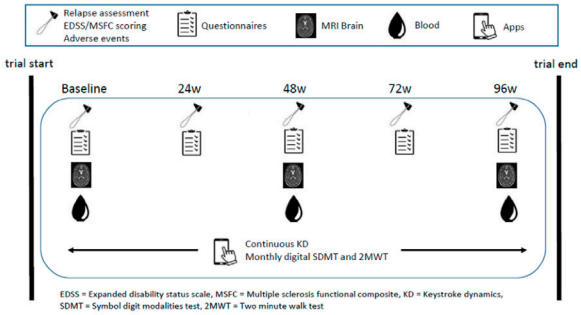

Fig. 2. Study visits BLOOMS trial.

Results: To conclude non-inferiority of personalized ocrelizumab two co-primary endpoints will be analysed: 1. percentage of relapse-free patients and 2. percentage of patients free from new/enlarging lesions on MRI.
Conclusion: Enrolment of patients started in April 2022. Results are expected in 2026. Clinicaltrials.gov Identifier:NCT05296161
Disclosure: J. Killestein report personal fees from Genzyme, Biogen Idec, Teva Pharmaceutical Industries, Merck Serono, Roche, Novartis.

EPO-333

Transcriptome analysis in the retina of mice with experimental autoimmune encephalomyelitis

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Background and aims: Visual disabilities often occur in multiple sclerosis (MS) and experimental autoimmune encephalomyelitis (EAE) an animal model of MS, but little is known about the mechanisms underlying the pathogenesis of retinitis in EAE. The aim of the study is to identify hub genes and pathways in the retina with EAE to explore its etiologies.
Methods: Differential expressed genes analysis was performed. Genes with a log 2 fold-change value >2 and false discovery rate(FDR) adjusted p-value<0.05 were considered differentially expressed genes (DEGs). Gene ontology (GO) analysis, gene set enrichment analysis (GSEA) with leading-edge analysis were conducted and constructed a protein-protein interaction (PPI) network using STRING database.
Results: 660 differentially expressed genes were identified, including 2 downregulated genes and 345 upregulated genes. GO analysis revealed that upregulated genes were associated with immune response, myofibrillar protein and extracellular matrix in the retina of mice with EAE-affected

mice. The 12 hub genes including were identified by the PPI network. Based on a curated gene set from molecular signatures database (MSigDB), GSEA showed that the upregulated genes in the retina with EAE were associated with electron transport chain and oxidative phosphorylation, and that downregulated genes are related to neuronal system and phototransduction cascade.

Conclusion: The hub genes related to immune response and phototransduction cascade pathway may be associated with the development of visual dysfunction in EAE mice. This study provided transcriptome profiles of the retinas of mice with EAE, which may help to identify new therapeutic targets.

Disclosure: There are no financial conflicts of interest to disclose.

EPO-334

Selective Vulnerability of Retinal Ganglion Cells in Multiple Sclerosis Regardless of Disease Subtypes

S. Huang[1], M. Pisa[1], S. Guerrieri[1], G. Dalla Costa[1], G. Comi[3], L. Leocani[2]

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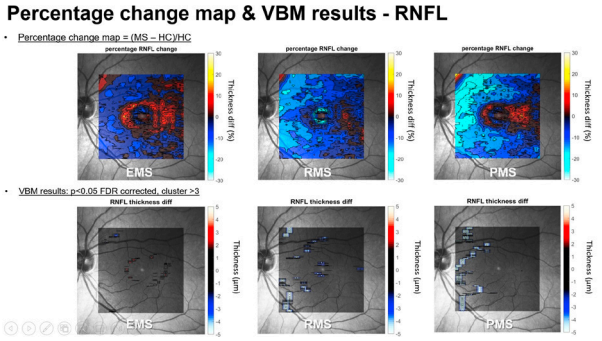
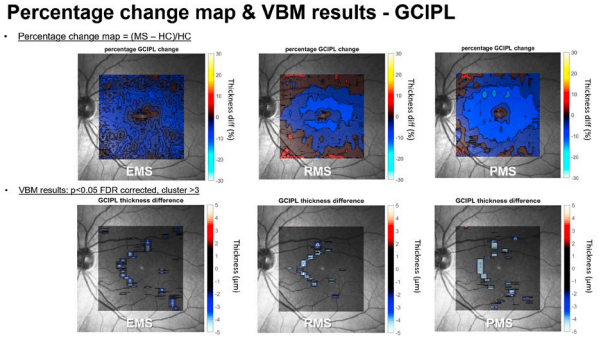
Background and aims: Neurodegeneration is the main contributor to disability accumulation in Multiple Sclerosis (MS). Studies in neuro-ophthalmology demonstrated that neurodegeneration in MS correlates with neuroretinal atrophy measured by optical coherence tomography (OCT). Thinning of retinal layers is recognized as biomarkers for axonal/neuronal loss. However, current analytical tools are unable to provide topographical information or detect focal atrophy. Here we aimed at verifying Whether applying voxel-based morphometry (VBM), a neuroimaging tool, may offer topological information on how neurodegeneration spreads among the central nervous system (CNS).

Methods: 110 people with MS (36 early, 37 relapsing-remitting, and 37 progressive MS) and 50 healthy subjects were enrolled. Only eyes with normal global peripapillary retinal nerve fiber layer (pRNFL) thickness and without histories of optic neuritis (ON) were considered. VBM was applied to macular OCT and voxel-wise ANCOVA was delivered with general linear model (GLM).

Results: Significant nasal macular ganglion cell/inner plexiform layer (GCIPL) atrophy was detected across all the MS subgroups at the same location, the thinning increases as the disease progresses. While RNFL atrophy spreads from the optic nerve head (ONH) toward the fovea as the disease moves toward the progressive phase.



VBM-OCT reults of RNFL



VBM-OCT results of GCIPL

Conclusion: Our results support primary retinal ganglion cell damage since disease onset in eyes without ON, its location implies selective vulnerability. Further, the evolution of the RNFL atrophy as the disease progresses suggests retrograde degeneration from the brain. Our data demonstrate bidirectional neurodegeneration coexists in MS and we may monitor and quantify the two mechanisms with VBM-OCT in the retina.

Disclosure: The authors have nothing to disclose.

EPO-335

Incidence and correlates of autoimmune comorbidities in multiple sclerosis: a prospective registry-based study

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Background and aims: : Multiple Sclerosis (MS) is an autoimmune disease affecting the central nervous system. Although current evidence is conflicting, people with MS (pwMS) have a higher risk to develop autoimmune comorbidities and it is reasonable that both share the same genetic susceptibility. The aims of this study are to evaluate the frequency of autoimmune comorbidities in pwMS and the impact of such comorbidities among disease activity and progression.

Methods: We included patients with relapsing remitting MS and with a follow-up period of at least 15 years. We calculated incidence of autoimmune comorbidities and the Hazard ratios (HR) for secondary progression as well as the adjusted annualized relapse ratio (ARR) in patients with and without autoimmune comorbidities.

Results: From a total of 142 pwMS (age at diagnosis: 32.8 ±9.9 years; follow up: 23.5±6.5 years), three patients (2.1%) showed preexistent autoimmune comorbidity, while n=24 developed one during follow-up period (incidence rate= 0.7/100 patients/years) without sex differences (p=0.61). The overall prevalence for autoimmunity was 19% and the more common was Hashimoto's thyroiditis (12%) followed by psoriasis (2.1%). The presence of autoimmune comorbidity was associated with a reduced risk of secondary progression (HR= 0.42 [95% CI: 0.22–0.81]; p=0.02; Fig 1) and with a higher adjusted ARR (0.29 [95% CI: 0.28–0.32] vs 0.4 [95% CI: 0.35–0.45]; p<0.0001; Fig 2).

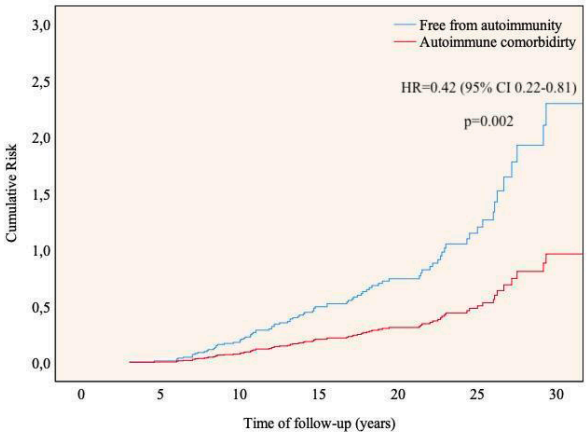

Figure 1: Cox regression analysis showing the different risk to secondary progression MS between patients with (red line) and without (blue line) autoimmune comorbidity

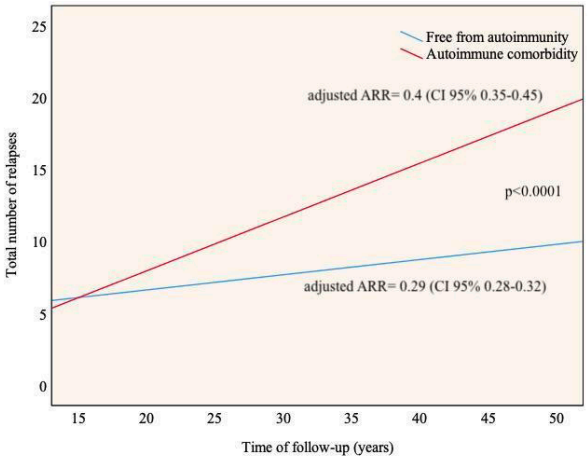

Figure 2: Scatterplot showing the different relapse rate between patients with (red line) and without (blue line) autoimmune comorbidity

Conclusion: Autoimmune comorbidities significantly affect the MS course suggesting that the accurate evaluation of these comorbidities may improve the clinical management of pwMS.

Disclosure: All authors declare that have no conflict of interests for this study.

EPO-336

Real clinical experience with alemtuzumab in patients with multiple sclerosis in Slovakia

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Background and aims: Alemtuzumab (ALEM), a monoclonal antibody targeting CD52 receptors of active lymphocytes has been monitored by several clinical studies. In our longitudinal study we evaluated efficacy of ALEM from 2014 to July 2022 in real clinical practice.
Methods: The study included patients from 10 out of 12 Multiple Sclerosis Centres in Slovakia. Neurologists from the centres provided data about their patients treated with at least 1 cycle of ALEM. Long-term efficacy was evaluated using NEDA-3 concept (absence of relapses, no new T2-hyperintense brain lesions on MRI, stabile EDSS).
Results: We obtained data about 146 MS patients. 119 patients (81.5%) received 2 ALEM cycles, 16 patients (10.9%) received 1 ALEM cycle, and 11 (7.5%) 3 cycles. Stability of NEDA-3 was 32.3 months (2–79), stability of EDSS was 28.5 months. The follow-up treatment was: ocrelizumab – 13 patients (8.9%), siponimod – 9 (6.2%), dimetyl fumarate – 3 (2.1%), cladribine – 3 (2.1%), glatiramer acetate – 2 (1.3%), and interferon beta Ia sc, cyclophospamid, aHSCT and cyclophosphamid – 1patient (0.7%) each. Four patients died after ≥2 years after the last ALEM: multiple myeloma, generalised carcinoma mammae (man), progressive multifocal leucoencephalopathy after switch to natalizumab, and sepsis after COVID-19 pneumonia. One other case of bilateral carcinoma mammae was diagnosed in a female patient after 1 cycle of ALEM. The most frequent were autoimmune thyreoidites
Conclusion: Our study adds information about real-life duration of ALEM effectivity and the need and details of further treatment.
Disclosure: The authors have nothing to disclose.

EPO-337

One year of B-cell directed therapy with ofatumumab s.c.: Results of a patient-centered real-world observational study

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Background and aims: Ofatumumab (Kesimpta™) is a subcutaneously applicable anti-CD20 antibody, which has been used for the treatment of relapsing-remitting multiple sclerosis. Home self-administration offers a high degree of independence from invasive forms of application while providing potent B-cell directed immunotherapy. In this study, we recorded the epidemiology and patient-centered experience in 99 of 127 patients. The objective was to investigate tolerability and acceptability from the patient's perspective.
Methods: Data collection was performed using physician documentation, questionnaires on tolerability and application of ofatumumab, and supplemental telephone interviews.
Results: Our cohort consists of 127 patients on ofatumumab. On average, patients received 2.8 (± SD: 1.7) prior therapies. The mean duration of ofatumumab therapy was 9.8 months (± SD: 3.5). Structured data were collected from 99 patients. 23% of the patients reported no side effects during the first application of the drug. 19% rated the side effects as "very mild" and 18% as "mild". Side effects included: 48% chills and fever, 46% headache. 19% of patients listed "other" symptoms, with fatigue being the most common here. During follow-up injections, 72% of patients reported no side effects, and 87% of patients found handling the drug "very easy." One relapse event occurred during therapy with ofatumumab.
Conclusion: Our prospective study shows that ofatumumab is well accepted and tolerated by patients. There has been one relapse event during the observation period. Side effects are mild and occur mainly during the initial application. The data suggest that ofatumumab is an effective and safe treatment option for patients with relapsing-remitting multiple sclerosis.
Disclosure: None related to this work.

EPO-338

Abstract withdrawn.

EPO-339

Probability of Cognitive Impairment Development in Patients with Multiple Sclerosis Depending on MRI Findings

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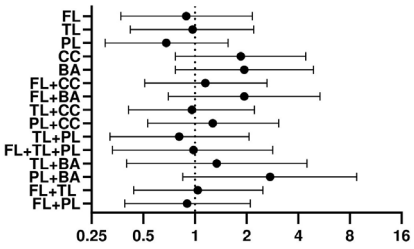
Background and aims: The aim was to assess probability of cognitive impairment (CI) development depending on location of demyelization lesions in the brain in relapsing-remitting (RR) multiple sclerosis (MS) patients.
Methods: The study enrolled 106 RR-MS patients (81 females; 25 males) from 22 to 67 years. They completed the Montreal Cognitive Assessment /MoCA (which was separated into domains: memory, language, attention, abstract thinking, visual-spatial/executive functions; Beck Depression Inventory (BDI); Hamilton Anxiety Rating Scale (HAM-A); The Pittsburgh Sleep Quality Index (PSQI); undergone MRI.
Results: During our research we discovered that perspective memory impairment was strongly associated with brain atrophy in combination with lesion of parietal lobe (OR=2.74 (0.85–8.77), p <0.0001). Probability of executive functions disorders was tied to simultaneous damage of frontal and parietal lobes (OR=3.68 (1.36–10.0), p=0.0080). Risk of anxiety onset was related to the presence of lesions in frontal and temporal lobe simultaneously (OR=2.67 (1.15–6.17), p=0.0202). Connection between MRI lesions and development of depression or sleep disorders was not found.



FL – frontal lobe, TL – temporal lobe, PL – parietal lobe, CC – corpus callosum, BA – brain atrophy

Fig. 1. Probability of development of memory decline in patients with relapsing remitting multiple sclerosis (risk assessment with 95%– OR (95%CI)).

Propability of memory decline development in RRMS patients (risk assessment with 95%-OR (95%CI))

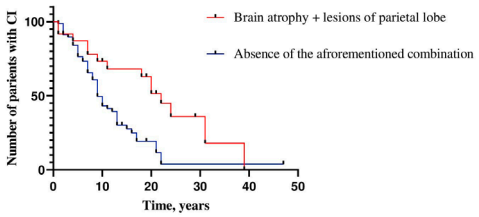
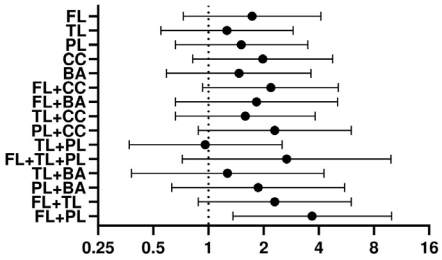


Fig. 2. Probability of development of memory decline in patients with relapsing remitting multiple sclerosis.

Propability of memory decline development in patients with RRMS



FL – frontal lobe, TL – temporal lobe, PL – parietal lobe, CC – corpus callosum, BA – brain atrophy

Fig. 3. Probability of development of executive functions disorders in patients with relapsing remitting multiple sclerosis (risk assessment with 95%– OR (95%CI)).

Propability of executive functions disoders development in RRMS patients (risk assessment with 95%-OR (95%CI))

Conclusion: Based on the location of demyelization lesions of the brain, development of CI, in particular memory and executive functions disorders, and anxiety can be predicted and potentially prevented in RRMS patients.
Disclosure: Nothing to disclose.

EPO-340

Anti GAD 65 encephalitis overlapping with multiple sclerosis : a case report

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Background and aims: Autoimmune encephalitis is a severe disorder revealed by neuropsychiatric manifestations. The concurrence with demyelinating diseases is described with NMDA-R antibodies.This overlapping is rare specifically with multiple sclerosis.
Methods: A single case presentation.
Results: A 32 year old female, is followed since 2016 for relapsing remitting multiple sclerosis and has been under Natalizumab since 2018. She was in NEDA status and the EDSS was stable at 2. In 2022 she presented a status epilepticus without any evident etiology.Sedation and Intubation were required to control the seizures. Later on, she presented visual hallucinations, memory and attentional disorders and dyskinesia. Cerebral MRI showed new lesions described as T2 and FLAIR hypersignals of the internal and medial-temporal regions in both sides without any enhancement.The CSF analysis was normal.Biological assessment, HSV and JCV PCR were negative. The immunological screening revealed positive anti-GAD65 antibodies in serum .No associated neoplasm was detected. Intravenous immunoglobulin was initiated and progressive improvement was noticed.The therapeutic protocol included the maintenance of the DMT and a monthly perfusion of IGIV during six months. The patient improved rapidly after the initiation of immunotherapy and her MS remained stable.
Conclusion: To the best of our knowledge,this is the first case describing the overlapping of relapsing remitting MS and Anti GAD65 autoimmune encephalitis.These overlap syndromes are strongly suggestive of a common dysimmune mechanism in their pathophysiology. Their Recognition is essential to avoid delay in diagnosis and treatment.
Disclosure: Nothing to disclose.

EPO-341

Effect of high-efficacy disease-modifying treatment on spinal cord lesion development in multiple sclerosis

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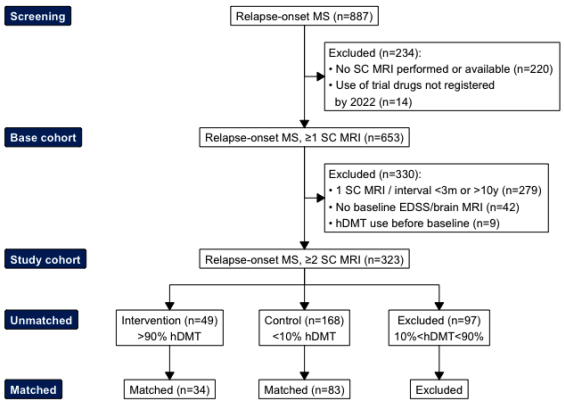
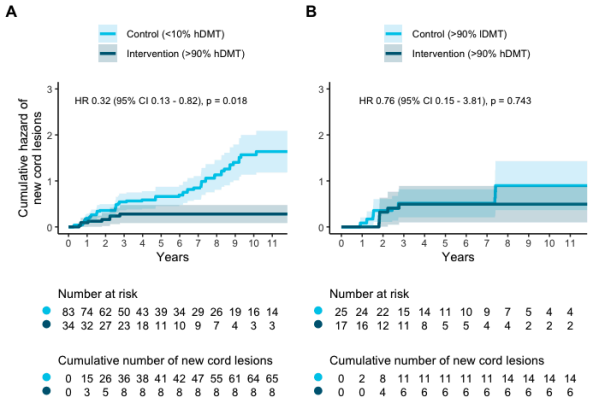
Background and aims: Spinal cord lesions in MS are an important contributor to disability. Knowledge on the effect of disease-modifying treatment (DMT) on cord lesion formation is sparse, as cord outcomes are seldom included in MS treatment trials. We aim to investigate whether high-efficacy DMTs (hDMT) can reduce spinal lesion formation, compared to low-efficacy DMTs (lDMT) and/or no treatment.

Methods: Relapse-onset MS patients with spinal cord MRI data available. were retrospectively identified. Patients with ≥2 spinal MRIs (interval >3 months and <10 years) were included. The intervention group was defined as patients that, after starting treatment, were treated with hDMTs ≥90% of spinal MRI follow-up time. Patients receiving hDMTs <10% (lDMT or no treatment ≥90%) of follow-up, served as controls. In a secondary analysis, only patients using lDMT for ≥90% of follow-up were considered controls. Patients were matched using propensity-scores. Cox proportional hazards models were used to estimate the risk of new spinal lesions.

Results: 653 patients had ≥1 spinal cord MRI and 323 an additional one with sufficient baseline data: 49 satisfied intervention and 168 control group criteria. 34 intervention group patients were matched to 83 controls. Patients in the intervention group were significantly less likely to develop new spinal cord lesions at follow-up (HR 0.32 [0.13–0.82], p=0.018). When the intervention group was matched to only controls using lDMT >90% of follow-up, the difference was not statistically significant (HR 0.76 [0.15–3.81], p=0.743).



Flowchart of screening, inclusion and matching of study population



Cumulative hazard of new spinal cord lesions. (A) Primary analysis, with patients <10% hDMT usage during follow-up as control group. (B) Secondary analysis, with patients >90% lDMT usage during follow-up as control group.

Conclusion: Treatment with hDMTs significantly reduces risk of new spinal cord lesions when compared to matched patients receiving no treatment and/or lDMTs.

Disclosure: DK, AM, RS and OG have nothing to disclose; RH received institutional research grants and fees for lectures and advisory boards from Biogen, Merck and Genzyme-Sanofi.

EPO-342

The Central Vein Sign to differentiate multiple sclerosis from migraine

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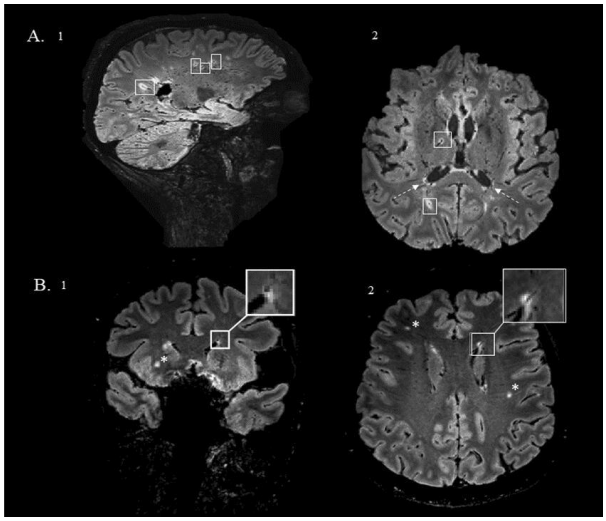
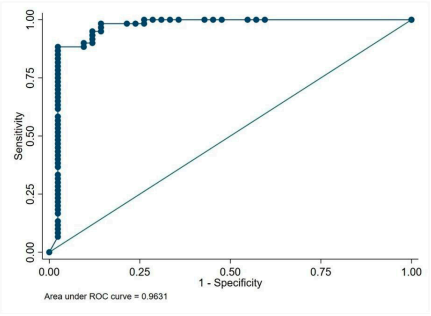
[1]IRCCS Ospedale Policlinico San Martino Genoa, Genoa, Italy, [2]University of Genoa, Genoa, Italy, [3]DISSAL, University of Genoa, Genoa, Italy, [4]DINOGMI, University of Genoa, Genoa, Italy

Background and aims: Background The Central Vein Sign (CVS) has been demonstrated its potential in differentiating multiple sclerosis (MS) from its comorbidities. Migraine represents the most common MS mimic.Aims The aims of this study were to investigate, in two cohorts including MS and migraine patients (i) the prevalence of CVS, (ii) the spatial distribution of CVS+ lesions, (iii) the best CVS threshold able to differentiate them.
Methods: 60 MS patients and 50 age and gender-matched migraine patients underwent a 3T MRI scan. A ROC-curve analysis was performed to identify the best threshold in terms of proportion of CVS+ lesions and the absolute number of CVS+ lesions able to differentiate MS from migraine.
Results: Lesion volume (LV) was different between CVS+ and CVS− lesions (median=1,273 mm³ vs 181.5 mm³ for MS cohort; median = 35.1 mm³ vs 52.2 mm³ for migraine cohort; p<0.001 for all). CVS+ LV and number were higher in MS with respect to migraine both considering whole brain and its subregions (p<0.001). The proportion of CVS+ lesions in juxtacortical and infratentorial areas was higher in MS than migraine (p=0.016 and p=0.034 respectively). The best CVS proportion-based threshold able to differentiate MS from migraine was 23% (sensitivity 90%, specificity 90.5%). The "pick 6" rule seemed to be preferable in terms of specificity with respect to the "pick 3" rule.



Example of CVS in migraine and MS patients



ROC Curve analysis to identify the best cut-off in terms of %CVS+ lesions able to differentiate MS from migraine patients

Conclusion: A CVS proportion-based threshold of 23% is capable to distinguish MS from migraine with high sensitivity and specificity. The "pick 6" algorithm may be useful in the clinical setting.
Disclosure: Authors declare no disclosures for this work.

EPO-343

Primary HIV infection as atypical cause of demyelination

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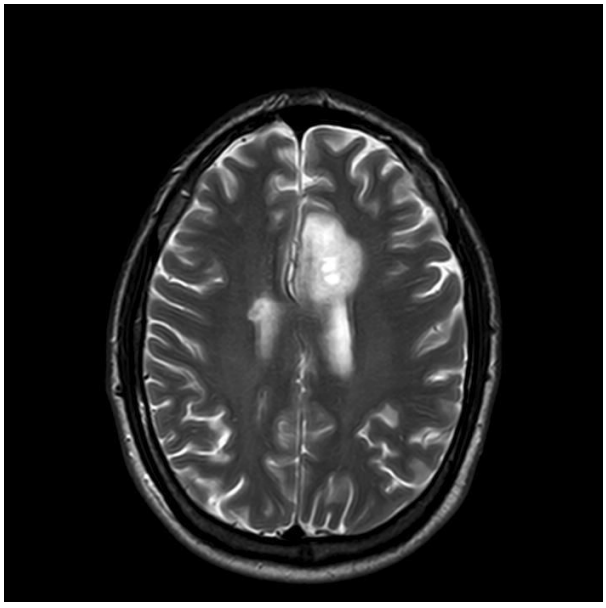
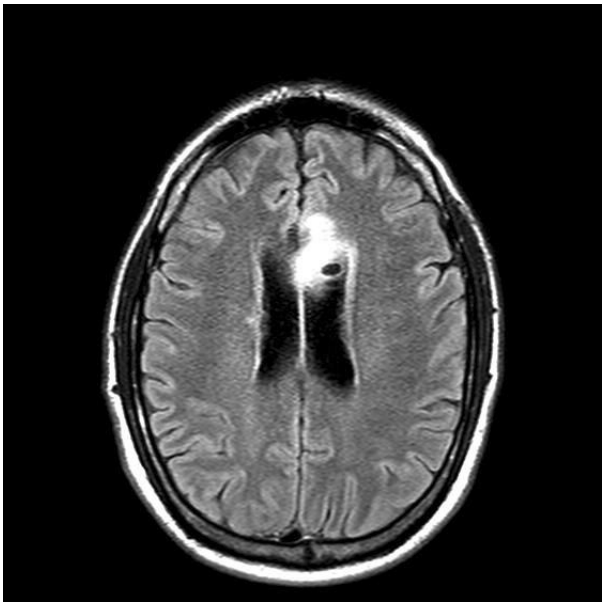
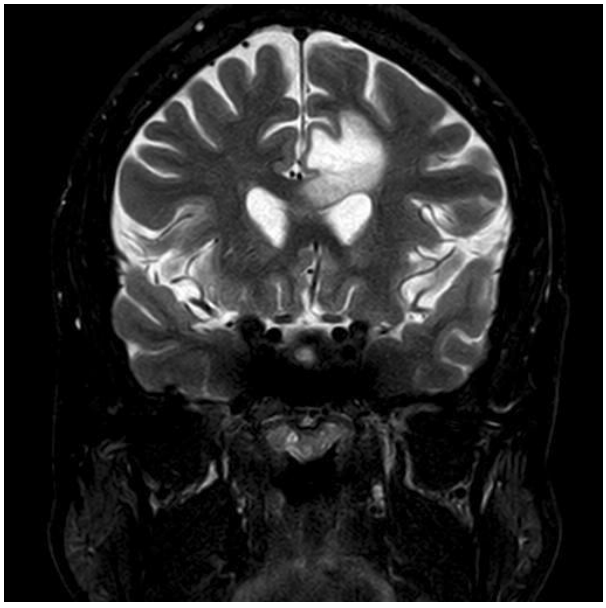
Background and aims: Demyelinating lesions secondaries to primary HIV infection are highly infrequent, with only a few case reports published in the literature. In this context, we should rule out other diagnosis, such as progressive multifocal leukoencephalopathy, primary CNS lymphoma, acute disseminated encephalomyelitis, toxoplasmosis, cytomegalovirus, cryptococcosis and multiple sclerosis. We present a case about this rare entity.
Methods: A 38-year-old male, current smoker and diagnosed with hypertension under no treatment, presented blurry vision and a hypertensive crisis. One month ago, he had experimented similar symptomatology, with completely spontaneous recovery. On physical examination he showed a right temporal hemianopsia, without delirium or another focal neurologic deficit.
Results: Brain MRI showed a lesion in the corpus callosum and left frontal lobe, hypointense on T1 and hyperintense on T2 and FLAIR, with little restriction (predominantly peripheral) in diffusion and no enhancement after gadolinium administration; stable in successive imaging tests. The brain biopsy was compatible with demyelinating disease. The results of the blood analysis were: HIV positive; serology tests for HCV, syphilis, toxoplasma and cryptococcal negative; CMV IgM negative, CMV IgG positive; CD4 428. The CSF showed a hyperproteinorraquia, IgG OCBs with a mirror pattern and negative cytology. Clinical stability had been achieved after starting antiretroviral therapy, with no new lesions.



Brain MRI: axial T2



Brain MRI: axial FLAIR



Brain MRI: coronal T2

Conclusion: An exhaustive approach in HIV patients who shows demyelinating lesions is essential for making a right diagnosis because the primary infection can be the cause.
Disclosure: Nothing to disclose.

ePosters

Monday, July 03 2023
Sleep-wake disorders

EPO-344

Confusional arousal parasomnias and the sleep factors associated with in-lab registration of episodes

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Background and aims: Non-rapid eye movement (NREM) sleep parasomnias include three subtypes: sleepwalking, sleep terrors, and confusional arousals (CA). CA are frequent but stay unnoticed in many patients, however with higher chances to be recorded during polysomnography (PSG). Our aim was to study the possible associations between CA parasomnias recorded during PSG night and sleep parameters.
Methods: We performed a retrospective review over a period of 5 years of PSGs of patients with NREM parasomnia diagnosed at a tertiary sleep center. They underwent somnological interview and a single-night PSG study preceded by a partial sleep deprivation night. PSG parameters, data on the frequency of parasomnia events, and their duration were taken into consideration. Spearman's correlation (r) and Chi-squared test were used for statistical analysis.
Results: Overall, 60 participants (mean age - 15.23±10.7 (7-89), males=86.7%, mean BMI-21.9 kg/m^2) were included, with mean CA episodes – 1.2 (0-5). The main descriptive results of the parasomnia-related parameters are presented in Table 1. Correlations with PSG parameters showed among other findings some interesting positive correlations between number of recorded episodes per PSG night and leg movement (LM) parameters (Table 2).

Parameter	Results	SD
Confusional arousals by PSG	58.3%	n/a
0 RE	41.7%	n/a
1 RE	26.7%	n/a
2 RE	15%	n/a
3 RE	8.3%	n/a
4 RE	6.7%	n/a
5 RE	1.7%	n/a
Minimum ED	32.1sec	23.98
Maximum ED	43.7sec	23.69
Average ED	37.9sec	22.26
Average difference between the longest and shortest ED	10.9sec	16.09

Table 1. Descriptive statistics of parasomnia-related data. PSG – polysomnography, RE- recorded episodes, ED- episode duration, SD- standard deviation, n/a – not applicable

PSG parameters	Spearman's *r*	P
Total sleep time	-0.204	>0.05
Wake after sleep onset	0.208	>0.05
Sleep onset	0.158	>0.05
Sleep efficiency	-0.201	>0.05
Awakenings number	**0.332**	**0.05**
Latency NREM1	0.059	>0.05
Latency NREM2	0.293	>0.05
Latency NREM3	0.299	>0.05
Latency REM	0.313	0.07
Apnea hypopnea index	0.174	>0.05
Oxygen desaturation index	0.122	>0.05
NREM1%	**0.349**	**0.04**
NREM2%	-0.018	>0.05
NREM3%	0.012	>0.05
REM%	-0.083	>0.05
Wake%	0.201	>0.05
Leg Movement Index	**0.361**	**0.03**
Periodic Leg Movement Index	0.163	>0.05
Arousal Index	0.183	>0.05

Table 2. Correlation of the number of confusional arousal episodes per recording night with PSG parameters. PSG – polysomnography

Sleep Complaints	CA by PSG	No CA by PSG	P
Insomnia	11.11%	18.18%	>0.05
Unrefreshing sleep	7.41%	9.09%	>0.05
Sleepiness	11.11%	22.73%	>0.05
Snoring	14.81%	27.27%	>0.05
Shortness of breath	7.41%	0.00%	>0.05
Restlessness in legs before sleep	7.41%	27.27%	0.06
Repetitive movements in legs in sleep	11.11%	34.78%	**0.04**
Bruxism	7.41%	18.18%	>0.05

Table 3. Association of sleep complaints with the presence of confusional arousals by PSG. CA – confusional arousal, PSG - polysomnography

Conclusion: Our results suggest the parasomnia-related parameters among patients with CA by PSG are associated with leg movements and possibly restless legs syndrome, while we found no association with sleep stage-related and respiratory variables. Probably RLS may delay sleep and worsen quality of sleep. Overall, recording CA subtype of NREM parasomnias may have added value for understanding interactions between different sleep disorders.
Disclosure: Nothing to disclose.

EPO-345

"A sleep disorder never comes alone: the association between rem sleep behaviour disorder and obstructive sleep apnoea"

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[1]Neurology Department, Hospitalar and Universitary Center of Coimbra, Coimbra, Portugal, [2]Pulmonology Department, Hospitalar and Universitary Center of Coimbra, Coimbra, Portugal, [3]Neurology Department, Braga Hospital, Braga, Portugal, [4]Sleep Medicine Center, Hospitalar and Universitary Center of Coimbra, Coimbra, Portugal

Background and aims: REM sleep behaviour disorder (RBD) is a parasomnia associated with synucleinopathies such Parkinson's disease (PD). In patients with RBD, obstructive sleep apnoea (OSA) can occurs as comorbid condition. The main goals of our study were determine the prevalence of OSA in isolated RBD (iRBD) or RBD plus synucleinopathy (RBDpS) patients and evaluate the impact of positive airway pressure therapy in RBD symptoms.
Methods: We included patients with RBD and OSA (defined as apnoea-hypopnea index(AHI)≥5/h) diagnosis followed in a tertiary sleep centre. Data on demographics, clinical characteristics, video polysomnography(VPSG) and in self-reported RBD symptoms following positive airway pressure therapy were collected. Non-parametric tests were used in statistical analyses.
Results: The prevalence of OSA in 53 RBD patients was 73.6%(n=39): 46.2% mild, 33.3% moderate and 20.5% severe. 16 patients(41.0%) with concomitant RBD and OSA, also had diagnosis of synucleinopathy, the vast majority PD(93.8%;n=15). No statistically significant differences were found between iRBD plus OSA and RBDpS plus OSA regarding male sex, age at diagnosis of RBD, BMI, AHI, total sleep time, REM-AHI and NREM-AHI. AutoCPAP, CPAP and BIPAP therapy were used by 48.7% (n=19), 7.7% (n=3) and 5.1% (n=2), respectively. These therapies improved self-reported RBD symptoms in 72.7% of the iRBD patients and in 54.5% of RBDpS patients. The main subjective improvement was the reduction in abrupt movements (87.5%-iRBD and 100.0%-RBDpS).
Conclusion: Positive airway pressure therapy may improve self-reported RBD symptoms, including in those with a coexistent synucleinopathy.
Disclosure: Nothing to disclose.

EPO-346

Suicidal tendencies and sleep disorders in epilepsy: insomnia takes the lead

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Background and aims: Suicide is more prevalent in epilepsy compared to the general population. Adults with epilepsy (AWE) report worse sleep quality. We aimed to assess subjective sleep among AWE who exhibit suicidal tendencies (ST).
Methods: AWE were assessed in a sleep and epilepsy center. AWE remained on same treatment scheme for past 3 months (or were drug-naive). Sleep complaints (SC) and their total number were addressed during structured interview (insomnia, sleep-disordered breathing, behavioral and movement disorders). Subjective sleep quality (SSQ) was measured by Pittsburgh Sleep Quality Index (PSQI). Participants were evaluated using Hamilton rating scales for depression (HAMD) and anxiety. The point on ST from HAMD was used to grade them. We divided the sample into two groups according to any suicide point positive response (SG) against none (NSG). Statistical analysis included Mann-Whitney U and Chi-squared tests.
Results: We included 168 AWE (mean age – 35.75 years, F=46.4%). Depression and anxiety rates were higher and SSQ was worse in SG. Overall, higher SC number was associated with ST (Table 1). Insomnia and its phenotypes were the most outstanding variables connected to ST. Also, abnormal behaviors in sleep, sleep paralysis and sleep bruxism were more prevalent in SG (Figure 1). No differences were obtained for sleepiness and sleep-disordered breathing, still the sleep attacks were more prevalent in SG.

Total Sample	SG	NSG
168	24	144

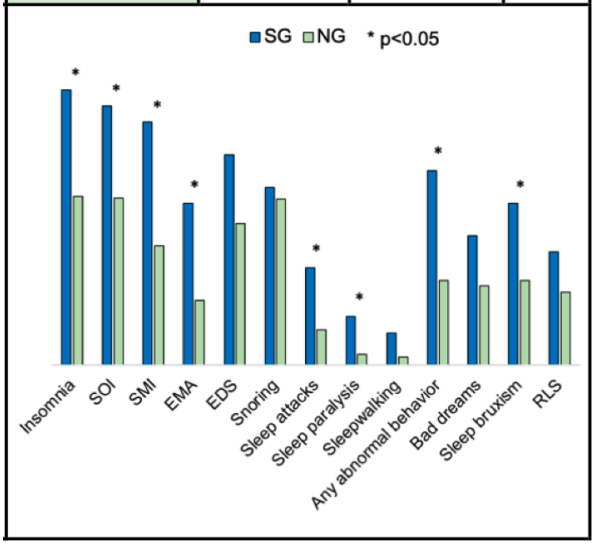
	SG	NSG	P
Age (mean, yrs)	37.0 (±12.6)	34.5 (±13.6)	>0.05
Sex (%)	58.3/41.7	52.8/47.2	>0.05
HAMD (mean)	21.1 (±7.5)	11.2 (±6.8)	<0.01*
HAMA (mean)	21.8 (±10.6)	13.4 (±9.1)	<0.01*
PSQI (mean)	10.3 (±5.4)	7.5 (±4.8)	<0.05*
SSC (num.)	5.5 (±3.8)	3.6 (±2.7)	<0.05*

Suicidal tendencies in general sample	Proportion
Suicidal tendencies total	14.3%
Feeling life is not worth living	8.3%
Thoughts of harm/possible death	4.2%
Suicidal ideas	1.2%
Suicide attempts	0.6%

SG - suicidal tendencies group, NSG – absent group, HAMD – Hamilton Depression Rating Scale, HAMA – Hamilton Anxiety Rating Scale, PSQI – Pittsburg Sleep Quality Index, SSC – Subjective Sleep Complaint.

Table 1. Descriptive data, depression, anxiety and sleep quality rates presented for two groups of epilepsy patients: with and without suicidal tendencies.

	SG	NSG	P
Insomnia	70.8%	43.4%	<0.05*
SOI	66.7%	43.1%	<0.05*
SMI	62.5%	30.6%	<0.05*
EMA	41.7%	16.7%	<0.05*
EDS	54.2%	36.4%	>0.05
Snoring	45.8%	42.7%	>0.05
Sleep attacks	25%	9.1%	<0.05*
Sleep paralysis	12.5%	2.8%	<0.05*
Sleepwalking	8.3%	2.1%	>0.05
Other behavior	50%	21%	<0.05*
Any behavior	50%	21.7%	<0.05*
Bad dreams	33.3%	20.3%	>0.05
Sleep bruxism	41.7%	21.7%	<0.05*
RLS	29.2%	18.75%	>0.05



SG - suicidal tendencies group, NSG – no suicidal tendencies group, SOI – sleep-onset insomnia, SMI – sleep-maintenance insomnia, EMA – early morning awakenings, EDS – excessive daytime sleepiness, RLS – restless legs syndrome.

Figure 1. Subjective sleep complaints are presented for both groups of adults with epilepsy with and without suicidal tendencies.

Conclusion: Sleep quality is worse and sleep complaints are more prevalent in adults with epilepsy with suicidal tendencies. Insomnia was the leading disorder for these people. Epilepsy patients with suicidal tendencies show higher burden of sleep complaints.
Disclosure: Nothing to disclose.

EPO-347

Fatigue in hypersomnolence disorders

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Background and aims: In narcolepsy and other hypersomnolence disorders besides of excessive daytime sleepiness, many patients describe rapid exhaustion, tiredness and fatigue, often associated with limitations in performance. There are only few studies on fatigue in hypersomnolence disorders.
Methods: The aim of this study was to prospectively and systematically investigate patients with different hypersomnolence disorders (narcolepsy, idiopathic hypersomnia (IH), daytime sleepiness associated with obstructive sleep apnea) for symptoms of daytime sleepiness, fatigue and affective disorders as well as the influence of therapies (medication, CPAP, others) on the symptom fatigue. Therefore, we used an online survey with multiple questionnaires like the Fatigue Scale for Motor and Cognitive Functions (FSMC), Epworth Sleepiness Scale (ESS) and others.
Results: Currently included are 176 participants (73.9% female), 72 with type 1 narcolepsy (NT1), 41 with NT2, 17 with IH, and 41 healthy controls. On average, participants were 36.6 years old (SD +/- 13.8). Participants with NT1 had a mean ESS of 16.5 (SD +/- 3.8), NT2 15.0 (SD+/- 3.8), and IH 16.5 (SD+/- 4.0). 96.9% of NT1, 97.4% of NT2 and 92.9 % of IH patients described fatigue, according to the FSMC total score (74.36; SD +/-15.9 for NT1, 77.3; SD +/-13.1 for NT2, and 75.6; SD+/- 20.0 for IH). FSMC total scores indicate a "severe" level of fatigue in all 3 disorders. Final results will be presented at the congress.
Conclusion: Preliminary results indicate that fatigue is practically always present in narcolepsy and in IH. Many patients seem to be severely affected.
Disclosure: No conflict of interest.

EPO-348

REM sleep behavior disorder in Parkinson's disease: motor and non-motor characteristics, severity and levodopa aspects

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Background and aims: REM sleep behavior disorder (RBD) is a premotor biomarker of Parkinson's disease (PD) and may accompany it during the course. Our aim was to

study the relationship of RBD, PD clinical characteristics and treatment with levodopa.
Methods: Patients with PD were diagnosed using UK PDS Brain Bank criteria and assessed by UPDRS scale and Hoehn&Yahr (H&Y). Probable RBD diagnosis (referred to as RBD) was placed based on dreams with enactment mentioned by patients and caregivers (not confirmed by polysomnography). Mann-Whitney U and Chi-squared tests were used for statistical analysis.
Results: Sample description: n=107, mean age-62.9 years (43-87), F=52.3%. UPDRS and H&Y profiles are presented in Table 1. Two groups were formed according to the RBD variable (27.4% had RBD). Mean age, sex, BMI and age of PD onset and duration were similar for both groups. Daily levodopa dose average tended to be lower in RBD ($p>0.05$), and, interestingly, the number of intakes of levodopa per day were fewer in PD patients with RBD than in patients without RBD ($p<0.05$). Table 2 encompasses comparisons for continuous and dichotomous variables in relation to RBD. PD patients with RBD had more fatigue ($p<0.05$) and vivid dreaming ($p<0.05$).

Variable	Mean	SD
UPDRS_I	2.7	2.15
UPDRS_II	11.9	5.4
UPDRS_III	30.1	14.8
UPDRS_Total	44.6	105
Hoehn&Yahr rating	2.15	0.67

Table 1. Parkinson's disease-related general descriptive data (UPDRS – Unified Parkinson Disease Rating Scale, SD – Standard Deviation).

Variables	RBD	No RBD	P value
UPDRS I	3.5	2.4	**<0.05**
UPDRS II	12.9	11.6	=0.05
UPDRS III	32.4	29.4	>0.05
UPDRS Total	48.2	43.4	>0.05
H&Y rating	2.3	2.1	**<0.05**
Restless legs syndrome %	29.6	17.2	>0.05
Fatigue %	89.7	70.15	**<0.05**
Olfactory dysfunction %	55.2	50	>0.05
Vivid dreaming %	60.9	27.1	**<0.05**
Sleep onset insomnia %	51.85	45.8	>0.05
Sleep maintenance insomnia %	66.7	52.8	>0.05
Daytime sleepiness %	58.6	50	>0.05
Levodopa in the scheme %	80.8	74.1	>0.05
Nocturnal akinesia %	66.7	62.8	>0.05
Nocturnal tremor %	50	44.2	>0.05

Table 2. Continuous and dichotomous variable distribution according to the presence or absence of RBD in patients with PD. Abbreviations: RBD – REM sleep behavior disorder, UPDRS – Unified Parkinson's Disease Rating Scale, H&Y - Hoehn&Yahr.

Conclusion: Our results show high prevalence of RBD in PD. PD patients with RBD had more fatigue and vivid dreaming. PD patients with RBD had worse results on mood, cognition, and behavior domain, while other domains were similar. Finally, the disease was more severe in the presence of RBD.
Disclosure: Nothing to disclose.

EPO-349

Sleepiness in functional motor disorders: the mismatch between self-reporting and the multiple sleep latency test.

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Background and aims: Sleep symptoms, including sleepiness, are frequently reported by patients with functional motor disorders (FMD). We aimed to identify the comorbid sleep disorders in FMD, and to investigate the relationship between subjective sleepiness and objective measures of hypersomnia.
Methods: Twenty-six patients (mean age 49.5 (SD 10.0) years) with clinically definite FMD, and 16 patients (mean age 47.9 (SD 9.6) years) with central hypersomnia (CH) were included in the study. The study protocol consisted of a medical and sleep history, neurological examination, polysomnography (PSG), multiple sleep latency test (MSLT), and questionnaires assessing sleepiness, fatigue, and depression.
Results: Fifteen FMD patients reported sleepiness as their major sleep complaint and/or scored above the cut-off for excessive daytime sleepiness. Sleep comorbidities were found in the following proportions: 11 restless legs syndrome; 13 obstructive sleep apnoea; and 2 periodic limb movements in sleep; however, their relation to sleepiness was not observed. FMD patients with sleepiness reported higher depression ($p=0.018$), and had longer sleep latencies in the MSLT ($p<0.001$) compared to the CH patients. Depression ($p=0.006$) and fatigue ($p=0.003$) positively correlated with self-reported sleepiness in FMD patients.
Conclusion: This study did not find the objective correlation of subjective sleepiness reported by patients with FMD. Although sleep abnormalities were found to be common in FMD, they were not associated with increased sleepiness. Correlations between self-reported sleepiness, depression, and fatigue support the current unified model for the development of functional symptoms. Supported by: Czech Ministry of Health Project AZV NU20-04-0332.
Disclosure: Supported by: Czech Ministry of Health Project AZV NU20-04-0332; National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107) – Funded by the European Union – Next Generation EU; Charles University: Cooperatio Program in Neuroscience; General University Hospital in Prague project MH CZ-DRO-VFN64165. The authors have no conflict of interest to disclose.

EPO-350

Sex-related differences in symptoms and impairment in patients with narcolepsy: findings from the TENAR project

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Background and aims: Recent pre-clinical findings suggest the existence of sex-related differences in narcolepsy. We aimed at comparing severity of symptoms and psychosocial impairment of female and male patients with narcolepsy.

Methods: Secondary analysis of baseline data of 106 female and 102 male patients with narcolepsy (mean age of 33.9 and 34.1 years respectively) participating in the TENAR (TElemedicine for NARcolepsy) randomized controlled trial (Italian Ministry of Health funded project RF-2016-02364742). Baseline data included: sociodemographics (educational level, sentimental, marital and occupational status), sleepiness (Epworth Sleepiness Scale, ESS), frequency and duration of cataplexy attacks, disease severity (Narcolepsy Severity Scale, NSS), depressive symptoms (Beck Depression Inventory, BDI), pharmacological treatment, and main narcolepsy-related problems.

Results: Female and male patients did not differ regarding sociodemographics, cataplexy, and pharmacological treatment. Compared with male, female patients had significantly higher ESS (11.2 vs 9.4), NSS (22.3 vs 17.1), and BDI scores (11.7 vs 6.9). With the exclusion of cataplexy and of the item "relationships with the others", compared with male, female patients reported significantly ($p<0.05$) more frequently as a problem all the narcolepsy-related problems investigated: sleepiness (71.7% vs 46.1%), sleep attacks (45.3% vs 26.5%), concentration and memory problems (65.1% vs 35.3% and 42.5% vs 27.5% respectively), and maintain the work pace and achieve goals (54.7% vs 23.5% and 40.6% vs 21.6% respectively).

Conclusion: Narcolepsy may impair differently female and male patients calling for better understanding of sex-related differences to improve management and care of narcolepsy.

Disclosure: Funding source: Italian Ministry of Health funded project RF-2016-02364742

EPO-351

Positive Effects of pregabalin and duloxetine on Sleep and Pain in Painful Diabetic Polyneuropathy (PDPN): Blossom Trial

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Background and aims: The secondary outcome of Blossom Clinical Trial was to measure effects of pregabalin (Pregabalin Krka) and duloxetine (Dulsevia®) on sleep patterns and depression in PDPN patients.

Methods: 201 PDPN patients from 5 countries were randomized to pregabalin (99) or duloxetine (102) for 12 weeks. Pain was evaluated using visual analogue scale (VAS) and Douleur Neuropathique questionnaire (DN4), insomnia with insomnia severity index (ISI), excessive daytime sleepiness with Epworth sleepiness scale (ESS) and depression with major depression inventory (MDI).

Results: After 12 weeks, worst pain intensity in last 24-hours (WPI) decreased from 69.2±16.7 to 27.7±20.6 (pregabalin) and from 67.4±16.0 to 27.4±21.0 (duloxetine). DN4 decreased from 6.9±1.6 (both arms) to 3.6±2.4 (pregabalin) and to 3.6±2.5 (duloxetine); ISI from 11.1±7.0 to 6.0±5.6 (pregabalin) and from 10.9±6.9 to 7.4±6.4 (duloxetine); ESS from 7.0±4.4 to 6.7±4.4 (pregabalin) and from 6.0±4.1 to 5.8±3.6 (duloxetine); MDI from 16.0±11.4 to 10.2±8.3 (pregabalin) and from 15.4±9.4 to 10.8±8.1 (duloxetine). On average, patients had subthreshold insomnia without excessive daytime sleepiness or depression. At the end of the treatment period, WPI, DN4, ISI and MDI scores significantly decreased ($p<0.001$) without change in daytime sleepiness.

Conclusion: According to results, pregabalin and duloxetine may have beneficial multimodal effect. The mood and sleep of PDPN patients improved after 12 weeks of treatment.

Disclosure: Krka, d.d., has financially supported this clinical trial.

EPO-352

Sociodemographic characteristics of female narcolepsy patients

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Background and aims: Narcolepsy is a rare neurological disorder, which affects men and women about equally often. Narcolepsy often results in limitations of workability and quality of life, but gender-specific data are very limited. We aimed at analyzing sociodemographic data from narcolepsy females compared to healthy female controls.
Methods: For assessment, we used an online survey. Adult female patients were invited from the outpatient clinic of a tertiary sleep and narcolepsy center. Data assessment included demographic data, use of exogenous noxae, education, work, and co-morbidities.
Results: We included 113 female narcolepsy (NC) patients and 199 healthy (HC) female controls. Mean age was 33.8 (SD 9.8) for NC and 35.4 (SD 10.1) for HC (n.s.). Mean BMI was 27.1 (SD 6.7) for NC and 25.1 (SD 3.5) in HC. In narcolepsy, the highest completed level of education reached only 29.2%, in contrast to 41.2% in HC ($p<0.05$). 19.5% of NC (vs. 12% of HC) did not complete any professional training ($p<0.05$). 81.4% of HC work full-time, but only 31.9% of NC ($p<0.01$). NC had less frequent a permanent partnership (incl. marriage): 33.6% vs. 39.7% ($p<0.05$). 32.7% of NC are smokers, whereas only 21.1% of HC ($p<0.05$). Depression was common in NC with 23% vs 9% in HC ($p<0.01$).
Conclusion: Women with narcolepsy are more often less educated and limited in their workability. Further efforts are needed to implement earlier diagnosis and treatment, as well as to pay particular attention to gender aspects in narcolepsy.
Disclosure: Nothing to disclose.

EPO-353

Involvement of sleep structure in patients with a selective stroke of the basal ganglia: An observational, cohort study.

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Background and aims: Selective basal ganglia (BG) stroke is a rare event observed after revascularization procedures. The primary endpoint of the study was the analysis of sleep structure in patients with selective ischemic BG lesions. Secondarily, we aimed to determine the prognostic role of sleep parameters in the same population.
Methods: In this observational, cohort study we included consecutive adult patients admitted to our Stroke Unit (SU) who presented a selective BG lesion consequent to a M1 occlusion treated with mechanical thrombectomy (BG group). Each BG subject was age- and sex-matched with a patient who underwent polysomnography for syncope and/or suspected sleep-related breathing disorders (CG). All BG patients underwent polysomnography during their SU stay within 10 days from stroke onset. Statistical analyses were performed through Mann-Whitney U-test and logistic regression.
Results: 45 patients were enrolled. Several sleep parameters differed between BG and CG patients in the univariate analysis. In logistic regression, BG subjects presented a lower percentage of REM sleep ($p=0.002$) and more daytime sleep ($p=0.012$) than controls. 25/39 (64%) patients presented a good outcome (3-month modified Rankin Scale (mRS)≤2). Percentage of REM sleep ($p=0.001$) and CAP rate ($p<0.001$) were higher in subjects with a good outcome than those with mRS>2.

	Patients (n=45)		**Controls (n=45)**		
	Mean	SD	Mean	SD	p
Macrostructure					
Total sleep time (min)	353	92	371	89	**<0.001**
Sleep efficiency index (%)	67	18	80	13	**<0.001**
Sleep latency (min)	30	39	18	22	0.364
WASO (min)	147	87	76	64	**<0.001**
REM/TST (%)	10	7	21	9	**<0.001**
N1/TST (%)	11	8	9	5	0.197
N2/TST (%)	50	14	48	12	0.329
N3/TST (%)	23	13	23	10	1.000
Awakenings > 2 min (n)	11	6	6	5	**<0.001**
All arousals (per hour)	15	14	11	15	0.333
Daytime sleep (min)	63	60	25	41	**<0.001**
Microstructure					
CAP rate (%)	34	22	47	22	**0.009**
A1 (%)	22	17	29	18	0.060
A2 (%)	32	17	23	8	**<0.001**
A3 (%)	41	24	48	18	0.147
Respiratory parameters					
central AHI (per hour)	4	10	0	1	**0.024**
obstructive AHI (per hour)	32	29	15	20	**0.003**
ODI (per hour)	26	24	14	18	**0.037**

Table 1. Results of the univariate comparison between patients with a selective basal ganglia stroke and the control group. Significant differences are reported in bold. All the statistical comparison were performed through the Mann-Whitney U-test.

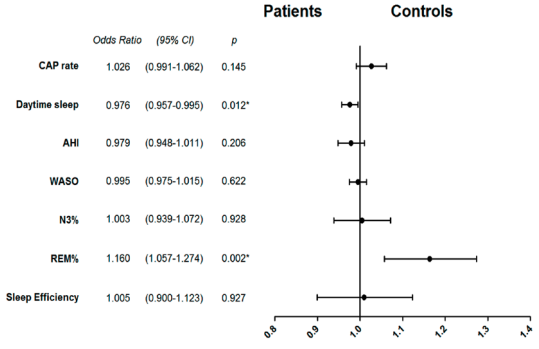

Figure 1. The Forest Plot of the logistic regression comparing patients with a selective basal ganglia stroke with the control group. Patients of the BG group presented a lower percentage of REM sleep and a higher amount of daytime sleep than controls.

	Good outcome (n=25)		Poor outcome (n=14)		
	Mean	SD	Mean	SD	p
Macrostructure					
Total sleep time (min)	533	51	529	56	0.050
Sleep efficiency index (%)	69	19	64	16	0.072
Sleep latency (min)	22	28	40	49	0.296
WASO (min)	142	83	156	94	0.481
REM/TST (%)	13	7	7	5	**0.002**
N1/TST (%)	13	8	9	6	0.174
N2/TST (%)	47	12	54	15	0.065
N3/TST (%)	24	13	21	13	0.098
Awakenings > 2 min (n)	9	3	14	9	0.518
All arousals (per hour)	12	9	20	18	0.065
Daytime sleep (min)	52	48	79	71	0.257
Microstructure					
CAP rate (%)	43	17	22	21	**<0.001**
A1 (%)	28	18	14	12	**0.002**
A2 (%)	33	11	31	23	0.545
A3 (%)	35	19	50	26	0.406
Respiratory parameters					
central AHI (per hour)	5	8	3	12	**0.033**
obstructive AHI (per hour)	35	24	28	35	0.100
ODI (per hour)	33	24	17	22	**0.033**

Table 2. A table depicting the results of the univariate comparison between the subgroups of patients with good (mRS≤2) and those with poor (mRS>2) 3-month stroke outcome. Significant differences are reported in bold.

Conclusion: A low amount of REM sleep and an increase in daytime sleep time characterize patients with selective BG stroke. A low CAP rate and a reduced proportion of REM sleep are related to poor 3-month stroke outcome. Polysomnography is a useful tool for patients with a BG stroke.
Disclosure: The authors declare no disclosures.

EPO-354

Sleep-onset REM in polysomnography is an important indicator to diagnose narcolepsy in sleep clinic patients

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Background and aims: The differential diagnosis of excessive daytime sleepiness (EDS) includes narcolepsy and sleep apnoea. In sleep medicine, the vast majority of polysomnography (PSG) is performed in order to identify sleep apnoea. In general sleep clinic patients, the frequency of sleep-onset REM (SOREM) in polysomnography is <1%. In narcolepsy, it is found in 15-44%. The aim of this study is to identify the frequency and the impact of SOREM periods in diagnostic PSG on the final sleep diagnosis.
Methods: A literature review on SOREM periods in PSG. Retrospective data analysis of consecutive sleep clinic patients on demography, clinical data, PSG and Multiple Sleep Latency Test (MSLT) data, and final diagnosis.
Results: Interim analysis includes data of 286 consecutive patients with the suspected diagnosis of sleep aponea. In 3 (1.05%) patients SOREM periods in PSG were found. SOREM occurred after 2, 8.5 and 14 minutes. Two of them were male and one was female. They were aged 34, 44 and 59 years. Epworth Sleepiness Scale (ESS) was 14, 15 and 17 points. Further diagnostic work-up showed >2x SOREM also on MSLT. Final diagnosis of the patients was narcolepsy type 1 (n=1) and type 2 (n=2).
Conclusion: PSG is an important tool for the diagnosis of sleep disorders. SOREM in PSG should be used as an important indicator for further differential diagnosis, in particular with a view to narcolepsy. This will also help to shorten the latency between symptom onset and diagnosis.
Disclosure: Nothing to disclose.

EPO-355

Sleep architecture of patients with idiopathic hypersomnia and identification of neurophysiological markers for subtypes

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Background and aims: Idiopathic hypersomnia (IH) is a rare neurologic disease characterised by excessive need of sleep including prolonged nocturnal sleep and excessive daytime sleepiness. Previously, IH has been classified into "with/without long sleep". The aim of the study is to systematically examine differences in sleep architecture, including sleep cycle features and sleep stages of patients with IH in order to identify particular neurophysiological parameters for subtypes.
Methods: In this retrospective pilot study, clinical data, and data on questionnaires, Polysomnography and Multiple Sleep Latency Tests of 60 consecutive IH patients from two major sleep centres are analysed.
Results: Interim results of 11 patients (8 female, 3 male): Mean age is 22 years. Mean score of Epworth Sleepiness Scale questionnaire is 11.0. Mean total sleep duration is 561 mins with a standard deviation (SD) of 107. Mean number of sleep cycles (MNSC) including incomplete last sleep cycle is 5.45 (SD = 1.37). Mean sleep efficiency is 93.41%. Mean sleep latency is 12 mins. Mean wake after sleep onset is 5 mins. Mean sleep cycle duration (MSCD) excluding incomplete last sleep cycle is 114 mins (SD = 20). 5 patients have a MSCD between 88 – 108 minutes (SD = 8), their MNSC is 6.0 (SD = 1.87). 6 patients have a MSCD >110 mins (SD = 18), their MNSC is 5.0 (SD = 0.63), 2 of these patients have a MSCD >140 mins. Detailed results will be presented at the congress.
Conclusion: Preliminary data indicates two subtypes of IH, one associated with long sleep cycles.
Disclosure: Nothing to disclose.

EPO-356

Sleep – wake disorders for patients with Parkinson's disease: relationship with motor and non-motor symptoms

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Background and aims: Sleep – wake disorders are among the main non-motor symptoms (NMS) that occur for the patients with Parkinson's disease (pwPD), affecting 60-90% of them [1,2,3]. Usually patients complain of insomnia, increased daily sleepiness, circadian rhythm disturbances, restless leg syndrome (RLS), REM sleep behaviour disorders (RBD) [2,3]. Recent studies show that RBD occur 10-15 years before PD specific motor symptoms evolve and is associated with increased risk of developing other neurodegenerative diseases [4].

Methods: We involved 43 patients (25 patients with PD and 18 control group patients) who underwent clinical evaluation of motor (UPDRS III scale) and non-motor symptoms (Table 1): NMS-quest, Sniffin'Sticks-12 (SS-12) test, Montreal cognitive assessment (MoCA) and sleep questionnaires (Table 2). 15 PD and 16 control group patients underwent polysomnography (PSG) and were evaluated for objective sleep disorders (Table 3).

Results: More than 75% of pwPD were diagnosed with insomnia and/or significant RLS. PSG findings suggested of longer sleep onset, reduced total sleep time, reduced sleep efficiency and more frequent arousal for pwPD compared to controls. 75% of pwPD were diagnosed with RBD, 50% - with obstructive sleep apnea syndrome (OSA) and periodic leg movement disorder (PLMD). PwPD suffering from RLS and RBD reported having significantly more NMS. PwPD having severe motor symptoms complained of insomnia more often.

Clinical characteristics	PD group (n=25)
Age, mean ± SD [min÷max]	62.8 ± 8.77 [46 ÷ 77]
Sex - Men, n (%) - Women, n (%)	 15 (60%) 10 (40%)
MoCA, mean ± SD [min÷max] - Normal, n (%) - Mild cognitive impairment, n (%) - Intermediate cognitive impairment, n (%)	22.23 ± 3.83 [13 ÷ 27] 10 (40%) 13 (52%) 2 (8%)
Brain trauma in the past, n (%)	3 (12%)
UPDRS III scale, mean ± SD [min÷max]	22.25 ± 8.6 [9 ÷ 34]
PD stage according to *Hoehn-Yahr*, mean ± SD [min÷max]	2.56 ± 0.88 [1 ÷ 4]
PD NMS questionnaire, mean ± SD [min÷max]	10.92 ± 2.97 [6 ÷ 16]
Smell test, mean ± SD [min÷max]	6.18 ± 1.99 [4 ÷ 10]
Family history of PD: - negative, n (%) - positive, n (%) - unknown, n (%)	 6 (24%) 9 (36%) 10 (40%)
Complain of sleep problems, n (%) - Cannot initiate sleep, n (%) - Arouses, n (%) - Experience nightmares, n (%)	21 (84%) 5 (20%) 20 (80%) 12 (48%)

Abbreviations: mean ± SD - mean ± standard deviation, n – number of cases, *% – percentage, PD – Parkinson's disease, UPDRS – Unified Parkinson's Disease Rating Scale, NMS – non-motor symptoms*

Table 1. Clinical characteristics of patients with Parkinson's disease

Indicators	PD group (n=25)	Control group (n=18)	p value
Insomnia severity index (ISI), mean ± SD [min÷max]	11.94 ± 6.86 [3 ÷ 24]	12.28 ± 5.51 [1 ÷ 20]	0,873
International Restless Leg Syndrome Scale (IRLS), mean ± SD [min÷max]	14.73 ± 11.39 [0 ÷ 32]	9.06 ± 11.73 [0 ÷ 39]	0,136
Berlin sleep apnoea scale - Low risk, n (%) - High risk, n (%)	 21 (84%) 4 (16%)	 5 (27,8%) 13 (72,2%)	**0,002**
Ullanlina Narcolepsy Scale (UNS), mean ± SD [min÷max]	7.5 ± 3.65 [2 ÷ 16]	8 ± 4.68 [2 ÷ 18]	0,723
Innsbruck RBD assessment scale, mean ± SD [min÷max]	0.25 ± 0.20 [0 ÷ 0,66]	0.22 ± 0.22 [0 ÷ 0,67]	0,606
RBD Single-Question screen (RBD1Q) - Yes, n (%)	 7 (28%)	 1 (5,6%)	**0,013**
Epworth Sleepiness Scale (ESS), mean ± SD [min÷max]	8.88 ± 4.34 [4 ÷ 19]	10.61 ± 5.88 [0 ÷ 18]	0,332

Abbreviations: PD – Parkinson's disease, RBD – REM sleep behaviour disorder, mean ± SD - mean ± standard deviation, n – number of cases

Table 2. Comparison of subjective sleep parameters using specific sleep questionnaires

Indicators	PD group (n=15)	Control group (n=16)	*p* value
Overall sleep time, min, mean ± SD [min÷max]	309.42 ± 86.67 [148 ÷ 465]	352.07 ± 51.21 [273,0 ÷ 432,5]	0,150
Overall sleep time, hr, mean ± SD [min÷max]	5.16 ± 1.44 [2,47 ÷ 7,75]	5.87 ± 0.85 [4,55 ÷ 7,21]	0,150
Sleep quality, %, mean ± SD [min÷max]	66.34 ± 13.24 [38,1 ÷ 83,8]	58.81 ± 12.26 [40,1 ÷ 76,1]	0,835
Sleep latency, min, mean ± SD [min÷max]	29.62 ± 44.69 [0 ÷ 147]	39.79 ± 28.01 [4,0 ÷ 96,5]	0,193
REM sleep latency, min, mean ± SD [min÷max]	188.54 ± 116.35 [23,5 ÷ 402,0]	199.10 ± 115.94 [38 ÷ 389,5]	0,945
N1 (%), mean ± SD [min÷max]	11.93 ± 10.86 [2,7 ÷ 35,2]	11.84 ± 9.16 [3,5 ÷ 37,6]	0,645
N2 (%), mean ± SD [min÷max]	48.88 ± 12.04 [21,1 ÷ 69,4]	52.81 ± 10.69 [38,6 ÷ 72,6]	0,728
N3 (%), mean ± SD [min÷max]	22.86 ± 17.85 [2,6 ÷ 72,2]	19.31 ± 9.65 [5,9 ÷ 40,8]	0,809
REM sleep (%), mean ± SD [min÷max]	16.48 ± 8.79 [2,5 ÷ 35,3]	17.12 ± 9.1 [4,1 ÷ 37,2]	0,928
AHI, e/hr, mean ± SD [min÷max]	8.33 ± 10.43 [0,4÷37,5]	34.93 ± 28.05 [3,9 ÷ 81,1]	**0,001**
AHI (on the back), e/hr, mean ± SD [min÷max]	10.8 ± 16.25 [0 ÷ 59,1]	48.95 ± 29.84 [5÷93,7]	**<0,001**
RERA, e/hr, mean ± SD [min÷max]	2.71 ± 3.63 [0,2 ÷ 13,2]	33.89 ± 31.54 [2,5 ÷ 103,5]	**<0,001**
SAI, e/hr, mean ± SD [min÷max]	18.46 ± 12.22 [2,4 ÷ 47,33]	27.19 ± 12.49 [13,9 ÷ 51,3]	**0,028**
Leg movement related arousals, e/hr, mean ± SD [min÷max]	7.29 ± 11.79 [0,3÷43,2]	2.69 ± 3.21 [0 ÷ 11,1]	0,114
Overall AI, e/hr, mean ± SD [min÷max]	30.91 ± 18.1 [9,1 ÷ 65,9]	65.43 ± 41.45 [23,1 ÷ 168,4]	**0,007**
PLMI, e/hr, mean ± SD [min÷max]	37.04 ± 32.29 [0,7 ÷ 98,5]	11.12 ± 14.89 [0 ÷ 47,4]	**0,009**
PLM-AI, e/hr, mean ± SD [min÷max]	6.24 ± 10.36 [0÷39,7]	1.64 ± 2.14 [0 ÷ 6,9]	**0,037**

Abbreviations: mean ± SD - mean ± standard deviation, n – number of cases, min – minutes, hr – hours, % – percentage, e/hr – events per hour, PD – Parkinson's disease, N1 – first sleep stage, N2 – second sleep stage, N3 – third sleep stage, REM sleep – rapid eye movement sleep stage, AHI – apnea-hypopnea index, RERA – respiratory effort related arousal, SAI – spontaneous arousal index, PLMI – periodic limb movement index, PLM-AI – periodic limb movement arousal index, AI – arousal index

Table 3. Polysomnography (PSG) results

Conclusion: Sleep – wake disorders for pwPD have a significant negative effect on other motor and NMS. Increased attention for sleep – wake disorders for pwPD may help improve management of Parkinson's disease.

Disclosure: Authors report no conflict of interest.

EPO-357

Update on SPHYNCS: the Swiss Primary Hypersomonlence and Narcolepsy Cohort Study

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Background and aims: Central disorders of hypersomnolence (CDH) comprise Narcolepsy type 1 (NT1), Narcolepsy type 2 (NT2), Idiopathic hypersomnia (IH), Insufficient sleep syndrome (ISS) and Hypersomnia associated with psychiatric disorders (NOH). Apart from NT1, further understanding of pathophysiology, diagnosis and treatment is urgently required. SPHYNCS addresses this lack of knowledge on CDH and aims at identifying new biomarkers for narcolepsy and its borderland (NBL) and thus improving diagnostic criteria and treatment.

Methods: Since 2020, 6 Swiss sleep centers have been enrolling patients with the suspected diagnosis of CDH; healthy persons are recruited as controls. Follow-up comprises 3 years. Clinical and electrophysiological data as well as blood, cerebrospinal fluid (CSF) and stool samples are collected for quantitative assessments of new biomarkers using proteomics/peptidomics, immunological, genetic, microbiome studies.

Results: 113 patients and 12 controls have been included. 92 (74%) are female and the median age is 26 (21, 34) years. The mean BMI is 23.1 (21.0, 27.1). 28 (22%) patients were diagnosed with NT1. Serum (n=125), stool (n=90) and CSF (n=81) were collected, and 110 participants agreed to wear a Fitbit device for one year. Preliminary results including Fitbit, Microbiome, CSF analyses, SART, and MINI, will be presented.

Characteristic	N	N = 125[1]
Gender (Female)	125	92 (74%)
Age	125	26 (21, 34)
BMI (calculated automatically)	119	23.1 (21.0, 27.1)
Diagnosis type	125	
Narcolepsy Type 1		28 (22%)
Other central hypersomnias		79 (63%)
Diagnosis missing		6 (4.8%)
Healthy controls		12 (9.6%)
Diagnosis certainty	107	
Definite		35 (33%)
Probable		62 (58%)

Table 1: demographics of the SPHYNCS population

Conclusion: The report shows the feasibility of the ongoing multicenter study. Hypothesis and data driven (e.g. unsupervised patient clustering) analyses are currently being explored in order to identify new CDH markers towards better patient characterization and treatment.

Disclosure: The study is supported by the Swiss National Science Foundation.

EPO-358

The Swiss Narcolepsy Network (SNaNe) and its Registry

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Background and aims: The mission of SNaNe is to foster cooperation in Switzerland among health professionals, scientists, patient organizations and the general public to promote diagnosis, treatment, psychosocial support, research and awareness of narcolepsy and central disorders of hypersomnolence (CDH). The creation of a Swiss registry for CDH is essential to collect uniform data and evaluate specified outcomes.
Methods: Sleep centers with SNaNe membership will prospectively submit patient registry information to the SNaNe REDCap database (set up at the Clinical Trials Unit (CTU) Bern). Clinical, polysomnographic and biological information are collected at baseline and follow-up visits. To be compliant with the European Narcolepsy Network (EU-NN) database, key features of the EU-NN database were adopted for the SNaNe registry. Data from the Swiss Primary Hypersomnolence and Narcolepsy Cohort Study are transferred electronically to the SNaNe database. The database regulation has been accepted by the local ethics committee.
Results: To date, we transferred data from 230 visits of 119 individuals (31 patients with narcolepsy type 1, 74 patients with other CDH or missing diagnosis and 14 controls) from the SPHYNCS to the SNaNe database.
Conclusion: The SNaNe registry aims to answer open clinical, diagnostic and therapeutic questions, support research for innovative therapeutic solutions and improve care for patients with CDH. This is needed, because Narcolepsy and other CDH are rare, debilitating and still relatively poorly understood diseases. Compatibility with the EU-NN and SPHYNCS RedCap databases enables accurate data transfer between the three databases.
Disclosure: Nothing to disclose.

Neurogenetics 1

EPO-359

Expanding the spectrum: Chorea on CANVAS.

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Background and aims: Cerebellar Ataxia, Neuropathy and Vestibular Areflexia Syndrome (CANVAS) is a recently described type of hereditary ataxia, produced by AAGGG expansions in the RFC1 gene, presenting with cerebellar, sensory and vestibular dysfunction. A multitude of other neurological symptoms have been associated with this genetic alteration, and the clinical spectrum is expanding.
Methods: We report a case of CANVAS presenting with chorea.
Results: A 60-year-old male patient, with history of chronic cough and 2 relatives affected by ataxia, started with a progressive gait disorder. The examination revealed cerebellar syndrome (dysarthria, ataxia), apalesthesia and altered Vestibulo-Ocular Reflex, suggestive of CANVAS. However, it also stands out motor impersistence, and irregular, arrhythmic and purposeless movements of the limbs, worsening with dual-task, suggestive of generalized chorea (videographic record). Complete analytical study was normal, electromyogram showed sensory neuronopathy (Figure-1), brain MRI showed cerebellar and basal ganglia atrophy (Figure-2). A CANVAS genetic study was performed with pathological results.

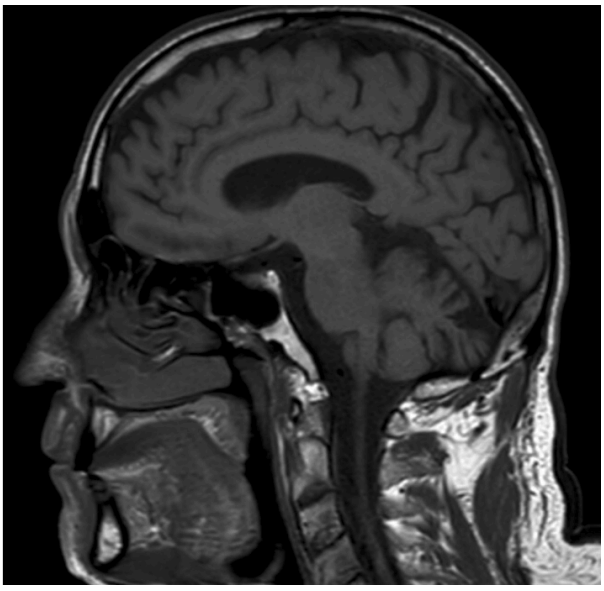
VC Sensitiva

Nervio / Lugares	Reg.	Latencia ms	Ampl µV
R Mediano - y Ulnar Dedos			
Dedo I	Muñ	NR	NR
Dedo II	Muñ	NR	NR
Dedo III	Muñ	NR	NR
Dedo V	Muñ	NR	NR
R Radial			
Ant	Tab ana.	NR	NR
R Sural - Mal Exter			
Sura	Mal Lat	NR	NR
L Sural - Mal Exter			
Sura	Mal Lat	NR	NR
R Peroneo superficial			
Pant Later	Dorso pie	NR	NR
L Peroneo superficial			
Pant Later	Dorso pie	NR	NR

VC Motora

Nervio / Lugares	Latencia ms	Ampl. mV	Dur. ms	Dist. mm	VC m/s	Reg
R Mediano - Apb						
Muñeca	4,11	8,3	4,58			APB
Codo	8,85	7,5	4,90	240	50,6	
Axila	15,26	2,6	4,74			
Erb	15,36	7,8				
R Cubital - Adm						
Muñeca	2,66	4,7	5,26			ADM
Infracodo	6,46	4,6	5,52	200	52,6	
Supracodo	8,54	4,6	5,89	110	52,8	
Axila	11,82	3,8	6,25			
EP	14,53	3,6				
R Peroneo - EDB						
Dorso Pie	3,28	4,6	5,63			EDB
Distal CP	11,46	4,3	6,77	310	38,9	
Prox CP	12,97	4,2	6,04	130	86,1	
L Peroneo - EDB						
Dorso Pie	4,48	2,5	5,68			EDB
Distal CP	12,34	2,3	6,30	320	40,7	
Prox CP	14,06	2,1		130	75,6	

Electromyogram showed sensory neuronopathy (Figure-1)



brain MRI showed cerebellar and basal ganglia atrophy (Figure-2)

Conclusion: The number of reported cases of CANVAS is increasing, progressively expanding the phenotypic spectrum, being frequent the presence of parkinsonism, sleep disorders, etc. Chorea has been described anecdotally in the past. Recently, atrophy predominantly involving cerebellum and Basal Ganglia (as in the presented case) has been described, as well as increased expression of the RFC1 gene in these locations, what could justify the presence of chorea and other dyskinesias. Although more reports are needed in this regard, chorea and other movement disorders are probably part of the clinical spectrum of CANVAS, and several authors postulate that their description will increase in the coming years.
Disclosure: the authors have no conflict of interest to report.

EPO-360

Clinical and genetic characterization of a Portuguese cohort with hereditary spastic paraparesis

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Background and aims: Hereditary spastic paraparesis (HSP) represents a heterogeneous group of neurodegenerative disorders manifested mainly by spasticity and lower limb paresis. More than 70 genes have been identified that are associated with different clinical phenotypes and inheritance patterns. The description of case series with identified genotype may help to clarify the phenotypic spectrum associated with each genetic form.

Methods: Retrospective clinical and molecular study of HSP patients enrolled in the database of the Neurogenetics and Movement Disorders Outpatient Clinic of Hospital Santa Maria, Lisbon, since January 2021.
Results: We identified 37 patients with HSP, 59.5% female; mean age at symptom onset was 24 years. Genetic mutations were found in 70% of patients, of which 69% had a molecular diagnosis and 31% were a variant of unknown significance. SPG4 (43%), SPG3A (15%), SPG11 (14%), SPG5, SPG28, SPG76 (7% each) corresponded to the majority (78%) of HSP with molecular diagnosis and 22% formed other genetic disorders. Other neurological signs occurred in HSP, including retinal disease (SPG11), ophthalmoparesis, cerebellar ataxia and parkinsonism (SPG78), peripheral polyneuropathy (SPG11), dysautonomia (SPG4, 11, 78) and cognitive dysfunction (SPG3A). The correlation found between phenotype and genotype was consistent with the literature, except for 2 cases of SPG3A with later onset and complex forms and 1 case of SPG11 with retinopathy.
Conclusion: The clinical characterization of rare forms of HSP in the present case series and the possible association with genes whose classic phenotypes do not include spasticity and paraparesis may help to clarify the broad clinical and molecular spectrum of HSP.
Disclosure: This is an original article. We do not have conflict of interests.

EPO-361

A new heterozygous variant in the STUB1 gene linked to Spinocerebellar Ataxia type 48

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Background and aims: Spinocerebellar ataxias (SCA) are a group of clinically and genetically heterogeneous disorders, characterized by a predominant cerebellar syndrome, that can afflict other neurological systems. The number of known genes associated with disorders is constantly expanding with the use of Next Generation Sequencing (NGS). Originally associated with autosomal recessive SCA16 (SCAR16), homozygous variants in the STUB1 gene have recently been linked to autosomal dominant SCA48 (SCA48) in some patients.
Methods: A 45-year-old male was referred due to cognitive changes that began at the age of 31 years (difficulty in sustaining attention and planning tasks). In the past 6 years he additionally presented difficulties in verbal articulation and fine motor coordination, and progressive gait imbalance. His maternal grandparents were consanguineous, and his mother began experiencing progressive gait and cognitive dysfunction when she was 50. Neurological examination highlighted a multiple-domain cognitive impairment, hypermetric saccades, appendicular dysmetria, low-amplitude intention tremor, dystonic posture of the left hand, 4-limb hyperreflexia and wide-based gait.
Results: Blood analysis excluded reversible causes of ataxia and brain MRI-scan showed olivopontocerebellar atrophy. NGS panel showed a new heterozygous variant (c857T>C) in the STUB1 gene (classified as deleterious by the bioinformatic analysis). Segregation study of the variant in the family identified his mother with the same variant.
Conclusion: We present a clinical case of ataxia caused by SCA48, demonstrating the genotypic and phenotypic expansion seen in these patients. The recently reported SCA48 cases show cerebellar and extrapyramidal involvement, as well as cognitive dysfunction, which are also features seen in SCAR16.
Disclosure: The authors have no potential conflict of interest to disclose.

EPO-362

Genotype-phenotype correlation in Italian patients affected by Tuberous Sclerosis

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Background and aims: Tuberous Sclerosis complex (TSC; MIM #191100, MIM #613254) is a rare genetic multisystem disorder characterized by the presence of widespread hamartomatous lesions in multiple systems. TSC is caused by mutations in either TSC1 or TSC2 genes leading to dysfunction of hamartin or tuberin, respectively. In this study, we aimed to investigate the molecular spectrum of TSC genes and evaluate the genotype-phenotype correlation in an Italian study cohort.
Methods: Our series includes 41 familial/sporadic TSC patients, enrolled at Division of Neurology, Neurofibromatosis and Rare Diseases Center of AOU Luigi Vanvitelli and at Division of Pediatric Neurology of Santobono-Pausilipon Children's Hospital. All TSC patients were clinically evaluated according to NIH diagnostic criteria and a combination of targeted next-generation sequencing and multiplex ligation-dependent probe amplification (MLPA) was performed for molecular analysis.

Results: In our study the mutation detection rate was 93%, TSC2 or TSC1 variants were reported respectively in 25 and 13 TSC patients. We identified 25 different pathogenic or likely pathogenic variants and 18% of identified mutation were novel. TSC1 mutations were associated with a less severe phenotype than TSC2. No retinal manifestations were detected in TSC1 patients.
Conclusion: This study offered an important contribution to identify further novel genotype–phenotype correlation in TSC pathogenesis that may improve the management of TSC patients.
Disclosure: The authors declare that the research was conduct in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

EPO-363

Biallelic variants in ARHGAP19 cause mixed demyelinating and axonal polyneuropathy

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Background and aims: Rho GTPases are members of the large superfamily of small GTPase proteins considered as molecular switches in various cellular events. One of the major regulators of Rho GTPases are Rho GTPase-activating proteins (GAPs), which stimulate intrinsic GTPase activity and are important in actin organisation, cellular migration, cycle control and adhesion. We identified 16 individuals from 14 families with biallelic variants in Rho GTPase-activating protein 19 (ARHGAP19) presenting with young age of onset progressive weakness in lower limbs. Nerve conduction studies reveal mixed demyelinating and axonal polyneuropathy.
Methods: We are using in-vitro GAP assays to assess GAP activity in ARHGAP19 mutant proteins, complemented by an in-vivo Drosophila model to test for movement, lifespan and neuromuscular junction integrity.
Results: Ongoing in-vitro GAP assays show that ARHGAP19 has GAP activity towards RhoA but not Rac1 or Cdc42. Three of the mutations found in patients are being tested for their GAP activity and preliminary data suggest a loss of the GAP activity in a frame shift mutation. Visualisation of the endogenous expression pattern of ARHGAP19 ortholog in fly, RhoGAP54D, suggest the protein is expressed in perineural or subperineural glia in the fly brain. Preliminary results indicate that RNAi knockdown of RhoGAP54D in flies reduces both overall movement and startle responses to light-dark transitions.
Conclusion: This is a first association of ARHGAP19 with neurological disease and deep phenotyping analysis in conjunction with the in-vivo animal model and the in-vitro GAP assay will help highlight he importance of the gene in early human brain development and function.
Disclosure: Nothing to disclose.

EPO-364

Clinical and molecular study of familial Infantile Encephalopathy

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Background and aims: IInfantile Encephalopathy (IE) is a group of neuro-developmental disorders. The genetic and clinical heterogeneity of this condition constitutes a major diagnostic and consequently therapeutic challenge. In recent years, next generation sequencing (NGS) technologies enabled the discovery of numerous genes involved in IE. However, the interpretation of a large amount of NGS data is particularly laborious. The aim of this study was to describe the clinical features and the bioiformatics workflow implemented to investigate Tunisian children with familial IE.
Methods: We conducted a retrospective study of a group of 10 unrelated Tunisian families with familial IE over two years (from January 2019 to December 2020). The probands were investigated by whole exome sequencing (WES).
Results: Bioinformatics analysis of 480 prioritized genes were conducted in the 10 VCF files generated. Twenty different variants of interest were identified in 16 distinct genes. They included five likely pathogenic variants, ten variants of uncertain significance, four likely benign variants, and one benign variant. We extended our analysis to other genes associated with IE. We detected five additional variants in six different genes. The mutated genes were implicated in various molecular pathways involving ion channels and protein needed for regulatory and developmental functions. Our study expands the phenotypic and genetic landscape of IE in Tunisia and emphasizes the complexity of genotype-phenotype correlations.
Conclusion: The results of our current study could allow more accurate management of this pathology and may guide the development of a molecular diagnostic strategy for IE in Tunisia
Disclosure: The authors declare no conflict of interest.

EPO-365

An Italian family affected by SCA 45, a rare autosomal dominant cerebellar ataxia

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Background and aims: SCA 45 is a rare autosomal dominant cerebellar ataxia caused by mutations in FAT2. To date three families and two sporadic cases have been described.
Methods: A 41 year-old man presented to our clinic with a history of slowly progressive gait imbalance since the age of 26. His sister, mother, and grandfather had developed gait imbalance between age 30 and 55. He also reported to have intermittent diplopia. On examination the patient had an ataxic gait, dysarthria, impaired smooth pursuit, gaze evoked nystagmus, action and postural tremor of the hands with no bradykinesia or dystonia. SARA score was 12. Eye examination and EMG were normal. Brain MRI revealed cerebellar atrophy. After SCA 1, 2, 3, 6, 7, 8, 12, 17 were ruled out, he underwent an NGS panel and resulted heterozygous for the variant FAT2 c.12798_12799delCT (p.C4267fs*3) which was confirmed by Sanger sequencing and segregated within the family.
Results: FAT2 encodes for a transmembrane adhesion molecule expressed in the cerebellar granule cells and implicated in cerebellar development. So far, all cases reported presented with a slowly progressive late-onset ataxia. Our patient presented with an early onset cerebellar ataxia with postural tremor whereas the other members of the family affected had gait imbalance later in life. The novel variant found is predicted to cause a frameshift and to result in a truncated protein.
Conclusion: Our case suggests that SCA 45 should be considered as a possible cause of autosomal dominant cerebellar ataxia in younger patients as well.
Disclosure: Nothing to disclose.

EPO-366

Hanac syndrome as a cause of cerebrovascular disease in young patient: about a case

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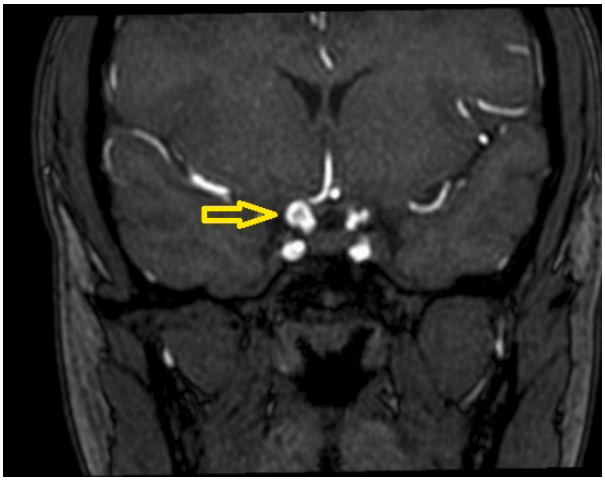
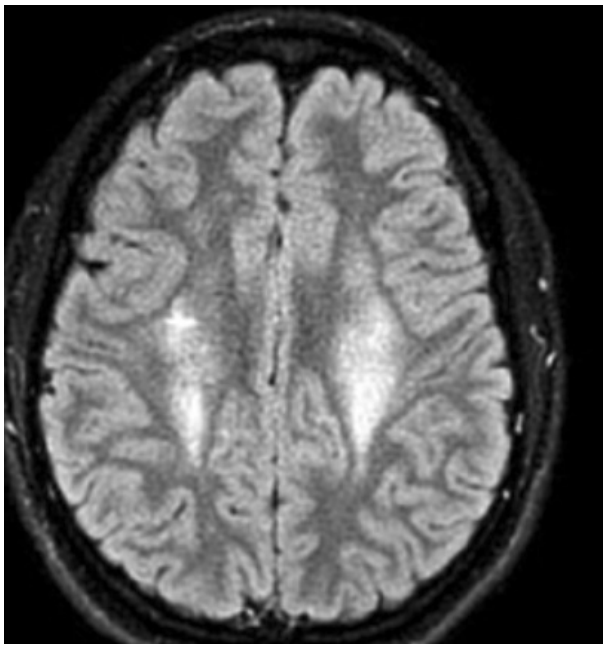
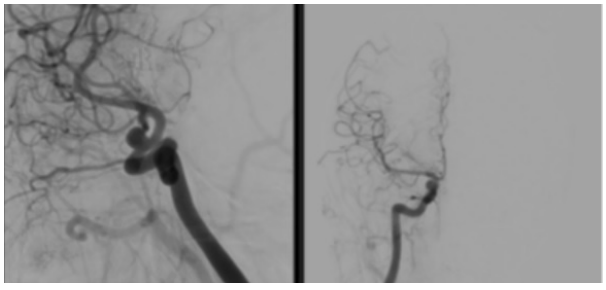
Background and aims: Heterozygous mutations in the COL4A1 gene, which encodes the alpha-1 subunit of type IV collagen, is an extremely rare cause of cerebrovascular disease in young patients. Among its phenotypic spectrum is the HANAC syndrome (hereditary angiopathy-nephropathy-aneurysms-muscle cramps syndrome), a multisystem condition that manifests as small and large vessel cerebrovascular disease, accompanied by ocular and nephrological abnormalities, and myalgias.
Methods: Description of a clinical case.
Results: We present the clinical case of a 23-year-old patient. She is admitted to Neurology due to refractory intense holocranial headache. A cerebral AngioMR was performed, showing a 5mm aneurysm in the ophthalmic region of the right ICA (Figure 1), and severe leukopathy (Figure 2). Diagnostic arteriography is performed (Figure 3). On examination, the presence of bilateral microcornea and a history of cataract intervention stand out. There is no family history. The genetic study showed the mutation c.2317G>A p.(Gly773Arg) in heterozygosity in the COL4A1 gene. The patient is diagnosed with HANAC syndrome.



Saccular aneurysm dependent on the ophthalmic region of the right ICA (yellow arrow). Coronal plane 3D TOF MR sequence.



Axial plane MRI FLAIR sequence. Severe leukopathy is seen in both corona radiata.



Diagnostic arteriography of right carotid aneurysm. Oblique (left) and AP (right) projection.

Conclusion: Genetic diseases individually represent a rare etiology of cerebrovascular disease. However, taken together, they represent a significant percentage of the causes of stroke in young patients. Among them we find the HANAC syndrome, which is produced by heterozygous mutations in the COL4A1 gene.
Disclosure: Nothing to disclose.

EPO-367

Exploring of shared genetic architecture between Alzheimer's disease and multiple sclerosis

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Background and aims: Neuroinflammation is involved in early and late disease phases of Alzheimer's disease (AD). Recent GWAS data revealed several immune-linked genetic variants and molecular pathways linked to proinflammatory interleukins and cytokines in AD pathology. Multiple Sclerosis (MS) is a chronic central nervous system immune-mediated disease with both genetic and environmental risk factors. Here we investigated shared genetic susceptibility between AD and MS, to identify pathological mechanisms between neurodegeneration and the immune system.
Methods: We analysed GWAS for late-onset AD (Wightman et al., 2021, n cases=64549, n controls=634442) and MS (n cases=14802, n controls=26703, IMSGC, 2019). We used statistical genetics methods as gaussian causal mixture modelling (MiXeR) for characterisation of genetic architecture and overlap between the two disorders. The conditional/conjunctional false discovery rate framework (cFDR) was used to identify specific shared genetic loci. Functional annotation was performed with FUMA and Open Targets.
Results: We showed comparable polygenicities for AD and MS and genetic overlap with 20 % of shared trait-influencing variants despite negligible genetic correlation (rg=0.03). Around 1.8 thousand were identified by MiXeR as associated variants. cFDR analysis identified 16 shared genetic loci. Annotated genes were enriched in molecular signalling pathways linked to inflammation and neuron structure.
Conclusion: The current results provide evidence for a polygenic overlap between AD and MS, beyond genetic correlation. The shared loci between AD and MS suggest the important role of the immune system and neurodegeneration in the pathophysiology of disorders, and highlight new opportunities for future studies.
Disclosure: No special disclosures. This work was supported by an RCN grant 324252.

EPO-368

RNA studies in neurogenetical disorders: a new diagnostic tool beyond Next Generation Sequencing.

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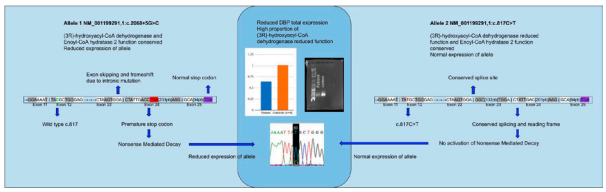
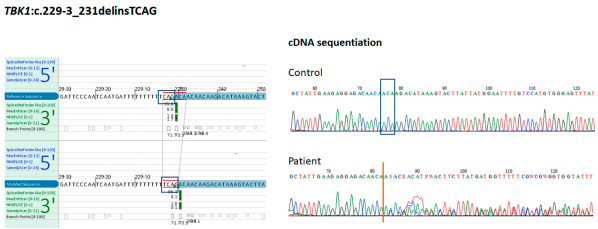
Background and aims: Next Generation Sequencing (NGS) has expanded the diagnostic field of neurogenetical disorders. However, inconclusive results require further studies to confirm pathogenicity of the variants found.

Here, we show two examples where blood-derived RNA was employed to confirm diagnosis.
Methods: Written informed consent was obtain for genetical studies. The effect on splicing was studied through SpliceAI software. Blood RNA was purified and complementary DNA (cDNA) was obtained through reverse transcription. Final time PCR was run and Biodonostia Genomics Platform performed Sanger sequentiation of PCR products. Quantitative PCR (qPCR) were performed in order to measure expression levels.
Results: Patient 1 is a 41 years-old male with sensorineural deafness, intellectual disability, sensorimotor neuropathy and cerebellar ataxia. Whole exome sequencing showed two variants in HSD17B4 gene related to Perrault syndrome: c.817C>T, (pathogenic) and c.2068+5G>C (considered of unknown significance). As the mutation was in the exon-intron boundary, impaired splicing was hypothesized. SpliceAI predicted exon skipping; consequently, a premature stop codon would arise and Non-Sense Mediated Decay would degrade RNA. qPCR and Sanger sequencing confirmed reduced RNA expression of the splice-site mutation allele (Fig.1). Patient2 is a 66 years-old male with frontotemporal dementia. NGS panel showed a mutation in TBK1 (c.229-3_231delinsTCAG) predicted to impaired splicing. Careful revision showed the mutation probably produces a codon loss and, consequently, the absence of Thr79, previously considered pathogenic. Sanger sequencing of blood cDNA confirmed this hypothesis (Fig.2)



Schematic view of the mutations in HSD17B4 found in patient 1. Experiments showed reduced expression of the allele carrying the splicing-site mutation.



Schematic view of the mutation found in TBK1. Although predicted to affect splicing, careful revision show the effect of ACA deletion, resulting in absence of Thr79 which has been previously described as pathogenic.

Conclusion: RNA studies are cost-effective, relatively easy and very useful in selected patients and they should be included in hospital's genetic departments.
Disclosure: No conflicts of interest.

EPO-369

The Role of Bdnf Pathway in Energy Homeostasis deficit in Smith-Magenis syndrome mice

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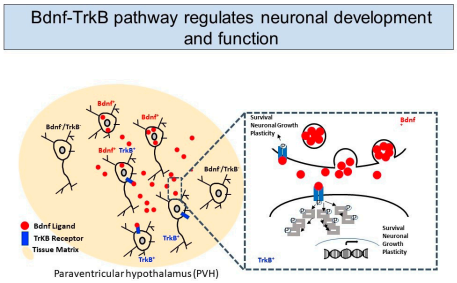
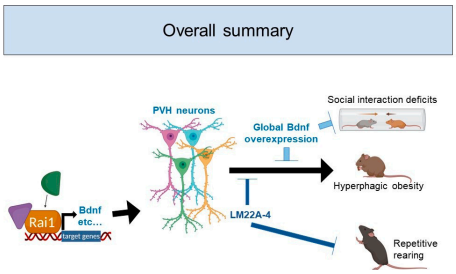
Background and aims: Severe hyperphagia, metabolic defect, and obesity are debilitating features of Smith-Magenis syndrome (SMS), a monogenetic disorder caused by haploinsufficiency of retinoic acid induced 1 (RAI1). Rai1 regulates the transcription of neurodevelopmental genes including brain-derived neurotropic factor (Bdnf). Bdnf is downregulated in the hypothalamus of SMS mice. We further analyzed the contribution of Bdnf signalling in SMS pathology and therapeutically targeting Bdnf pathway.



Schematic for the Bdnf-TrkB Pathways

Methods: We first performed reverse phase protein analyses (RPPA) using a cocktail of antibodies that probe downstream of Bdnf-TrkB pathway. Next, we generated Rai1 conditional knock out (cKO) model (Rai1-deletion in Bdnf producing neurons) to decipher the function of Rai1 in a discrete set of Bdnf-producing cells, which regulates energy homeostasis in the hypothalamus. We explored the therapeutic potential of targeting Bdnf downstream signalling by using a pharmacological agent, LM22A-4 (a TrkB partial agonist).
Results: We found multiple Bdnf downstream targets to be downregulated in SMS mice. Loss of Rai1 from Bdnf-producing cells contributes to obesity in SMS by selectively altering fat deposition. 3-weeks old cKO mice also showed reduced neuronal excitability in the PVH. Our drug treatment data demonstrate that LM22A-4 treatment significantly reduces the body weight in SMS mice and delays the onset of obesity. Moreover, this reduction in body weight is followed by improved blood leptin and lipoprotein levels in the treatment group.
Conclusion: Our work shows the pathological contribution of Bdnf pathways in SMS and demonstrate that targeting Bdnf signaling has a potential to ameliorate obesity associated with SMS.



Summary of results

Disclosure: We declare no confilict of interest.

EPO-370

Neuropsychiatric symptoms in Friedreich's ataxia assessed by the Mild Behavioral Impairment Checklist (MBI-C)

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Background and aims: Neuropsychiatric symptoms (NPS) are common in hereditary ataxias. In Friedreich's ataxia (FRDA), depressive symptoms were previously reported, but little is known about other NPS. The MBI-C is a questionnaire assessing NPS in early stages of neurodegenerative diseases. Using the MBI-C, we aimed to assess the presence and severity of NPS in FRDA and examine their relationship with disease severity.

Methods: 27 FRDA patients and 37 healthy controls (HC) were recruited at the Centre of Hereditary Ataxias. Close informants of all participants filled in the MBI-C. Disease severity was assessed by the Scale for the Assessment and Rating of Ataxia (SARA), and the scale of the Activities of Daily Living (ADL).

Results: Mean MBI scores in FRDA and HC were 6.70 (SD=8.70) and 2.59 (SD=3.20) respectively. 25.9% of FRDA patients had at least one MBI symptom compared to 18.9% HC. Prevalence of specific NPS in FRDA was 25.9% (vs. 18.9% HC) for decreased motivation, 55.6% (vs. 32.4%) for emotional dysregulation, 48.1% (vs. 37.8%) for impulse dyscontrol, 18.5% (vs. 8.1%) for social inappropriateness and 11.1% (vs. 13.5%) for psychotic symptoms. Patients had significantly higher score only in the emotional dysregulation domain (p=0.026). ADL correlated with motivation (r=0.39, p=0.044) and emotional dysregulation (r=0.39, p=0.048). SARA did not correlate with any MBI-C score.

Conclusion: NPS are common in FRDA, particularly in the affective domain, are linked to impairment of ADL but not ataxia severity. NPS should be addressed in clinical care due to their potential impact on quality of life and the possibility for therapeutic intervention.

Disclosure: Supported by Charles University Grant Agency (GAUK) projects No. 224522 and 309121 and project National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107). The authors are members of the European Reference Network for Rare Neurological Diseases (ERN-RND).

EPO-371

Broadening the clinical spectrum of brain-lung-thyroid syndrome. The first patient treated with bipulmonary transplant

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Background and aims: Benign hereditary chorea is part of the "brain-lung-thyroid syndrome", which is caused by mutations in the NKX2.1 gene (also known as TTF1). This gene plays an important role in the embryological development of the brain (ventral telencephalon and hypophysis), lungs and thyroid gland. Pathogenic variants in NKX2.1 have been associated with chorea, hypothyroidism, and lung or thyroid carcinomas.

Methods: We describe the case of the first patient treated with bipulmonary transplantation for lung interstitial fibrosis in the context of a "brain-lung-thyroid syndrome" associated with NKX2.1 and review the clinical spectrum of the disease reported in the literature.

Results: We report the case of a 42-year-old woman who presented delayed motor development and previously undiagnosed choreoathetosic movements since early childhood. Subclinic hypothyroidism was found when she was 30. At 38 years of age, she developed an interstitial lung disease which progressively worsened until requiring lung transplantation. In the lung explant, mucinous adenocarcinoma was discovered in both lungs, with differences in the genetic biomarkers; no lymph nodes were affected. Given the atypical presentation and the combination of clinical signs, the diagnosis was reconsidered. Exome sequencing identified a pathogenic variant in NKX2.1 gene (frameshift mutation). Four more cases of lung cancer in relation to NKX2.1 mutations have been reported, none of them were considered elective to surgery.

Figure 1.- Timeline of the disease development and clinical manifestations. ILD= Interstitial lung disease

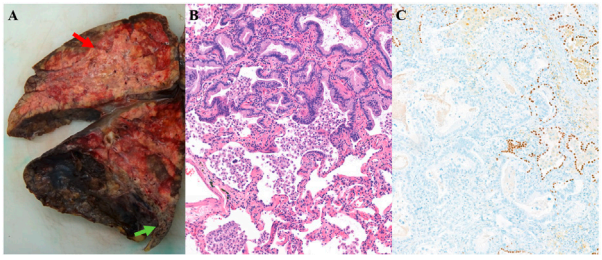

Figure 2.- A. Macroscopic sample of the lung explant. Whitish areas correspond to the lung adenocarcinoma (red arrow) and fibrous tissue in the lung base (green arrow). B,C. Microscopic view of the mucinous adenocarcinoma (upper half). and TTF1 staining.

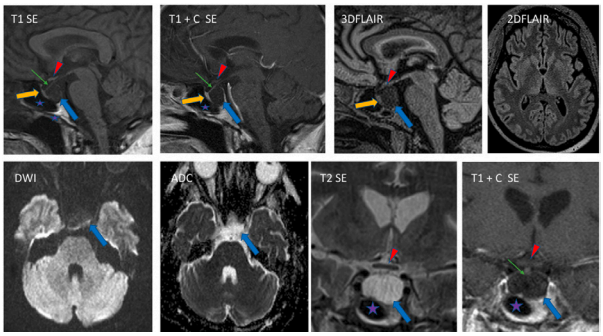

Figure 3.- Intrasellar cystic structure (blue arrow) that causes anterior displacement of the adenohypophysis (orange arrow) and bilateral hyperintensity of the thalamus in FLAIR. Pituitary stalk (green arrow). Optic chiasm (Red arrow).

Conclusion: The brain-lung-thyroid syndrome has a broad clinical spectrum. This case-report expands the clinical spectrum and presentations leading to suspect this rare disease. To our knowledge, this is the first patient treated with lung transplantation.
Disclosure: No conflicts of interest to disclose.

EPO-372

Hereditary ataxias: diagnostic yield with Next-Generation Sequencing

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Background and aims: Hereditary ataxias (HAs) are a group of progressive monogenic rare neurodegenerative disorders characterized by a wide spectrum of ataxia-dominated phenotypes. Despite the identification of many causative genes, up to 50% of HAs cases still remain without molecular diagnosis, mainly due to their vast clinical and genetic heterogeneity. Massive parallel next-generation sequencing (NGS) analysis broadened our knowledge of HAs genetic aetiology, consequently stimulating the trend towards genetically specific therapies. In this study we aimed to assess the diagnostic yield of NGS panel and exome analysis in the clinical practice of our setting.
Methods: A cohort of 100 patients with a clinical diagnosis of HA but no molecular confirmation was studied. NGS panel (26 genes) and/or clinical exome sequencing (CES) were performed in the case of inconclusive first-line genetic tests for spinocerebellar ataxias (SCA1-3, 6-8,12,17), DRPLA, Friedreich's ataxia (FRDA) or phenotype-guided specific single gene sequencing.
Results: By means traditional genetic tests a molecular diagnosis was achieved in 35% of patients. Of 65 patients with HAs of indeterminate genetic origin, 36 underwent new molecular evaluations: in 12 of 36 (33,3%) known pathogenic mutations or putative pathogenic variants were found, using NGS panel and CES. Furthermore, in 30,6% of patients (11/36) one or more variants of unknown significance were detected.
Conclusion: Overall, we present daily practice evidence that for one third of the patients with a clinical diagnosis of HA, but no molecular diagnosis on routine genetic testing, a definitive diagnosis can be reached with NGS approach.
Disclosure: The authors have no conflicts of interest to declare.

Cerebrovascular diseases 3

EPO-373

Analysis of clinical characteristics and functional outcome in patients with cervical artery dissection.

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Background and aims: Cervical artery dissections (CAD) are responsible for 20-25% of ischaemic strokes in young patients. Non-traumatic dissections are the most frequent and, although their cause is unknown, it is believed to be due to a weakness of the arterial wall.
Methods: We conducted a retrospective review of patients with CAD admitted in our hospital between 1-1-2011 and 31-12-2022. We recorded baseline clinical features, treatment, functional outcome, and mortality rate.
Results: We identified 32 cases of CAD (20 carotid/ 12 vertebral); mean age was 48.3 years and 67.7% were men. Four patients (13%) had a history of physical effort. The average baseline NIH Scale score was 3.87 (range, 0-19). Code stroke was activated in 15 patients. Six patients (18.75%) were treated with intravenous thrombolysis and 10 (31.25%) with acute endovascular treatment, 7 of them with stent placement. Five of these patients received both treatments; at 3 months, functional independence (modified Rankin Scale scores 0-2) was achieved by 90% of the patients. One patient died. The average mRS scores for each subgroup were the following: thrombolysis + endovascular treatment 2.2 points, only thrombolysis 1 point, and only endovascular treatment 2.4 points.
Conclusion: Cervical artery dissection is an uncommon cause of ischaemic stroke, which tends to occur in younger patients compared to other aetiologies. Reperfusion therapies appear to be safe in these patients, but more studies are needed to confirm this.
Disclosure: The authors declare no conflict of interest.

EPO-374

Carotid web as a possible cause of ipsilateral ischemic stroke of undetermined origin: experience in a tertiary hospital

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Background and aims: Carotid web (CW) has been observed in cases of embolic strokes of undetermined origin (ESUS). We hypothesize it might be the responsible of the formation of emboli, given no other plausible cause is found. Our objective was to determine the optimal management of these patients by analyzing baseline patient characteristics, acute-phase treatment, functional status at 90 days, secondary prevention, and stroke recurrences.
Methods: Retrospective single-center observational study of a prospectively recorded database from 2017 to 2022 of patients with acute ischemic stroke (AIS) and ipsilateral CW in a tertiary hospital. Patients with a diagnosis of AIS and confirmation of CW in digital subtraction angiography were included. Data regarding baseline characteristics, diagnostic study, presence of recurrence and secondary prevention were recorded.
Results: 12 patients were included, with a median age of 50 years. 1 had a previous stroke. 10 (83%) underwent mechanical thrombectomy (MT), 4 of them with combined intravenous thrombolysis. The diagnostic study revealed 1 patient with atrial fibrillation (AF), 2 with a patent foramen ovale (PFO), 1 with an antiphospholipid syndrome, and 8 with a negative study. Carotid stenting was placed in 7 patients, 1 received acenocumarol (coexistence of PFO and pulmonary thromboembolism) and 1 rivaroxaban (AF) and single antiplatelet therapy. No recurrences were observed.
Conclusion: In our series, CW was the only finding in 58% of patients, being the probable cause of stroke. Although there is no consensus on secondary prevention management, carotid stenting could be a safe and effective alternative.
Disclosure: The authors declare they have no conflict of interest.

EPO-375

Strokes mimics and chameleons on the prehospital level in Emergency Center of Bishkek, Kyrgyzstan

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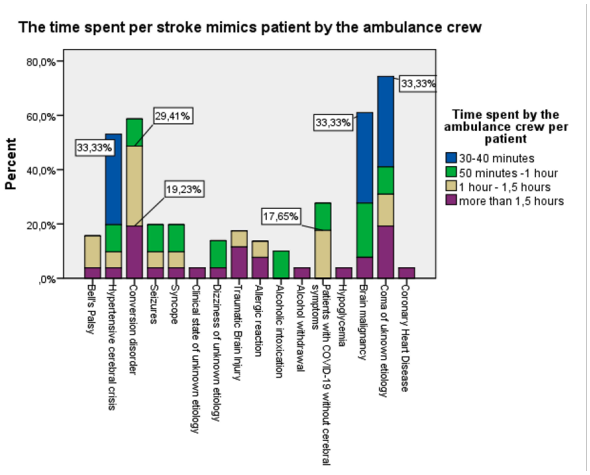
Background and aims: In Kyrgyzstan which is on the way of the thrombolytic therapy implementation and where there is the lack of trained emergency service personnel for stroke recognition and management, early and accurate diagnosis of stroke and differentiating it from stroke mimics is an important task for healthcare. We aimed to identify and describe stroke mimics patients among all the patients with the stroke code.
Methods: We analyzed 535 medical records of patients with a stroke code at the Emergency Medical Center of Bishkek, Kyrgyzstan. We described demographics, clinical and logistical parameters of stroke mimics patients. Comparisons of continuous variables between stroke and stroke mimics patients were made with Independent Samples Test and ANOVA.

Results: There were 10,1% patients with stroke mimics and they were significantly younger: median age was 57 (56;75) while for stroke patients median age was 65 (45;69), p=0,003. Stroke mimics were represented by conversion disorder (19,3%), coma of unknown etiology (15,79%), brain malignancy (8,7%) and others. Stroke mimics patients with seizures and syncopes tend to call to emergency services earlier (median time 0,9 and 1,4 hours) compared to patients with alcohol withdrawal and cardiological diseases (167 hours). Ambulance crew spent around 1-1,5 hours in 30% examining the patients with stroke mimics and in 18% in patients with COVID-19.
Conclusion: New implemented order for the obligatory NIHSS evaluation of the all patients with stroke code will improve diagnostics and may shorten time of the crew spent with stroke mimics patients.
Disclosure: Nothing to disclose.



EPO-376

Tendencies of public stroke knowledge in Vilnius

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Background and aims: Stroke remains the common cause of death and disability in the world. A visible decline in disabling outcomes can be attributed to the increasing frequency of reperfusion therapies. Stroke recognition and urgent admission of patients to specialized stroke centres after the onset of first stroke symptoms are essential for treatment outcomes. This study aims to evaluate public stroke awareness and its change since 2019.
Methods: An anonymous cross-sectional study, involving 802 Vilnius residents was conducted in 2019 and 2022. The closed-ended questionnaire was used. Statistical analysis was performed with SPSS software, with a significance level of $p<0.05$.
Results: Stroke as an acute cerebrovascular disorder was identified by 83.3% of the respondents in 2022 (less than a 1% increase since 2019). At least one correct warning sign of stroke was reported by 98.7% of respondents (96.4% in 2019). The most mentioned symptoms of stroke were one-sided face, arm or leg sensory disturbances, paralysis or weakness (90.0%) and speech disorder (83,3%) – 82.1% and 81.5% respectively in 2019. Only 58% (45.4% in 2019) of respondents reported visual impairment as a stroke symptom. Females have better knowledge of stroke than males ($p<0.05$).
Conclusion: Stroke awareness is improving since 2019 in Vilnius. Women have better knowledge of stroke compared to men. Visual impairment is the least known stroke symptom. Therefore, BE-FAST campaigns should be directed to the target audience through the most used informational means to provide reliable information and be more gender sensitive.
Disclosure: Nothing to disclose.

EPO-377

Opalsky syndrome secondary to medulla oblongata hemorrhage: case report and review of the literature

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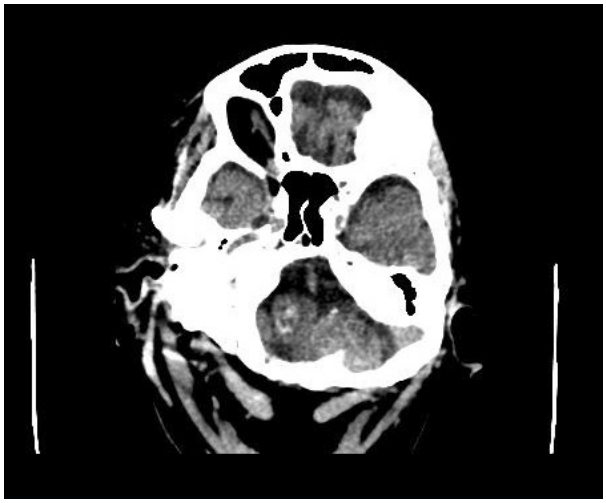
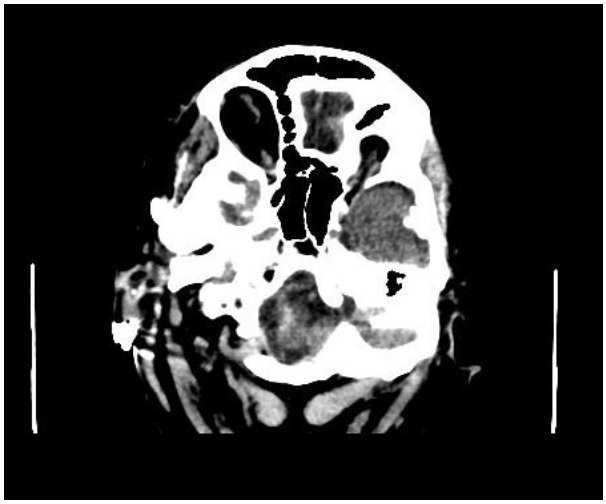
Background and aims: Opalsky syndrome (or sub-bulbar syndrome) was first described by A. Opalsky in 1946, as the presence of a lateral medullary syndrome (Wallemberg syndrome) and ipsilateral hemiplegia. It can be explained by the involvement of the ipsilateral corticospinal tract after the piramidal decussation, and it is considered as a variant of Wallemberg Syndrome.
Methods: We describe a case of Opalsky Syndrome secondary to medulla oblongata hemorrhage. We performed a literature review in PubMed of previous publications on Opalsky Syndrome and the different etiologies reported.
Results: A 80-year-old woman with moderate cognitive decline under heparin treatment due to deep vein trombosis 1 month before, presented with a 3-days history of right leg weakness followed by dysphagia, dysarthria and headache. Neurological examination revealed moderate dysarthria, downbeat nystagmus, right-sided Horner Syndrome (with partial ptosis and miosis), right facial palsy, right limbs 4/5 hemiparesis and left limbs hypoesthesia. Urgent CT showed bleeding in the right margin of medulla oblongata. Urgent blood analysis and EKG were normal. 48h hours later the patient died due to respiratory insuficiency. Literature describe over 62 Opalsky Syndrome with different etiologies: ischemic (53) due to atherotrombosis or vertebral artery dissection (6), vertebral artery giant-cell arteritis (1), cavernome bleeding (1), brainstem tumors (2), multiple sclerosis lessions (2), infective demyelinating event due to scrub typhus (1) or lateral compression by megadolicobasilar artery (1).



Axial CT: Bleeding in the right margin of medulla oblongata



Axial CT: Medulla oblongata hemorraghe

Conclusion: Infarcts are the most common etiology of Opalsky Syndrome. To our knowledge this is the second Opalsky Syndrome secondary to hemorraghe described in the literature.
Disclosure: The authors declare no conflicts of interest.

EPO-378

Telemedical acute stroke management improves performance and patient outcome: evaluation of the NEVAS stroke network

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Background and aims: Timely acute stroke management improves functional outcome considerably. In countryside hospitals without stroke specialization, telemedical consultation by comprehensive stroke centers is an effective concept to provide timely treatment decision making and improve clinical performance.
Methods: In this study, clinical data of stroke patients were collected for the years 2014-2020 from three regional hospitals of the Neurovascular Network of Southwest Bavaria with telemedical stroke support by our centre. Door-to-imaging and door-to-needle times as well as the modified ranking scale (mRS) at discharge were analyzed over the years to examine if performance and clinical outcome improve over time through participation in the network.
Results: The number of admitted stroke patients nearly doubled between 2014 and 2020 with a mean thrombolysis rate of 15%. The percentage of door-to-imaging time <30 and <60 min for all stroke patients declined over time, presumably due to the increasing patient number. However, for thrombolysis candidates, the percentage of door-to-imaging and door-to-needle times <30 and <60 min increased over time. Door-to-needle time was slightly lower comparing thrombolysis indication by the local neurologist vs. telemedicine while improving over time for both scenarios. The percentage of thrombolysed patients with mRS 0-2 at discharge increased significantly (79% in 2020 vs. 59% in 2014). There was no substantial difference in critical time intervals or mRS at discharge during the pandemic year 2020 compared to previous years.
Conclusion: Telemedicine networks can significantly improve stroke care in rural hospitals with limited experience through timely thrombolysis indication by telemedical neurovascular expertise and continuous on-site training of professionals.
Disclosure: No disclosure.

EPO-379

Basilar Artery Occlusion strokes in patients admitted to the Neurological Clinic of Pisa: a retrospective analysis

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Background and aims: Basilar artery occlusion (BAO) is a subtype of stroke burdened by high mortality and disability. The aim is to analyze a cohort of patients with BAO, admitted to the Neurological Clinic of Pisa between January 2001 and December 2021, in order to individuate anamnestic, clinical or neuroradiological features, as well medical treatment, related to the outcome at 90 days, defined by the modified Rankin Scale (mRS).
Methods: The endpoint was mortality or significant disability at 90 days. We performed a binary logistic regression with the significant variables ($p<0.05$) at the univariate analysis.

Results: We have analysed 74 patients (37 males) with BAO admitted to our Unit in the selected timeframe. The median age was 72 years. 50 patients (67.6%) had hypertension, 56 (75.7%) atherosclerosis, 6 (8.1%) previous strokes/TIA, 17 (23%) diabetes, 10 (13.5%) tabagism, 14 (18.9%) atrial fibrillation, 32 (43.2%) structural cardiopathies. During hospitalization, 24 (32.4%) developed dysphagia, 20.3% infections, 8.1% ICH, 29% required intubation, and 8.1% tracheostomy. NIHSS at discharge was 0-10 in 65 (87.8), >10 in 9 (12.2). 18 patients received medical therapy, 11 systemic fibrinolysis, and 45 endovascular treatment. The 90 days mortality occurred in 5 (6.7%), while functional dependance (mRS 3-5) in 22 (29.7%). Dysphagia ($p = 0.01$), atrial fibrillation ($p = 0.03$), atherosclerosis ($p=0.04$) and NIHSS score at discharge ($p < 0.01$), were related to the endpoint.
Conclusion: The importance of primary prevenction (especially AF and atherosclerosis) and the management of complications during hospitalization, are crucial to avoid mortality and disability.
Disclosure: Nothing to disclose.

EPO-380

Total antioxidant status(TAS) in the serum of patients with acute ischemic stroke(AIS) -Is constant attention warranted?

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Background and aims: The impact of oxidative stress on neuronal injury in ischemic stroke has been a focus of stroke research. The aim of this study was to estimate TAS in the serum of patients with AIS within 2-5 days after symptom onset in northeastern Poland.
Methods: 175 patients with AIS, including 85 who received thrombolysis/thrombectomy, and 88 healthy controls were studied. TAS in the serum was measured spectrophotometrically using Randox kits and clinical details were collected from medical records.
Results: 57.2% of patients with AIS had TAS values outside the reference range (1.3-1.77mmol/L). TAS correlated with BMI index, hemoglobin values,and Cd/Pb molar ratios. TAS levels were higher in LVD than in CE/SVD ($p=0.043$) according to the TOAST classification. No significant differences in TAS concentrations were found between AIS patients and healthy controls ($p=0.41$). In patients with AIS, no statistically significant variations were observed with atrial fibrillation, smoking status, T2DM, or administered treatment (intervention vs.conservative). A linear model indicated that conservative treatment had a significantly higher TAS (0.79). A generalized linear regression model showed that higher BMI index, male gender, and LVD etiology were significant predictors of elevated TAS. No association of TAS was found with demographics, NIHSS(lowest values:21-42)/MRS scales,stage of atherosclerosis, brain lesion size,CRP,homocysteine,uric acid,fibrinogen,or lipid profile.
Conclusion: Patients in the initial phase of ischemic stroke show no change in blood TAS concentrations compared to controls, suggesting that at onset, they have an effective antioxidant defense which is depleted over time. The investigation has revealed the potential of using antioxidants for stroke-related oxidative stress.
Disclosure: Nothing to disclose.

EPO-381

Acute Cerebrovascular Accident during the pandemic of a new coronavirus infection in the Ural Federal District

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Background and aims: Acute cerebrovascular accidents (ACVA) are the main causes of death and disability in the population. The study of identifying signs of morbidity with acute cerebral circulation in the context of a pandemic of a new coronavirus infection COVID-19 is an urgent task. Purpose - to conduct a comparative analysis of the primary incidence of ACVA, including transient ischemic attacks (TIA), in the adult population of Russia, the Urals Federal District (UFD) and the constituent entities of the Russia during the pandemic of a new coronavirus infection.
Methods: The primary incidence of transient cerebral ischemic attacks, intracerebral and other intracranial hemorrhages, cerebral infarctions and strokes, not specified as hemorrhage or infarction, was studied. A comparative analysis of the primary incidence of ACVA in the adult population in the UFD and in individual subjects of the district during the 2020 pandemic was carried out relative to the average long-term indicators for 2015-2019.
Results: During the COVID-19 pandemic, the levels of primary incidence of certain ACVA in the whole Russia and the UFD decreased in relation to the average long-term indicators of 2015-2019 in all classes (table).
Conclusion: In real clinical practice, in a pandemic, healthcare resources are more directed towards combating COVID-19, which may affect the statistical indicators of the incidence of stroke. The data obtained require further confirmation by continuous dynamic monitoring of the epidemiology of stroke.

Table. The incidence of selectivity of cerebrovascular accidents in the Russian Federation, Ural Federal District, and also, in consideration of the Ural Federal District (per 100,000 adults)

	Average annual level	2020 year	2020 growth to standard deviation (percentage)
All acute cerebrovascular accidents			
Russian Federation	399,9±7,4, Kv1,9	371,1	-7,2
Ural federal district	421,2±15,0, Kv3,6	378,1	-10,2
Kurgan district	483,9±46,8, Kv9,7	414,2	-14,4
Sverdlovsk district	541,0±35,1, Kv6,5	480,3	-11,2
Tyumen region without autonomous okrug	399,3±24,9, Kv6,2	391,9	-1,9
Khanty-Mansi Autonomous Okrug – Yugra	239,9±8,6, Kv3,6	220,6	-8,0
Yamalo-Nenets Autonomous Okrug	198,2±53,4, Kv27,0	201,4	1,6
Chelyabinsk district	379,1±12,8, Kv3,4	335,2	-11,6
Stroke, unspecified as hemorrhage or infarction			
Russian Federation	29,4±6,1, Kv20,7	20,2	-31,3
Ural federal district	10,8±1,7, Kv15,7	10,5	-2,8
Kugran district	22,3±17,6, Kv78,7	5,1	-77,1
Sverdlovsk district	13,7±1,7,Kv12,2	15,5	13,1
Tyumen region without autonomous okrug	2,1± 3,4, Kv159,8	0,9	-57,1
Khanty-Mansi Autonomous Okrug – Yugra	6,9±2,1, Kv30,9	8,3	20,3
Yamalo-Nenets Autonomous Okrug	11,9±1,4, Kv11,5	6,5	-45,4
Chelyabinsk district	9,7±1,9, Kv19,3	11,4	17,5
Transient cerebral ischemic attacks [attacks] and related syndromes			
Russian Federation	49,3±1,5, Kv3,1	36,3	-26,4
Ural federal district	55,1±2,2, Kv4,5	39,3	-28,7
Kugran district	65,2±7,3, Kv11,2	53,6	-17,8
Sverdlovsk district	69,3±8,6, Kv12,4	50,8	-26,7
Tyumen region without autonomous okrug	48,5±5,4, Kv11,2	26,7	-44,9
Khanty-Mansi Autonomous Okrug – Yugra	39,5±3,4, Kv8,7	32,4	-18,0
Yamalo-Nenets Autonomous Okrug	31,5±12,7, Kv40,2	30,7	-2,5
Chelyabinsk district	47,9±4,8, Kv10,0	31,6	34,0
Intracerebral and other intracranial hemorrhage			
Russian Federation	42,8±1,0, Kv2,3	39,0	-8,9
Ural federal district	44,8±1,8, Kv4,0	41,0	-8,5
Kugran district	58,0±5,0, Kv8,6	61,3	5,7
Sverdlovsk district	52,3±3,4, Kv6,5	47,7	-8,8
Tyumen region without autonomous okrug	52,8±2,4, Kv4,5	52,4	-0,8
Khanty-Mansi Autonomous Okrug – Yugra	31,1±7,2, Kv23,0	23,8	-23,5
Yamalo-Nenets Autonomous Okrug	30,3±8,8, Kv29,1	32,2	6,3
Chelyabinsk district	37,1±1,9, Kv5,1	32,2	-13,2
Cerebral infarction			
Russian Federation	278,4±14,4, Kv5,2	275,6	-1,0
Ural federal district	310,5±14,6, Kv4,7	287,3	-7,5
Kugran district	338,4±36,2, Kv10,7	294,2	-13,1
Sverdlovsk district	405,7±29,2, Kv7,2	366,3	-9,7
Tyumen region without autonomous okrug	295,9±29,7, Kv10,0	311,9	5,4
Khanty-Mansi Autonomous Okrug – Yugra	162,4±6,2, Kv3,8	156,1	-3,9
Yamalo-Nenets Autonomous Okrug	124,5±35,9, Kv28,8	132,0	6,0
Chelyabinsk district	284,4±15,2, Kv5,3	260,0	-8,6

Disclosure: Nothing to disclose.

EPO-382

Moyamoya angiopathy in a Norwegian patient cohort: Characteristics and outcome

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Background and aims: Moyamoya angiopathy (MMA) is a rare intracerebral steno-occlusive, progressive vasculopathy. Increasing awareness of MMA in European populations has impacted on the incidence recently. This is the first description of a Norwegian MMA cohort.
Methods: A retrospective analysis of consecutive patients with MMA, treated with revascularization surgery or followed conservatively at Oslo University Hospital, between January 2010 to October 2021, was performed.
Results: We identified 63 MMA patients, 56 (89%) had moyamoya disease (MMD) and 7 (11%) moyamoya syndrome. 47 (75%) were females. Mean age for symptom onset was 36 (SD 15.6) years. The majority, 41 (65%), were of Caucasian ethnicity, followed by Asian 15 (24%), African 6 (9.5%) and Hispanic 1 (1.5%). Verified familial MMD occurred in 1 (1.5%) of patients. An acute clinical presentation occurred in 24 (38%) of patients, on imaging ischemic lesions were noted in 22 (35%) and hemorrhagic in 9 (14%). Cerebral vasculitis was initially misdiagnosed in 6 (9.5%) of patients. Revascularization treatment was performed in 30 (48%) patients. Mean years of follow-up was 8 (SD 6.9). At baseline, 29 (46%) were employed, vs. 18 (29%) at last follow-up (p <0.001). Initially, 55 (87%) had modified Ranking Scale ≤2 vs. 47 (75%) at last follow-up (p<0.001). Mortality for the cohort was 5 (7.9%) during a total of 498 years of follow-up.
Conclusion: MMA patients in our cohort had a decline in work capacity and functional independency over time. Our results underscore the importance of long-term follow-up and support of MMA patients.
Disclosure: Nothing to disclose.

EPO-383

Delayed neurological improvement in acute ischemic stroke patients treated with intravenous rtPA

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Background and aims: The aim was to investigate the phenomenon of neurological improvement delayed beyond the first 24 hours from admission in acute ischaemic stroke patients with special emphasis on intravenous thrombolysis.
Methods: This retrospective registry-based analysis included patients admitted with first-ever non-minor (NIHSS at least 4) ischaemic stroke within 24 hours from onset to a single tertiary stroke centre from January 2009 to December 2015. Patients treated with mechanical thrombectomy were excluded. Significant neurological improvement was defined as an 8-point reduction in the NIHSS score or reaching a score of 0 or 1. We compared neurological improvement at 24 h and day 7 in patients treated and not-treated with intravenous rtPA.
Results: Of N=463 included patients, n=316 (68%) received rtPA and n=147 (32%) not. There were no differences in median age, gender and baseline NIHSS (10 vs 9). Patients from the rtPA group had lower NIHSS at 24 h (5 vs 8, p=0.005) and day 7 (3 vs 5, p=0.024). Significant neurological improvement from baseline to 24 h was more frequent in the rtPA group (28% vs 10% p<0.001). However, the proportion of patients with significant improvement at day 7 not achieving improvement within the first 24 hours, was similar (22% vs 19%, p=0.493).
Conclusion: Delayed significant neurological improvement that takes effect beyond the first 24 hours from admission occurs in about 20% of acute ischaemic stroke patients with non-minor symptoms. Intravenous rtPA seems not to have an effect on this phenomenon.
Disclosure: We have no financial interests relevant to the submitted publication.

EPO-384

Causal evidence of anterior cingulate cortex function: an experimental study in patients with stroke in the frontal lobe

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Background and aims: The anterior cingulate cortex (ACC) is responsible for task regulation. ACC dysfunction has been linked to a wide spectrum of neuropsychiatric disorders, such as apathy, depression and Parkinson's disease. The Reward Positivity (RewP), an event-related brain potential (ERP), reflects the impact of midbrain dopamine signals on ACC and is a potential biomarker for depression. The RewP is thought to be generated in the ACC. The aim of this study is to (1) investigate the impact of ACC damage on task regulation and (2) localize the source of the RewP.
Methods: Patients with frontal lobe stroke are recruited at Ghent University Hospital, Belgium (recruitment started April 2021). Participants perform the coffee-tea task (CTT), a hierarchical sequence task, and the virtual T-maze task (vTMT) while scalp EEG is recorded. We compare data outcomes between ACC lesions and lesions in other parts of the frontal lobe using voxel-based lesion symptom mapping (VLSM). Beck Depression Inventory (BDI) is used to assess the prevalence of depression in this population.
Results: We have currently recruited 50 patients: mean age 61,4 (±13,3), 23 female. 24 participants (48,9%) successfully completed the CTT. Six patients (12%) had a BDI score greater than 20 and suffered from clinical depression. Average RewP was smaller for the group with rostral ACC lesions. VLSM-maps will be presented at the conference.
Conclusion: Preliminary analysis did not show a contribution of ACC lesions to worse performance of the CTT or higher BDI score. Preliminary ERP-analysis suggested rostral ACC as potential source of the RewP.
Disclosure: Nothing to disclose.

EPO-385

The prediction model for all cause of mortality after stroke

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Background and aims: Stroke is the second leading cause of mortality. Although it is important to stratify high-risk patients after acute ischemic stroke, few studies reported the risk stratification system for ischemic stroke. We aimed to develop a prediction model specific for ischemic stroke using machine learning (ML).
Methods: 3,413 patients were admitted within 7 days after ischemic stroke from 2014 to 2019. We developed a total of seven ML based prediction model composed of patient's demographics, laboratory results, clinical and imaging characteristics of stroke. We also developed a compact model by utilizing the top 10 key factors of the best-performing model.
Results: All cause of mortality was developed in 136 (3.98%) patients in the entire cohort. The CatBoost based prediction model showed the best discriminatory power for high-risk patients, and outperformed the other ML algorithms (Table). The compact model was not inferior to the best performing model using all features.

Table. Summary of Performance according to various ML model

Models	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
Internal validation						
Support Vector Machine	0.645	0.4779	0.752	0.074	0.972	0.741
Decision Tree Classifier	0.760	0.698	0.696	0.087	0.982	0.696
Random Forest	0.829	0.770	0.751	0.117	0.987	0.752
AdaBoost	0.725	0.770	0.750	0.116	0.987	0.751
XGBoost	0.818	0.857	0.282	0.038	0.983	0.301
LightGBM	0.781	0.857	0.282	0.038	0.983	0.301
CatBoost	0.803	0.610	0.797	0.111	0.980	0.789
Compact model	0.802	0.610	0.797	0.111	0.980	0.790

Conclusion: We demonstrated that the ML-based predictive model to predict all cause of mortality after ischemic stroke.
Disclosure: Nothing to disclose.

EPO-386

Timing of (code) stroke in southern Spain

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Background and aims: Stroke onset is influenced by circadian rhythms. Spain, with more daylight hours, different daily schedules and customs such as "siesta", could have a different hourly distribution for stroke onset than other European countries. Objective: To describe the temporal distribution of code stroke in southern Spain.
Methods: Descriptive analysis of the local registry of code stroke between 2018 and 2022.
Results: 1,677 stroke code activations were recorded, 88.1% of them considered ischemic strokes at the time of admission (after discarding bleeding, space-occupying lesions and other diagnoses). A peak can be seen in the activation of code stroke between 11:00am and 1:59pm. Taking only wake-up strokes into account, this peak is maintained but another one appears at 8:00-8:59am. Excluding wake-up strokes, starting at 7:00am there is an increase in incidence of onset ischemic stroke symptoms, which reaches its maximum at 10:00-10:59am, gradually

decreasing throughout the day towards a minimum at 3:00-3:59am. 39.40% of not wake-up ischemic strokes occur between 9:00am and 13:59pm. Considering only wake-up ischemic strokes, in which onset time is unknown, 11:00pm to 12:59am are the most frequent hours in which the patient was last seen asymptomatic. The indication for reperfusion therapy (thrombolysis and/or thrombectomy) is more frequent between 11:00am and 2:59pm.
Conclusion: In our population, we consider the time of not wake-up ischemic strokes from 9:00am to 1:59pm and the time when the patient was last seen asymptomatic in wake-up strokes from 11:00pm to 12:59am. This results in arrivals to the emergency room between 8:00am and 1:59pm.
Disclosure: Nothing to disclose.

EPO-387

Utility of External loop recorder cardiac rhythm monitoring in Cryptogenic stroke: An institutional experience

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Background and aims: Cryptogenic strokes (CS) consist of 30% of total strokes. These can be caused by Paroxysmal Atrial fibrillation(PAF), which is not detected in acute settings. Prolonged ECG monitoring may improve the detection of PAF
Methods: This was a single centre, prospective, longitudinal, observational study conducted at a tertiary care centre over 18 months. Consecutive patients of acute ischemic stroke (AIS) admitted in the study period were included. All patients were extensively evaluated for Stroke etiology (Routine investigations, ECG, CT angio head and neck, 2D echo, 24 hour holter monitoring). Patients with initial negative workup were considered as CS and extended loop recorder(ELR) (72 hours) was planned. All patients were followed up for 90 days on outpatient basis or by telephonic interview. mRS and Barthel index (BI) were calculated on admission, on discharge and after 90 days
Results: 113 subjects were enrolled. 61 subjects were identified as cryptogenic stroke and underwent ELR monitoring for 72 hours. After this monitoring 3 subjects (4.9%) were found to have AF, which were not found during routine evaluation by ECG or 24 hour holter monitoring Patients with AF had poorer NIHSS on admission, worse GCS, larger strokes and longer hospital stay compared to the non AF. mRS at discharge and after 90 days did not show any significant difference between patients with or without AF. BI was significantly worse for the patients with AF
Conclusion: In AIS, 72-hour ECG monitoring improves the detection rate of silent PAF
Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 3

EPO-388

Efgartigimod Demonstrates Consistent Improvements in Patients With gMG Regardless of Prior Treatment Failures

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Background and aims: In ADAPT, treatment with efgartigimod (a human IgG1 antibody Fc-fragment that blocks neonatal Fc receptor) resulted in clinically meaningful improvements in a broad population of anti-acetylcholine receptor antibody positive (AChR-Ab+) patients with generalised myasthenia gravis (gMG). We assessed efficacy of efgartigimod in a subset of AChR-Ab+ ADAPT patients with refractory gMG, defined as prior exposure to ≥2 immunosuppressive therapies or treatment with ≥1 immunosuppressive therapy and requiring plasma exchange or intravenous immunoglobulin multiple times within 1 year prior to study inclusion.

Methods: Patients received treatment cycles of 4 weekly intravenous infusions of efgartigimod (10 mg/kg) or placebo, with subsequent cycles initiated based on clinical evaluation. Baseline characteristics and proportion of patients achieving responder status were evaluated for refractory patients. Outcome measures included MG-ADL and QMG scores, with responder status defined as ≥2- and ≥3-point improvements for MG-ADL and QMG, respectively, for ≥4 consecutive weeks (with first improvement ≤1 week after last infusion).

Results: In refractory patients (AChR-Ab+), baseline characteristics were balanced between groups, with mean (SD) MG-ADL scores of 9.2 (1.95) for efgartigimod-treated patients and 8.8 (1.69) for placebo-treated patients (Table 1). More efgartigimod-treated patients (67.5%, n=27/40) were MG-ADL responders compared to placebo-treated patients (31.7%, n=13/41; P=.0029; Figure 1A). QMG results followed a similar pattern (Figure 1B). Common adverse events were mostly mild-moderate and included headache, nasopharyngitis, nausea, diarrhoea, and upper respiratory/urinary tract infections.

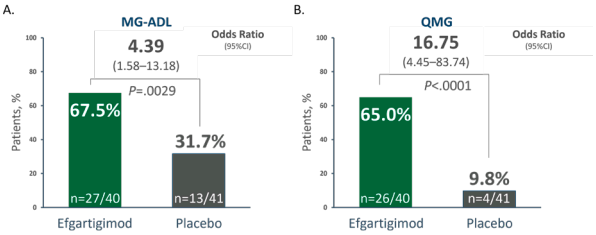

Figure 1: Proportion of MG-ADL (A) and QMG (B) responders in refractory AChR-Ab+ patients.

	Efgartigimod (n=40)	Placebo (n=41)
Age, mean, y (SD)	43.2 (13.89)	48.5 (14.95)
Female, n (%)	30 (75.0)	26 (63.4)
Time since diagnosis, mean, y (SD)	9.59 (7.62)	10.13 (8.07)
MG-ADL score, mean (SD)	9.2 (1.95)	8.8 (1.69)
QMG score, mean (SD)	15.9 (5.71)	15.4 (4.67)
MGFA class at screening, n (%)		
Class IIA	9 (22.5)	8 (19.5)
Class IIB	8 (20.0)	8 (19.5)
Class IIIA	11 (27.5)	10 (24.4)
Class IIIB	12 (30.0)	12 (29.3)
Class IVA	0	3 (7.3)
Prior treatment with steroids, n (%)	39 (97.5)	41 (100.0)
Prior treatment with NSISTs, n (%)	39 (97.5)	37 (90.2)

Refractory was defined as prior exposure to ≥2 immunosuppressive therapies or treatment with ≥1 immunosuppressive therapy and requiring plasma exchange or intravenous immunoglobulin multiple times within 1 year prior to study inclusion.

Table 1: Baseline demographics and clinical characteristics in refractory AChR-Ab+ patients.

	Efgartigimod (n=40)	Placebo (n=41)
AEs,[a] n (%)	29 (72.5)	34 (82.9)
SAEs, n (%)	2 (5.0)	4 (9.8)
Discontinued due to AEs, n (%)	1 (2.5)	2 (4.9)

Table 2: Safety data in the overall population. AE, adverse event; SAE, serious adverse event. aMost AEs were mild to moderate in severity.

Conclusion: Similar to results in AChR-Ab+ patients with gMG studied in ADAPT, efgartigimod demonstrated consistent and statistically significant improvements across outcome measures in patients with refractory gMG.

Disclosure: Multiple relationships financial and non-financial nature for authors CR, FS, JLdB, JV, SH, TV, VB, HM, EB, RK, SS, PU, NG, JV, RM and JFH Jr. stated at point of presentation.

EPO-389

A Real-life experience with Eculizumab and Efgartigimod in generalized Myasthenia Gravis patients.

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Background and aims: Eculizumab, a complement active monoclonal antibody, is reimbursed in Italy for anti-acetylcholine receptor antibody positive (AChR-Ab+) patients showing persistent symptoms, despite therapy with corticosteroids (CS) and ≥2 non-steroidal immunosuppressants (NSISTs). Efgartigimod, a neonatal Fc receptor blocker, is available in Italy through an expanded access program and treatment can be administered to both AChR-Ab+ and seronegative patients.
Methods: We included patients receiving either Eculizumab or Efgartigimod as part of our clinic practice and retrospectively collected data on their MG status using the MG activities of daily living (MG-ADL), quantitative MG scale (qMG), previous and current therapies, adverse events, and concomitant medication use.
Results: We enrolled 10 patients treated with Eculizumab and 12 with Efgartigimod. Demographics are shown in Table 1. Overall, MG-ADL decreased by -6.9 points ($p<0.001$), and qMG by -5.9 ($p<0.001$). Eculizumab reduced the MG-ADL by -6.6 points ($p=0.002$; Figure 1A), and the qMG by -7.4 ($p<0.001$; Figure 1B). Efgartigimod reduced the MG-ADL by -7.3 points ($p<0.001$; Figure 1A), and the qMG by -4.7 ($p<0.001$; Figure 1B). MG-ADL responders were 19 (86.4%), qMG responder were 19 (86.4%). Small non significant differeces emerged in the responder rate between treatments (Figure 2A). Mean prednisone reduction was -13.75 mg for the Eculizumab treated group ad -8.5 in the Efgartigimod group ($p=0.339$; Figure 2B).

Table 1. Baseline Demographics

Variable	Eculizumab (n=10)	Efgartigimod (n=12)	Total (n=22)
Gender (F/M)	5/5	10/2	12/10
AChR-Ab+	10	6*	16
Age	59.5±13.3	55.3±10.8	57.2±11.9
Previous Py use	9	12	21
Previous CS use	9	12	21
Previous NSIST = 0	2	4	6
Previous NSIST ≥1	8	8	16
Previous NSIST ≥2	8	4	12
Previous NSIST ≥3	2	0	2
Follow-up days (median)	116	84	91
MG-ADL	10.7±3.2	10.3±4.0	10.5±3.6
qMG	17.2±6.0	16.8±4.6	17.0±5.2

AChR-Ab+ = anti-acetylcholine receptor antibody positive; PY = Pyridostigmine; CS = Corticosteroids; NSIST = Non-steroidal Immunosuppressants; MG-ADL = Myasthenia Gravis Activities of Daily Living scale; qMG = Myasthenia Gravis quantitative scale. For gender significance is derived from a Fisher exact test, for Age, MG-ADL, qMG from a Mann-Whitney test. All comparisons were not significant. * 6 patients treated with Efgartigimod were seronegative, of these 2 were anti-MuSK-Ab+.

Table 1

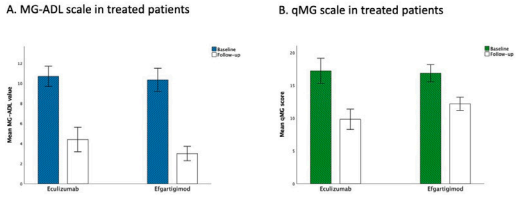

Figure 1

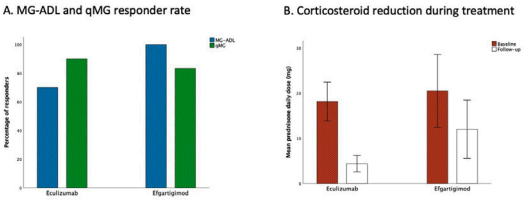

Figure 2

Conclusion: Eculizumab and Efgartigimod proved to be both effective treatments in a real world setting. They reduced MG-ADL and qMG in difficult to treat gMG patients. Responder rate was higher than previously reported in phase III trials.
Disclosure: FS received speaker honoraria from Alexion Pharmaceuticals, Inc, argenx, Biogen, Mylan, Novartis, Roche, Sanofi, and Teva; received honoraria from Alexion Pharmaceuticals, Inc, Almirall, argenx, Avexis, Biogen, Forward Pharma, Lexeo Therapeutics, Merk, Novartis, Pomona, Roche, Sanofi, and Takeda for consulting services; and served as PI in clinical trials supported by Alexion Pharmaceuticals, Inc, argenx, Immunovant, Novartis, Prilenia, and Sanofi. Other authors do not report disclosures.

EPO-390

Efficacy of innovative therapies in Myasthenia Gravis: review and meta-analysis.

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Background and aims: Therapy of Myasthenia Gravis (MG) is undergoing a profound change with new treatments being tested. These include: the complement inhibitors Eculizumab and Ravulizumab (humanized monoclonal antibodies), and Zilucoplan (self-administered peptide); the neonatal Fc receptor (FcRn) blockers Efgartigimod (human Fc-fragment), and Rozanolixizumab (sc-infused monoclonal antibody).
Methods: We present a meta-analysis of phase III trials with available efficacy results. In a second analysis round, we also included placebo-controlled trials with Rituximab. We assessed statistical heterogeneity across trials with Cochrane Q test and I2 values. We pooled mean differences with the random effect model. We derived treatment efficacy after 26 weeks of treatment with Eculizumab and Ravulizumab, 28 days with Efgartigimod, 43 days with Rozanolixizumab, 12 weeks with Zilucoplan, and after 16, 24 or 52 weeks with Rituximab.
Results: We observed an overall mean MG-ADL change of -2.17 points (95% CI -2.67, -1.67; $p<0.001$) as compared to placebo, without a significant difference between complement inhibitors and anti-FcRns ($p=0.16$; Figure 1A). The qMG change was -3.46 (95%CI -4.53, -2.39; $p<0.001$), with a higher reduction with FcRns (-4.78 vs -2.60; $p<0.001$;

Figure 1B). Rituximab did not significantly impact on MG-ADL (-0.92, CI95% -2.24, 0.39; p=0.17; Figure 2A), or qMG (-1.9, 95%CI -3.97, 0.18, p=0.07; Figure 2B).

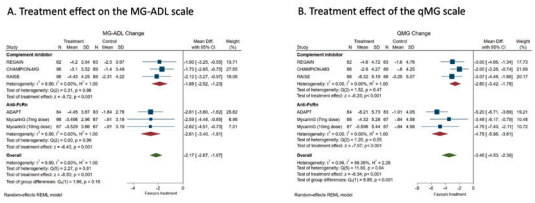

Figure 1. MG-ADL and qMG changes during treatment

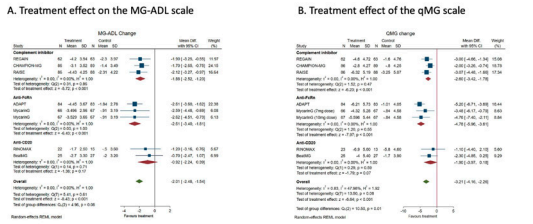

Figure 2. MG-ADL and qMG changes during treatment in the model including Rituximab

Conclusion: Anti-complement and FcRn treatments proved to be both effective in MG patients, whereas Rituximab did not show benefit in AChr-Ab+ patients. With the limitations of this meta-analysis, including efficacy time-points, FcRN treatments showed a short-term higher effect on the qMG.

Disclosure: FS received speaker honoraria from Alexion Pharmaceuticals, Inc, Biogen, Mylan, Novartis, Roche, Sanofi, and Teva; received honoraria from Alexion Pharmaceuticals, Inc, Almirall, argenx, Avexis, Biogen, Forward Pharma, Lexeo Therapeutics, Merk, Novartis, Pomona, Roche, Sanofi, and Takeda for consulting services; and served as PI in clinical trials supported by Alexion Pharmaceuticals, Inc, argenx, Immunovant, Novartis, Prilenia, and Sanofi. All other authors report no disclosures related to this abstract.

EPO-391

Rozanolixizumab in muscle-specific kinase autoantibody-positive myasthenia gravis: Further analyses from MycarinG study

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Background and aims: Muscle-specific kinase autoantibody-positive (MuSK-Ab+) generalised myasthenia gravis (gMG) is usually more clinically severe than acetylcholine receptor autoantibody-positive (AChR-Ab+) gMG. The Phase 3 MycarinG study analysed rozanolixizumab in patients with AChR-Ab+ or MuSK-Ab+ gMG.

Methods: MycarinG (MG0003/NCT03971422) randomised adults with Myasthenia Gravis Foundation of America Class II–IVa, AChR-Ab+ or MuSK-Ab+ gMG to weekly rozanolixizumab 7mg/kg, 10mg/kg or placebo for 6 weeks. The primary endpoint was Day 43 change from baseline (CFB) in Myasthenia Gravis Activities of Daily Living (MG-ADL).

Results: 200 patients (21 MuSK-Ab+) were randomised to rozanolixizumab 7mg/kg (n=66 [5 MuSK-Ab+]), 10mg/kg (n=67 [8]) or placebo (n=67 [8]). Among patients with MuSK-Ab+ gMG, a higher proportion experienced prior MG crisis and a lower proportion had thymectomy than the overall population, and their baseline MG-ADL score was higher (Table 1). Day 43 least-squares mean CFB in

MG-ADL for 7mg/kg, 10mg/kg and placebo groups were –7.28, –4.16 and 2.28, respectively, in patients with MuSK-Ab+ gMG and −3.37, −3.40 and −0.78 in the overall population. MG-ADL reduction in patients with MuSK-Ab+ and in overall population are shown in Figure 1. Mean percentage CFB in total immunoglobulin G (IgG) and IgG4 for patients with MuSK-Ab+ gMG and the overall population are presented in Table 2. Treatment-emergent adverse events occurred in 81.3% (7mg/kg), 82.6% (10mg/kg) and 67.2% (placebo) patients in the overall population and most were mild-to-moderate in severity.

		MuSK-Ab+*			Overall population†		
		Placebo (n=8)	RLZ 7mg/kg (n=5)	RLZ 10mg/kg (n=8)	Placebo (n=67)	RLZ 7mg/kg (n=66)	RLZ 10mg/kg (n=67)
Age at initial diagnosis, years, mean (SD)		37.1 (10.0)	37.2 (13.7)	43.6 (16.9)	41.4 (19.1)	46.6 (16.0)	42.6 (19.1)
Race, n (%)	Asian	0	2 (40.0)	2 (25.0)	5 (7.5)	9 (13.6)	7 (10.4)
	Black	0	0	1 (12.5)	1 (1.5)	0	4 (6.0)
	Native Hawaiian or other Pacific Islander	0	0	0	1 (1.5)	0	0
	White	8 (100)	3 (60.0)	5 (62.5)	46 (68.7)	41 (62.1)	49 (73.1)
	Missing‡	0	0	0	14 (20.9)	16 (24.2)	7 (10.4)
Duration of disease, years, mean (SD)		10.2 (9.8)	13.9 (7.6)	5.2 (5.0)	9.4 (9.3)	6.9 (6.8)	9.6 (9.9)
MG-ADL score at baseline, mean (SD)		8.8 (3.7)	11.0 (3.5)	9.3 (2.7)	8.4 (3.4)	8.4 (3.8)	8.1 (2.9)
QMG score at baseline, mean (SD)		17.9 (4.0)	17.0 (5.8)	14.0 (3.6)	15.8 (3.5)	15.4 (3.7)	15.6 (3.7)
MGFA disease class at baseline, n (%)	Class II	1 (12.5)	3 (60.0)	3 (37.5)	23 (34.3)	29 (43.9)	26 (38.8)
	Class III	4 (50.0)	2 (40.0)	5 (62.5)	41 (61.2)	34 (51.5)	39 (58.2)
	Class IVa/b‡	3 (37.5)	0	0	3 (4.5)	3 (4.5)	2 (3.0)
Prior MG crisis, n (%)		5 (62.5)	3 (60.0)	4 (50.0)	23 (34.3)	19 (28.8)	17 (25.4)
Baseline medications, n (%)	1 baseline MG-specific therapy (excluding AChEI)	1 (12.5)	1 (20.0)	4 (50.0)	23 (34.3)	19 (28.8)	26 (38.8)
	≥2 baseline MG-specific therapies (excluding AChEI)	4 (50.0)	3 (60.0)	4 (50.0)	27 (40.3)	20 (45.5)	34 (50.7)
Thymectomy at baseline, n (%)		3 (37.5)	1 (20.0)	0	31 (46.3)	32 (48.5)	20 (29.9)
Total IgG, g/L, mean (SD)		9.5 (3.0)	5 (9.2)	8 (9.3)	10.2 (2.6)	10.16 (3.18)	9.67 (2.61)

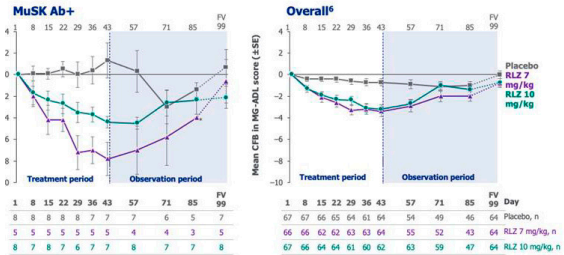
*Includes two patients who had positive AChR and MuSK autoantibody status.
†Includes both patients with AChR-Ab+ and MuSK-Ab+ gMG.
‡Data on race were not permitted to be collected in certain countries.
§Only 1 patient, who was randomised to the placebo group, had Class IVb disease.
AChEI, acetylcholinesterase inhibitor; AChR-Ab+, acetylcholine receptor autoantibody-positive; gMG, generalised myasthenia gravis; IgG, immunoglobulin G; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK-Ab+, muscle-specific kinase autoantibody-positive; QMG, quantitative myasthenia gravis; RLZ, rozanolixizumab; SD, standard deviation.

Table 1. Baseline characteristics of patients with MuSK-Ab+ gMG and in the overall population

	MuSK-Ab+*			Overall population†		
	Placebo (n=8)	RLZ 7mg/kg (n=5)	RLZ 10mg/kg (n=8)	Placebo (n=67)	RLZ 7mg/kg (n=66)	RLZ 10mg/kg (n=67)
Total IgG (%)	−1.3	−75.9	−77.6	−4.2	−69.1	−71.4
IgG4 (%)	10.14	−69.47	−66.95	5.29	−56.57	−59.87

*Includes two patients who had positive AChR and MuSK autoantibody status.
†Includes both patients with AChR-Ab+ and MuSK-Ab+ gMG.
AChR, acetylcholine receptor; gMG, generalised myasthenia gravis; IgG, immunoglobulin G; MuSK-Ab+, muscle-specific kinase autoantibody-positive; RLZ, rozanolixizumab.

Table 2. Mean percentage change from baseline in total IgG and IgG4 for patients with MuSK-Ab+ gMG and in the overall population



s not calculated for populations with n less than 3.
l visit; gMG, generalised myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK Ab+, muscle-specific kinase autoantibody-positive; RLZ, rozanolixizumab; SE, d error

Figure 1. Mean change from baseline in MG-ADL in (A) patients with MuSK-Ab+ gMG and (B) the overall population

Conclusion: Rozanolixizumab lowered total and subclass IgG levels and improved MG-specific outcomes in MuSK+ gMG, consistent with the overall study population. Funding: UCB Pharma.

Disclosure: This study was funded by UCB Pharma. Detailed author disclosures will be provided in the oral/poster presentation.

EPO-392

RevEal the burdeN on daily life for myotonic dyStrophy patients due to myotoniA: the ENSA survey.

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Background and aims: Myotonia is a symptom of myotonic dystrophy (DM) type 1 and 2. This can be debilitating and affects patients' everyday living, with a significant burden on Quality of Life (QoL) (1). Impact of DM on QoL has been evaluated (2,3), however, the specific contribution of myotonia remains unclear. The ENSA survey will assess the impact of myotonia on DM patients' daily lives.

Methods: Patients living in Europe, UK and North America, aged ≥18 years with a confirmed diagnosis of DM1/DM2, (or caregivers) will be invited to complete an anonymised online survey. Questions will explore the patient's description of DM symptom onset, time to medical consultation, the nature, frequency and location of myotonia, muscle weakness, fatigue, daytime sleepiness, gastrointestinal, and cardiorespiratory symptoms, along with disease management, treatment history and impact on daily life.

Results: Findings will be available in Q2-2023 and will aim to provide insight into the burden of myotonia on the daily life for DM patients, as well as increasing understanding of symptoms to support future clinical-trial outcome measures.

Conclusion: The ENSA survey will quantify the impact of myotonia on DM1 and DM2 patients' daily life and raise awareness of the need for appropriate management.

References: 1. Diaz-Manera J, et al. EMJ 2021;6[2]:37-46. 2. Rakocevic Stojanovic, S et al; J. Neurological Sciences, 2016;365, 158-161. 3. Landfeldt, E et al; Patient, 2019; 12(4): 365–373.

Disclosure: Zozulya-Weidenfeller is employed by Lupin. Other authors received honoraria from Lupin as consultants during the ENSA creation.

EPO-393

An unusual myopathy caused by a novel mutation in PNPLA2 gene

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Background and aims: The PNPLA2 gene encodes adipose triglyceride lipase, involved in adipose tissue triglyceride hydrolysis. Mutations of this gene are associated with neutral lipid storage disease with myopathy (NLSDM), a rare autosomal recessive condition.
Methods: Case report.
Results: Our case refers to a 35-year-old man history of severe acute heart failure by the age of 28, being identified a dilated myocardiopathy that required an implantable cardioverter-defibrillator implantation. His parents were consanguineous. He had no complaints of muscular weakness but had myalgias with intense physical exercise. On the neurological examination he had only a slight winged scapula, more evident on the left side. On blood workup he presented a high creatinine kinase level (200-800 U/L). A lipid deposition on the leukocytes known as Jordans anomaly was found on the blood smear. Abdominal CT and ultrasound were unremarkable. The muscle biopsy revealed a lipid accumulation on the muscle fibers, mainly on type 1 fibers. A genetic panel for myopathies revealed a novel homozygous pathogenic variant in the PNPLA2 gene (c.792del). He initiated bezafibrate 200mg 2id, which was suspended given the absence of therapeutic effect. He has been recently submitted to a successful heart transplant, from which he has been recovering uneventfully.
Conclusion: Our case of NLSDM seems to be singular as it started as a severe de novo dilated myocardiopathy, with subclinical involvement of skeletal muscle, associated with a novel mutation in PNPLA2 gene. The prognosis seems to be favourable, but it is limited by the cardiac involvement.
Disclosure: Nothing to disclose.

EPO-394

Patients in the Pompe Registry who switched from alglucosidase alfa to avalglucosidase alfa: Real-world experience

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Background and aims: Introduction: Marketing authorization for avalglucosidase alfa (AVAL) has been received in several countries for Pompe disease. Demographic and clinical characteristics of patients with Pompe disease who received alglucosidase alfa (ALGLU) for <5 versus ≥5 years before switching to AVAL are reported.
Methods: Real-world data were obtained from the Pompe Registry (NCT00231400), an international, observational, voluntary registry of patients with Pompe disease. For this analysis, eligible patients had ≥1 ALGLU treatment record immediately pre-switch to AVAL. Demographics, treatment duration and dose, plus respiratory, ambulatory, and biomarker measures are summarised pre-switch and, where data are available, for the last assessment post-switch.
Results: As of 2 December, 2022, data were available for 81 patients with late-onset Pompe disease (LOPD) and 8 with infantile-onset Pompe disease (IOPD); characteristics and treatment histories are summarised (Table 1). For patients with LOPD, last respiratory, ambulatory, and biomarker assessments pre-switch are summarised (Table 2) and for patients with both pre- and post-switch assessments these data are compared (Table 3). The preliminary results indicate an overall stabilisation in clinical outcomes following switch from ALGLU to AVAL, as well as improvement in the levels of biomarkers associated with disease burden, although more data will be needed from future data cuts to confirm these observations.

		LOPD	
		Time on alglucosidase alfa before switch to avalglucosidase alfa	
Parameter	IOPD (N=8)	< 5 years (N=26)	≥ 5 years N=55)
Sex, male, n (%)	3 (38)	12 (46)	31 (56)
Region, n (%)			
North America	2 (25)	26 (100)	46 (84)
Europe, Middle East, and Africa	5 (63)	0	7 (13)
Japan and Asia-Pacific	1 (13)	0	2 (4)
Age at diagnosis, mean±SD, years	0.4±0.30	32.4±22.29	33.7+21.59
Age at alglucosidase alfa initiation, mean±SD, years	0.5±0.29	33.3±22.76	37.6±21.34
First dose on alglucosidase alfa, 20 mg/kg qow,* n (%)	7 (88)	24 (100)	53 (100)
Last dose on alglucosidase alfa 20 mg/kg qow,* n (%)	5 (63)	23 (92)	41 (77)
Age at switch to avalglucosidase alfa, mean±SD, years	11.0±5.15	36.1±23.05	49.0±20.31
Time on avalglucosidase alfa, mean±SD (median [min, max]), months	5.4±8.98 (3.2 [0.0, 27.0])	6.7±20.36 (1.1 [0.0, 104.7])	3.5±3.79 (2.7 [0.0, 13.7])
First dose on avalglucosidase alfa 20 mg/kg qow,* n (%)		19 (73)	44 (80)
First dose on avalglucosidase alfa 40 mg/kg qow,* n (%)	6 (75)		
Last dose on avalglucosidase alfa 20 mg/kg qow,* n (%)		20 (77)	44 (80)
Last dose on avalglucosidase alfa 40 mg/kg qow,* n (%)	6 (75)		
*Most common dose for each group is shown; nominal dose 20 mg/kg (actual range: 14–27 mg/kg), nominal dose 40 mg/kg (actual range: 28–52 mg/kg); percentages based on number of patients with dose available. IOPD, infantile-onset Pompe disease; LOPD, late-onset Pompe disease; qow, every other week; SD, standard deviation.			

Table 1 Patient characteristics and treatment history (data cut-off: 2 December, 2022)

Parameter	LOPD: Time on alglucosidase alfa before switch to avalglucosidase alfa	
	< 5 years	≥ 5 years
FVC (upright) % predicted, mean±SD (median [min, max])	71.2±19.08 (76.0 [34.0, 104.0]) (n=17)	55.1±24.89 (50.0 [9.4, 124.0]) (n=52)
FEV_1 (upright) % predicted, mean±SD (median [min, max])	71.3±18.35 (74.0 [36.0, 100.0]) (n=16)	56.1±23.58 (50.0 [9.5, 121.0]) (n=50)
MIP, mean±SD (median [min, max]), cmH_2O	58.0±31.70 (59.0 [20.0, 120.0]) (n=11)	50.8±30.89 (43.0 [12.0, 134.0]) (n=35)
MEP, mean±SD (median [min, max]), cmH_2O	137.7±158.58 (84.5 [38.0, 571.0]) (n=10)	63.2±43.61 (52.5 [10.0, 246.0]) (n=30)
6MWT, mean±SD (median [min, max]), m	490.4±170.03 (491.0 [216.0, 869.0]) (n=11)	311.0±109.93 (316.5 [85.0, 500.0]) (n=30)
Urine Glc_4/Hex_4, mean±SD (median [min, max]), mmol/mol creatinine	4.6±2.12 (4.2 [1.6, 9.7]) (n=19)	12.3±20.83 (4.7 [1.6, 110.4]) (n=37)
Serum CK, mean±SD (median [min, max]), U/L	448±286 (366 [129, 976]) (n=18)	544±519 (411 [51, 2803]) (n=47)

*Data for infantile-onset Pompe disease patients not presented due to the small number of patients who had initiated avalglucosidase alfa at data cut-off.
6MWT, 6-minute walk test; CK, creatine kinase; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GLC_4, glucose tetrasaccharide; Hex_4; hexose tetrasaccharide; LOPD, late-onset Pompe disease; MEP maximal expiratory pressure, MIP, maximal inspiratory pressure; SD standard deviation.

Table 2 Last respiratory, ambulatory, and biomarker assessments for patients with LOPD* pre-switch from alglucosidase alfa to avalglucosidase alfa (data cut-off: 2 December, 2022)

Parameter	Patients, n	LOPD switch patients with assessments at both timepoints		
		Last assessment prior to switch	Last-post switch assessment (<1 year)	Change between visits
FVC (upright) % predicted, mean±SD (median [min, max])	16	60.4±23.45 (64.5 [25.0, 104.0])	61.5±23.99 (65.5 [19.0, 99.0])	1.1±5.09 (−1.0 [−6.0, 9.8])
FEV_1 (upright) % predicted, mean±SD (median [min, max])	16	61.8±22.67 (61.5 [28.0, 100.0])	63.3±24.31 (65.0 [22.0, 104.0])	1.5±6.13 (0.0 [−8.0, 13.0])
MIP, mean±SD (median [min, max]), cmH_2O	8	43.0±33.89 (31.0 [12.0, 120.0])	48.9±28.09 (43.5 [21.9, 107.0])	5.9±20.65 (−1.5 [−13.0, 49.2])
MEP, mean±SD (median [min, max]), cmH_2O	5	56.0±47.67 (42.0 [18.0, 138.0])	65.4±41.92 (46.0 [31.0, 126.0])	9.4±36.49 (−7.0 [−12.0, 73.8])
6MWT, mean±SD (median [min, max]), m	16	362.4±149.11 (392.5 [85.0, 640.0])	353.4±174.70 (401.0 [31.0, 650.0])	−8.9±66.15 (4.5 [−197.0, 80.0])
Urine Glc4/Hex_4, mean±SD (median [min, max]), mmol/mol creatinine	22	6.8±6.09 (4.4 [1.6, 25.0])	3.7±2.44 (2.8 [1.5, 10.8])	−3.1±5.67 (−0.8 [−19.3, 3.5])
Serum CK, mean±SD (median [min, max]), U/L	27	472.2±314.14 (424 [51, 1212])	390.8±273.93 (362 [61, 1105])	−81.4±194.56 (−21 [−735, 259])

*Data for patients with infantile-onset Pompe disease not presented due to the small number of patients who had initiated avalglucosidase alfa at data cut-off.
6MWT, 6-minute walk test; CK, creatine kinase; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GLC_4, glucose tetrasaccharide; Hex_4; hexose tetrasaccharide; LOPD, late-onset Pompe disease; MEP maximal expiratory pressure, MIP, maximal inspiratory pressure; SD standard deviation.

Table 3 Respiratory, ambulatory, and biomarker assessments pre- and post-switch (<1 year) from alglucosidase alfa to avalglucosidase alfa for patients with LOPD* who have both assessments (data cut-off: 2 December, 2022)

Conclusion: The Pompe Registry will continue to accrue data for patients switching from ALGLU to AVAL. Post-switch data will support the understanding of AVAL's effectiveness on respiratory and ambulatory outcomes and biomarker levels in the real-world setting.
Disclosure: Funding: Sanofi.

EPO-395

A Study Examining The Concordance Between Patient And Physician Assessment Of The MG-ADL

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Background and aims: Myasthenia Gravis (MG) is a rare, IgG-driven, autoimmune disease affecting vision, breathing, limb strength, and bulbar functioning. The most widely used primary endpoint in clinical trials is the MG-Activities of Daily Living (MG-ADL) scale, in which neurologists assesses patients on 8 symptoms. In contrast, real-world evidence studies often ask patients to complete the MG-ADL themselves. The objective of this study was to assess the concordance between the patient- and neurologist-reported MG-ADL scores.
Methods: An observational study was conducted in Italy and Germany, recruiting MG patients entering the hospital via emergency services or via a scheduled appointment. The MG-ADL was completed by patients at home and by neurologists during the consultation, in random order within 2 days (range 2-6) of each other. Concordance between the patient- and neurologist-reported MG-ADL assessments was calculated with Gwet's agreement coefficient for the 8 items, and with Intraclass Correlation Coefficients (ICC) for the total score.
Results: The ICC for the MG-ADL total score was 0.94 (95%CI 0.89-0.95), based on data from 137 adult MG patients and their neurologist, demonstrating excellent concordance. Gwet's AC showed substantial to almost perfect agreement for 7 items and moderate agreement for 1 item (eyelid droop). Neurologists assessed the patient's total symptom severity 0.6 points higher on a range of 0-24 (average 8.1 vs. 7.5 MG-ADL total score, respectively).

MG-ADL Items	Gwet's AC (p-value)
Chewing	0.77 (p<0.0001)
Double vision	0.74 (p<0.0001)
Breathing	0.73 (p<0.0001)
Rise from a chair	0.69 (p<0.0001)
Talking	0.66 (p<0.0001)
Swallowing	0.66 (p<0.0001)
Brush teeth or comb hair	0.58 (p<0.0001)
Eyelid droop	0.46 (p<0.0001)
	ICC (95% CI)
MG-ADL total score	0.94 (0.89-0.95)

Abbreviations: MG-ADL = myasthenia gravis activity of daily life score, ICC = intraclass correlation coefficient, CI = confidence interval

Table 1. Gwet's AC and ICC for item level and MG-ADL score

Conclusion: Excellent concordance of the assessment of MG symptoms with the MG-ADL was found between patients and neurologists. This evidence supports patient self-administration of the MG-ADL in MG-related clinical practice and research.
Disclosure: FS has received speaking honoraria and honoraria for attendance of advisory boards from Alexion and argenx BV. AM has received speaker honoraria, consulting fees or financial research support from Alexion, Argenx BV, Grifols, Hormosan, Janssen, Octapharma, and UCB. He serves as chairman of the medical advisory board of the German Myasthenia Gravis Society RM has received speaking honoraria from Biomarin, Alexion and UCB, served on advisory boards for Alexion, argenx BV and UCB and received support for congress participation from Merck, Teva and Biogen. SP is an employee of argenx BV, the sponsor of the study SD, owner of SHE, has been commissioned by argenx, the sponsor of the study, and is a member of the EuroQol Group. NT is an employee of SHE. MFJ is a paid consultants for argenx, the sponsor of this study, and received grant support from them.

EPO-396

Real-world experience with eculizumab in Japanese patients with myasthenia gravis: Post-marketing surveillance data

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Background and aims: Eculizumab (complement C5 inhibitor) is approved in Japan for treatment of adults with anti-acetylcholine receptor antibody-positive (AChRAb+) generalised myasthenia gravis (gMG) whose symptoms are difficult to control with high-dose intravenous immunoglobulin therapy or plasma exchange.

Methods: This interim analysis of post-marketing surveillance data assessed the effectiveness and safety of eculizumab in Japanese adults with gMG. Clinically meaningful response (≥3-point reduction in Myasthenia Gravis-Activities of Daily Living total score vs baseline) was evaluated at timepoints up to 104 weeks after eculizumab initiation in the analysis population overall and by patient and disease characteristics. Oral corticosteroid use was assessed. Safety was evaluated by recording adverse events.

Results: Data were available for 231 patients; the effectiveness analysis set comprised 223 patients. For patients with both baseline and follow-up data, 99/172 (57.6%), 104/167 (62.3%), 70/108 (64.8%) and 43/61 (70.5%) achieved clinically meaningful response at 12, 26, 52 and 104 weeks, respectively, after eculizumab initiation. Responder rates were similar and maintained through 104 weeks across analysed subgroups (Table). In patients receiving oral corticosteroids there was a trend towards reduced corticosteroid use and an increased proportion receiving ≤5 mg/day with continued eculizumab treatment (Figure). No new safety signals were observed.

Conclusion: The analysis findings align with previous real-world data, demonstrating eculizumab's sustained effectiveness and consistent safety profile in adults with AChRAb+ gMG, regardless of patient or disease characteristics. The observed reduction in concomitant oral corticosteroid use, also consistent with other real-world experiences, underlines the benefit of C5 inhibition in these patients.

Characteristic	MG-ADL responders, n/N (%)[a] Week 12	Week 26	Week 52	Week 104[b]
Sex				
Female	70/118 (59.3)	71/110 (64.5)	47/70 (67.1)	33/45 (73.3)
Male	29/54 (53.7)	33/57 (57.9)	23/38 (60.5)	10/16 (62.5)
Age at MG diagnosis (years)				
<50	59/103 (57.3)	65/102 (63.7)	47/68 (69.1)	28/39 (71.8)
≥50	40/69 (58.0)	39/65 (60.0)	23/40 (57.5)	15/22 (68.2)
Age at eculizumab initiation (years)				
≥18 to <40	20/32 (62.5)	22/35 (62.9)	14/23 (60.9)	10/15 (66.7)
≥40 to <65	53/96 (55.2)	58/93 (62.4)	42/59 (71.2)	24/33 (72.7)
≥65	26/44 (59.1)	24/39 (61.5)	14/26 (53.8)	9/13 (69.2)
Time from MG diagnosis to eculizumab initiation (years)				
≤2	30/45 (66.7)	33/43 (76.7)	21/30 (70.0)	13/15 (86.7)
>2 to ≤6	25/56 (44.6)	31/60 (51.7)	18/33 (54.5)	17/24 (70.8)
>6 to ≤14	28/42 (66.7)	23/35 (65.7)	16/26 (61.5)	6/13 (46.2)
>14	16/29 (55.2)	17/29 (58.6)	15/19 (78.9)	7/9 (77.8)
Inpatient/outpatient at eculizumab initiation				
Inpatient	28/38 (73.7)	27/35 (77.1)	18/24 (75.0)	11/15 (73.3)
Outpatient	71/134 (53.0)	77/132 (58.3)	52/84 (61.9)	32/46 (69.6)
History of thymoma				
Yes	50/76 (65.8)	48/67 (71.6)	36/44 (81.8)	20/25 (80.0)
No	49/95 (51.6)	56/99 (56.6)	34/63 (54.0)	23/35 (65.7)
Unknown	0/1 (0.0)	0/1 (0.0)	0/1 (0.0)	0/1 (0.0)
Severity of MG at first dose (MGFA classification)				
IIa	18/34 (52.9)	18/36 (50.0)	12/27 (44.4)	4/12 (33.3)
IIb	15/29 (51.7)	18/31 (58.1)	15/23 (65.2)	7/8 (87.5)
IIIa	26/40 (65.0)	29/39 (74.4)	13/18 (72.2)	10/13 (76.9)
IIIb	12/26 (46.2)	11/21 (52.4)	8/12 (66.7)	6/8 (75.0)
IVa	11/15 (73.3)	8/14 (57.1)	8/9 (88.9)	8/9 (88.9)
IVb	7/10 (70.0)	9/11 (81.8)	7/10 (70.0)	3/5 (60.0)
V	10/16 (62.5)	11/13 (84.6)	7/7 (100.0)	5/5 (100.0)
Unknown	0/2 (0.0)	0/2 (0.0)	0/2 (0.0)	0/1 (0.0)
Comorbidity				
Yes	70/120 (58.3)	76/118 (64.4)	52/80 (65.0)	28/41 (68.3)
No	29/52 (55.8)	28/49 (57.1)	18/28 (64.3)	15/20 (75.0)

The effectiveness analysis set (n=223) comprised all patients with ≥1 completed case report form at 26 weeks, except patients who received eculizumab in the REGAIN primary study (NCT01997229) or its open-label extension (NCT02301624). Data for each post-baseline timepoint are presented for those patients who had data at both baseline (eculizumab initiation) and the follow-up timepoint.

[a]MG-ADL responders were defined as patients with an MG-ADL total score improvement of ≥3 points vs. baseline (eculizumab initiation). [b]At time of data cut-off, 161 patients in the effectiveness analysis set were continuing treatment with eculizumab, of whom 82 had been treated for ≥2 years. MG, myasthenia gravis; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America.

Table: MG-ADL responder rates at Weeks 12, 26, 52 and 104 after eculizumab initiation in the overall population and according to patient and disease characteristics (effectiveness analysis set).

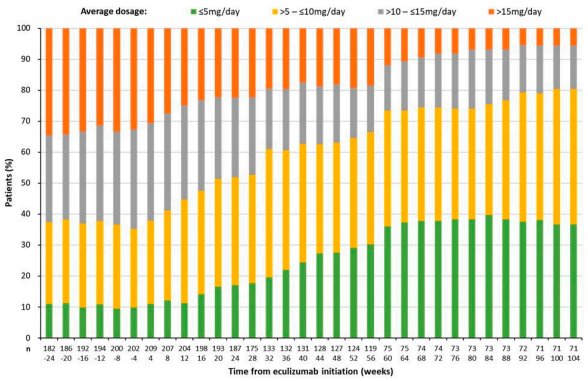

Figure: Mean corticosteroid use (daily dose) by time from eculizumab initiation.

Disclosure: Funded by Alexion Pharma GK, AstraZeneca Rare Disease

EPO-397

Diaphragmatic ultrasound:a promising tool for respiratory assessment in Facioscapulohumeral muscular dystrophy (FSHD)

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Background and aims: A restrictive respiratory impairment has been described in up to 40% of patients affected by Facioscapulohumeral muscular dystrophy (FSHD), one of the most prevalent muscular dystrophies in adults. Spirometry may underestimate early respiratory alterations in these patients, as inspiratory muscle impairment may occur before Forced vital capacity (FVC) variation. Ultrasonography has recently emerged as a non-invasive tool to assess the main inspiratory muscle, the diaphragm. The aim of this study was to thoroughly characterize the respiratory function of a small cohort of FSHD comparing spirometric and ultrasonographic data.

Methods: Genetically confirmed adult FSHD patients were enrolled. US diaphragmatic thickness at the end of a normal expiration (basal-DT), after a maximal inspiration (max-DT) and diaphragmatic excursion were calculated. The difference between max-DT and basal-DT represented "diaphragmatic thickening". FVC, forced expiratory volume in first second (FEV1), total lung capacity (TLC) and residual volume (RV) were also assessed by spirometry. Values were compared to normative data.

Results: Twenty FSHD patients (14 male and 6 female) were enrolled. Asymmetric abnormalities were found on US evaluation in 9 patients (45%), especially in diaphragmatic kinetic: median "diaphragmatic thickening" was 1,8 mm (range 0-4,6). A smaller portion of patients showed alteration on spirometric indexes. Inspiratory dysfunction with low TLC was detected in 5 (25%) patients, three of whom also displayed a restrictive pattern with a low FVC.

Conclusion: This pilot study suggests that diaphragmatic US could be a promising technique to identify early inspiratory dysfunction in FSHD patients and these results need to be confirmed in larger cohort.

Disclosure: The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the abstract and there is no financial interest to report.

EPO-398

IT engineered "smart-shoes" to digitally assess gait dynamics in FSHD patients

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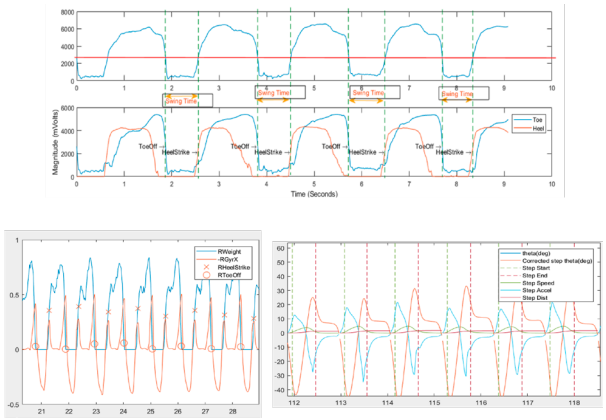
Background and aims: Facioscapulo-humeral muscular dystrophy is one of the most common myopathies in adult patients. Clinical trials are finally approaching also for FSHD, prompting understanding of molecular causes of clinical differences and precise phenotyping of different phenotypes, in order to identify suitable outcome measures. To highlight early signs of gait disturbances in FSHD patients without clinically detectable involvement of the lower leg, we tested the sensitivity of biosensors-featured "smart-shoes". The smart-shoes are integrated in the InGene2.0 software framework, which includes sections for collection of neurological examination, functional motor tests, muscular MRI, genetic data, muscle biopsies. Algorithms for artificial intelligence-mediated analysis and integration of data is applied to the whole software.

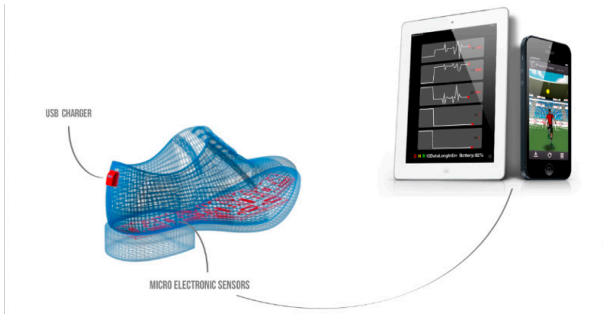
One of the smart shoes model, which is comfortably worn by patients and aesthetically indistinguishable from normal shoes.

Methods: We evaluated FSHD adult patients at baseline and for a 12-months follow-up period and in comparison to healthy controls. Variables collected by the smart shoes are speed gait, plantar pressures, joint angles. The tests included 6MTW, TUG, 10m run and time to climb and descend four stairs.
Results: The shoes are worn comfortably by the patients and can correctly and continuously detect the desired data. A worsening trend in patients' performance was found, although not statistically significant.



Real time collection of data during the tests is available on screen

Conclusion: Application of wearable devices such as the smart shoes could not only deliver digitized data on a personalized basis but also apply to a novel model of tele-monitoring of patients in daily life. The smart shoes will be tested on more patients, also with evident impairment of lower leg. Application of the smart shoes on a wider cohort is needed to validate our preliminary data.



The smart shoes could be integrated in e-health systems and help tele-monitoring of patients.

Disclosure: The authors have no disclosures to declare.

EPO-399

SRPKs in inflammatory muscle diseases

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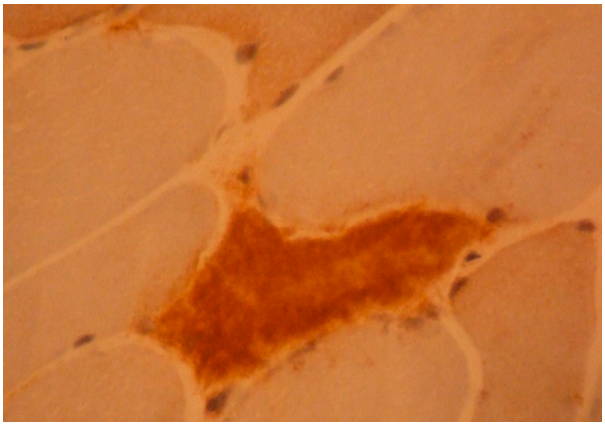
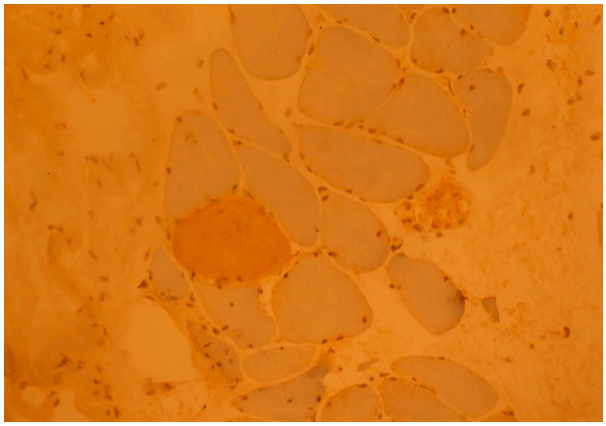
Background and aims: Idiopathic inflammatory myopathies (IIMs) consist an heterogeneous group of chronic autoimmune muscle diseases. Their pathogenetic mechanisms are not fully understood. Serine-arginine protein kinases (SPRKs) are a subgroup of serine-threonine protein kinases that phosphorylates substrates rich in Ser-Arg/Arg-Ser dipeptide repeats. Since many splicing factors contain RS domains, SRPKs play a major role in cell function via phosphorylation of these factors and therefore regulating alternative mRNA splicing. They have been implicated in oncogenesis but there are no data related to other disorders like autoimmune disorders.
Methods: Aiming to study the possible role of SRPKs on autoimmune disorders we sought to determine their expression on striate muscles in healthy individuals and patients with IIMs. We performed immunohistochemistry on frozen sections from muscle biopsies with diverse diagnosis, including dermatomyositis (DM), polymyositis (PM), sporadic inclusion body myositis (sIBM), immune-mediated necrotizing myopathy (IMNM), and myositis associated with antisynthetase syndrome (ASS).
Results: The results revealed an upregulation of both SRPK1 and SRPK2 in the cases with IIMs compared to healthy individuals. Interestingly only muscle fibers expressing other inflammatory markers showed this upregulation in SRPKs.





Conclusion: This results reveal a possible role of SRPKs in IIMs and possibly in other autoimmune disorders, apart from oncogenesis.
Disclosure: No conflict of interest.

EPO-400

The challenging interpretation of RYR-1 gene variants in three unrelated families.

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Background and aims: RYR-1 gene (Ryanodine Receptor type 1, 19q13.9) encodes a sarcoplasmic reticulum receptor, acting as a calcium release channel. RYR-1-related disorders encompass different conditions including central core disease (CCD), susceptibility to malignant hyperthermia and also asymptomatic hyperCKemia. The high phenotypic variability and the great number of emerging genetic variants require expertise and caution for their interpretation and clinical relevance.
Methods: We analyzed three families referred to our Unit with previously unreported RYR-1 heterozygous variants. An extensive phenotyping was performed through clinical examination, laboratory tests and, when available, muscle biopsy and magnetic resonance.
Results: Our cohort included a total of 8 patients, whose average age at first clinical evaluation was 39.1 years old [11-54]. The subjects taken into consideration were: father and daughter (Family A); three siblings (Family B); and mother and two sons (Family C). For each family a unique "in silico" pathogenic variant was identified, but different phenotypes were observed. In family A, the daughter presented a classical clinical and histopathological phenotype of CCD, while the father only mild signs of proximal weakness. In Family B and C, only one member showed clinical, histopathological, imaging, and laboratory characteristics of CCD, while the others' examinations resulted negative, except for a mild increase in serum Creatin kinase in one subject.
Conclusion: Our findings underline the complexity to interpret RYR-1 variants and to explain the genetic results and the clinical implications for a clinician. It also suggests possible incomplete penetrance or other genes' influence on RYR-1 mutated patients' phenotype.
Disclosure: The authors have no interests to disclose.

Motor neurone diseases; Muscle and neuromuscular junction disorder

EPO-401

Smartphone-based cough data in amyotrophic lateral sclerosis: a potential predictor of functional disability

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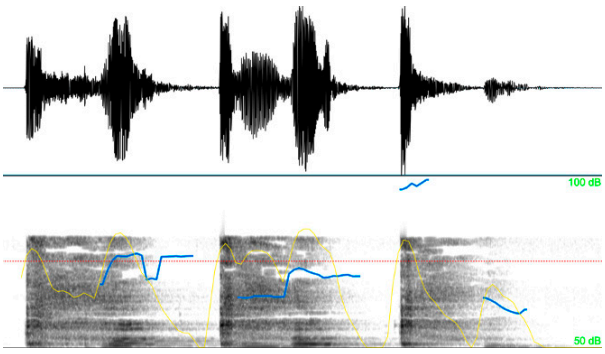
Background and aims: Amyotrophic lateral sclerosis (ALS) leads to severe functional disability. Cough depends on both respiratory and bulbar integrity. Correlations between cough sounds and ALS clinical features have been rarely performed. We aimed to assess the relationship between cough (and vocal) sound characteristics with respiratory and bulbar functions in ALS.

Methods: Single-center, cross-sectional and case-control study, consecutively collected on-demand cough recordings in ALS patients using a smartphone. The Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) was performed by a speech therapist. A quantitative acoustic analysis was conducted using time and frequency signal processing on the recordings. Correlation coefficients and multiple linear regression models were used.

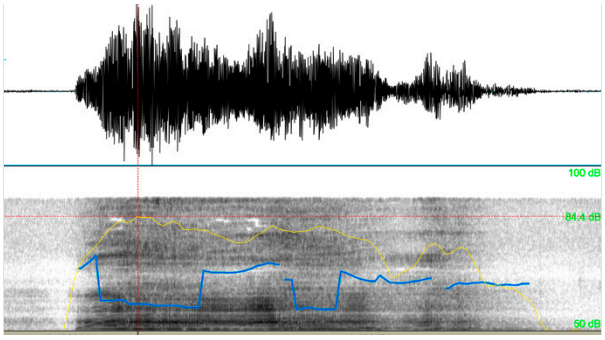
Results: We recruited 30 ALS patients: 19 females; mean age 61.36; mean 35 months disease duration; 10 with bulbar-onset; and a 37.5 mean ALSFRS-R total. Data from 20 controls were also included. Adjusting to age and gender, our results revealed clear differences between patients and controls on 9 (out of 31) cough sound features. The results revealed main difference between the two groups on sound frequency – significantly lower in ALS ($p=0.003$ for zero-crossing rate) – likely due to paralysis of laryngeal/bulbar muscles. The distance between signal peaks and sound energy were best correlated to ALSFRS total ($p<0.001$ and $p=0.003$, respectively) – demonstrating that worse patients have less intense cough sounds (likely due to respiratory impairment). We are now increasing our controls; and correlating findings with CAPE-V.



Healthy control cough bouts sounds: Signal in the time domain (upside); Signal in the frequency domain (downside).

Conclusion: Our results suggest that cough features could emerge as predictors of ALS functional evaluation, at the convenience of using a smartphone.

Disclosure: Nothing to disclose.



ALS patient cough bouts sounds: Signal in the time domain (upside); Signal in the frequency domain (downside).

EPO-402

Preliminary data on safety and efficacy of Risdiplam treatment in a small cohort of adult 5q spinal muscular atrophy

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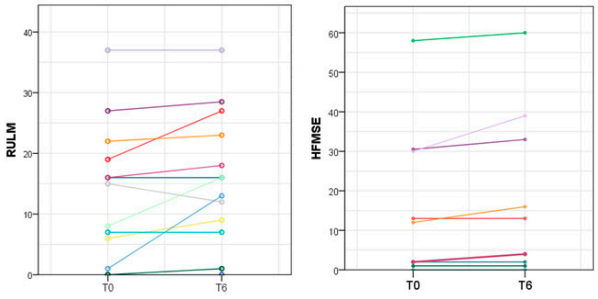
Background and aims: Risdiplam is an oral small-molecule drug recently approved for the treatment of Spinal Muscular Atrophy (SMA). It increases functional SMN (survival motor neuron) protein by modifying pre- mRNA splicing of the gene SMN2. Aim of the study was to investigate safety and efficacy of Risdiplam in our adult cohort of SMA patients.

Methods: Inclusion criteria were: clinical and molecular diagnosis of SMA2/SMA3; starting Risdiplam in adulthood; availability of clinical data and specific motor scale [Hammersmith Functional Motor Scale Expanded (HFMSE); Revised Upper Limb Module (RULM), six minute walking test (6MWT)] at treatment baseline (T0) and after 6 months (T6).
Results: We included 16 patients (10 SMA 2 and 6 SMA3), 41 years median age at first administration (IQR 21-54). HFMSE increased significantly from T0 to T6 (median values: 2, IQR: 0-13 vs 3, IQR: 0-15, p=0.026). The RULM significantly improved from T0 to T6 (median values: 15, IQR: 6-21 vs16, IQR: 9-26, p=0.024). No changes in 6MWT were detected at T6 in walking patients. Eleven patients (69%) were classified as responders at T6. Among all demographic and clinical variables, only the number of SMN2 copy was directly associated with clinical improvement (p=0.023). The one mild adverse effect was reversible diarrhoea in 18% of patients, requiring drug discontinuation. No severe-adverse events were reported.
Conclusion: Our data highlight the efficacy of Risdiplam even in the first six months of treatment, regardless of age/gender/functional clinical status at baseline and SMA type. Number of SMN2 copies influence positively clinical improvement.
Disclosure: Simone IL and E. D'Errico received grants from Biogen and Roche for educational events. All other authors have not disclosures.

		Median (IQR) or N. of patients (%)
Age at sampling (years)		41 (32-47)
Sex	Female	10 (62.5%)
	Male	6 (37,5%)
SMN2	2	5 (31,3%
	3	9 (56,3%)
	4	4 (12,5%)
Age at onset (months)		14 (9-36)
HFMSE	T0	2 (0-13)
	T6	3 (0-15)
RULM	T0	15.50 (6-21)
	T6	16.00 (9-26)



EPO-403

Clinical characteristics in amyotrophic lateral sclerosis with Sub-Saharan Africa ancestry

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Background and aims: Studies concerning epidemiological and clinical data of amyotrophic lateral sclerosis (ALS) in middle and low-incoming countries, including Sub-Saharan Africa (SA), are scarce. We attempted to characterize an ALS cohort with SA ancestry but followed in our ALS clinic in Lisbon.
Methods: A hospital-based retrospective study was conducted, including a total of 1633 ALS patients followed longitudinally. Patients were divided in two groups: SAALS (SA ancestry) and PALS (Portuguese ancestry). We looked for phenotype, genotype and prognosis.
Results: Thirty patients (1.8%) patients (15 men) were included in the SAALS group, with a median onset age of 51.5 years (15-73) and a predominant spinal-onset phenotype (23 patients, 76.7%). No patient had dementia. In this group onset age was lower ($p < 0.001$), and diagnostic delay longer (16 vs. 11 months, p=0.004). No other significant differences were found, including onset-region, familial history of ALS/FTD, rate non-invasive ventilation use or riluzole treatment. Ancestry was not an independent predictor of survival. C9orf72 repeat expansion testing was negative in SAALS group. One patient had a heterozygous FUS mutation identified by single-gene testing.
Conclusion: SAALS is a specific ALS population with a younger onset. Survival was not dependent on the ancestry. Regular follow-up and treatment in a specialized ALS Centre could explain the differences in survival between our results and previous data from African countries.
Disclosure: Nothing to disclose.

EPO-404

Epidemiology and comorbid disease of Spinal and bulbar muscular atrophy in South Korea

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Background and aims: Spinal and bulbar muscular atrophy (SBMA), also known as Kennedy's disease is caused by the increased CAG repeats in the Exon 1 of the androgen receptor. SBMA affects approximately 1:40,000 ~1:300,000 male people worldwide. The aim of this study was to investigate the prevalence and comorbidity of SBMA using Korean National Health Insurance database.
Methods: We conducted a retrospective cohort analysis of patients with the G12.25 code, registered from January 1, 2016 to December 31, 2019. Concomitant morbidity was assessed using various disease codes.
Results: A total of 294 SBMA patients with a G12.25 diagnosis were identified in the database during 2016-2019. The prevalence in South Korea of 2019 was 0.8:100,000. Comorbidities identified in more than 80% of SBMA were M79 (84%, Other soft tissue disorders), E78 (88.4%, Disorders of lipoprotein metabolism and other lipidemia), K30 (89.1%, Dyspepsia), K21 (90.5%, Gastro-oesophageal reflux disease), M54 (91.2%, Dorsalgia), J30 (92.2%, Vasomotor and allergic rhinitis), J20 (93.5%, Acute bronchitis), and K29 (99.7%, Gastritis and duodenitis). Of the 294 SBMA patients, 25 (8.5%) had accompanying cancer. The most common cancer was gastric cancer (5 patients).
Conclusion: According to our study, the prevalence of SBMA in South Korea is 0.8:100,000. In addition, there was increased association of dyslipidemia was found in 89% of the SBMA patients with accompanying cancer in 8.5%.
Disclosure: The authors have no disclosures.

EPO-405

Benchmarking care for adults living with spinal muscular atrophy (SMA) in Europe

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Background and aims: Spinal muscular atrophy (SMA) is a rare neuromuscular disease, leading to loss of motor milestones and reduced life expectancy. Individuals with SMA require complex care from a multidisciplinary team of healthcare professionals. Recommendations on standards of care (SoC) in SMA were updated before pharmacological treatments were widely available and are primarily focused on paediatric patients. SoC recommendations focused on the needs of adults are required. In partnership, F. Hoffmann-La Roche Ltd and SMA Europe are conducting a benchmarking project to assess how care is provided for adults living with SMA in 23 European countries, to identify gaps and to make recommendations for solutions and policy changes to improve SoC and quality of life for adults with SMA.
Methods: The study is being conducted in three phases: Phase 1: Reaching consensus on data collection methodology and benchmarking indicators. Phase 2: Collection and analysis of data from published sources; a structured survey targeting clinical experts, and semi-structured phone interviews with patient organisations. Phase 3: Summarisation of results, highlighting key gaps, best practices and recommendations. An expert committee of patients and healthcare professionals will advise on the project.
Results: Here we describe the study design of the project, focussing on the development of benchmarking indicators and data collection.
Conclusion: This study will help to identify care gaps for adults living with SMA in Europe. These results can be used by healthcare professionals, patient advocacy groups and policy makers to develop solutions to help improve SoC and quality of life.
Disclosure: This study is funded by F. Hoffmann-La Roche Ltd, Basel, Switzerland and is being conducted in partnership with SMA Europe. Data collection and analysis are being conducted by Hall and Partners, UK, and Weber Shandwick, Belgium, respectively. Writing and editorial assistance was provided by Chrysalis Medical Communications UK, in accordance with Good Publication Practice (GPP2022) guidelines (https://www.ismpp.org/gpp-2022). Data collection, analysis and medical writing support are funded by F. Hoffmann-La Roche Ltd.

EPO-406

Acoustic voice analysis as a useful tool to discriminate different ALS phenotypes.

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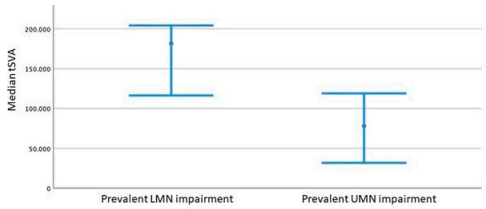
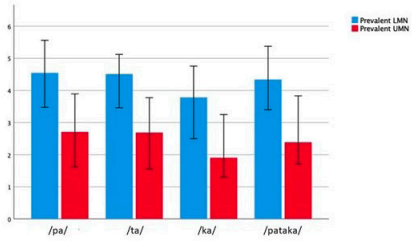
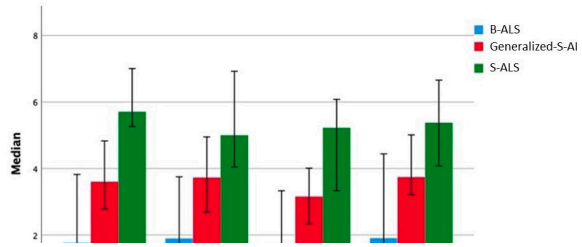
Background and aims: The assessment of upper (UMN) and lower motor neuron (LMN) impairment in bulbar regions remains still challenging in amyotrophic lateral sclerosis (ALS) patients. Particularly, there is a lack of quantitative measures able to discriminate spastic (UMN-impairment) by flaccid (LMN-impairment) dysarthria. Aim of the study was to evaluate acoustic voice analysis as useful tool to discriminate ALS phenotypes.

Methods: Thirty-six ALS patients were recruited (excluding severe dysarthrics). Patients' articulatory and motor speech production abilities were evaluated using the following acoustic parameters: Triangular Vowel Space-Area (tVSA), Alternating Motion Rates (AMR) and Sequential Motion Rates (SMR). The above-mentioned measures were tested in patients with prevalent UMN (pUMN) and LMN (pLMN) impairment (using the median of the Penn Upper Motor Neuron Scale-PUMNS, as a cut-off) and then in patients with bulbar-onset (B-ALS), with spinal-onset without bulbar symptoms (S-ALS) and with spinal-onset and bulbar symptoms at clinical evaluation (generalized-S-ALS).







Results: ALS patients with pUMN showed significantly lower values of tVSA, AMR and SMR than pLMNs. Among all the acoustic parameters, tVSA exhibited higher accuracy in discriminating patients with pUMN and pLMN (AUC: 0.83, CI:0.707–0.965, p<0.001). No differences were found in tVSA according to the site of onset. B-ALS patients showed significantly lower values of AMR and SMR compared to generalized-S-ALS and in turn, these latter exhibited lower values of the above-mentioned acoustic measures compared to S-ALS.
Conclusion: The acoustic voice analysis might be a useful tool to discriminate spastic by flaccid dysarthria and to incept the degree of bulbar involvement in ALS disease.
Disclosure: The authors have nothing to declare.

EPO-407

Ten-year Longitudinal Natural History and Prognosis in Amyotrophic Lateral Sclerosis in Southern Germany

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Background and aims: The ALS registry Swabia is an epidemiologic registry in Southern Germany covering a source population of 8.4 million inhabitants. We describe a 10 year follow-up of natural history and time to key clinical milestones (non-invasive ventilation (NIV), tracheostomy with invasive ventilation (TIV), percutaneous endoscopic gastrostomy (PEG)) and survival.
Methods: Between 10/2010 and 12/2020, n=1,171 people with ALS (pwALS) participated with annual follow-up. Three hundred forty-four pwALS were genetically tested.
Results: Overall, mean age at onset was 65.8 ± 11.2 years, 59.3% were male. Spinal/bulbar onset was observed in 65.3%/29.8%. A family history of ALS was reported by 6.2%. Median diagnostic delay was 7 months. 21.4% of pwALS used antidepressants at baseline and 73.5% Riluzole. Cumulative 5-year incidence for NIV, TIV, PEG and death was 28%/4%/17% and 83%, respectively. Median survival was 21.4 months (Q1 10.3, Q3 41.1). Thirty pwALS carried a C9ORF72, three a SOD1 mutation. C9ORF72 pwALS differed in age (61.3 ± 10.8) and onset (bulbar 40%) and had a faster progression (ALS-FRS-R -0.99/month versus -0.76/month in the entire cohort) with reduced survival. Each SOD1 pwALS had spinal onset and a positive family history, in contrast to C9ORF72 pwALS (50% with positive family history). Median diagnostic delay was 4 months in C9ORF72 and 3 months in SOD1 pwALS.
Conclusion: In Germany, TIV is rare while NIV/PEG is used in >25%/>15% of pwALS within 5 years. Riluzole treatment is regular and antidepressants used in up to 30%. Median survival was 21.4 months. Genetic forms alter clinical course and survival.
Disclosure: Specific data analysis in this investigator-initiated registry was supported by Biogen Inc. Biogen had no role in study design, and data collection within the registry, but gave input to the specific protocol, statistical analysis plan, and data interpretation for this project, and reviewed the final version of the abstract.

EPO-408

NIPA1 (GCG), NOP56 (GGCCTG) and NOTCH2NLC (GGC) expansion analysis in Italian Amyotrophic Lateral Sclerosis patients

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Background and aims: The discovery of hexanucleotide repeats expansion (RE) in C9Orf72 as the major genetic cause of ALS and the association between intermediate repeats in ATXN2 with the disorder suggest that repetitive sequence in the human genome plays a significant role in ALS pathophysiology. In this study, we aimed to define the frequency of REs in NIPA1, NOP56 and NOTCH2NLC genes; disclose the probable role of this expansion in ALS disease and the potential associations between phenotypes and the size of REs.

Methods: The REs were screened by both repeat-primed PCR and PCR-fragment analyses in 302 El Escorial diagnosed ALS patients. The distribution of repeats in the ALS cohort was evaluated and compared to a group of 197 healthy controls matched for age, gender, ethnicity. The chi-square test, Fisher exact test, Student's t-test and the Odd Ratio (OR) were used for statistical analysis.

Results: The REs distribution between ALS and control cases were similar (Fig. 1) with the presence of only a few borderline cases. There is a moderate association between long REs length and different clinical features such as age at onset, sex, site of onset, and family history.

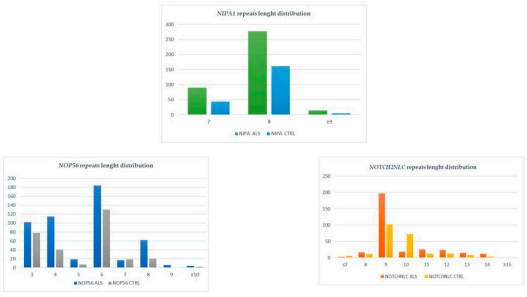

Fig 1

Conclusion: This study is the first to screen a cohort of ALS patients from southern Italy to evaluate the role of REs in the NIPA1, NOP56 and NOTCH2NLC genes in disease pathogenesis. Our results highlighted an extremely rare pathogenic REs in this gene not allowing an association with the disease.

Disclosure: The Authors disclose any conflicts of interest related to the manuscript.

EPO-409

Retinal degeneration in Amyotrophic Lateral Sclerosis phenotypes – preliminary data from a longitudinal study.

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Background and aims: Retinal measurements are biomarker candidates for many neurological diseases, but their significance in Amyotrophic Lateral Sclerosis (ALS) remains unestablished. We investigate retinal degeneration in ALS and its different phenotypes, its value as a progression biomarker and its prognostic implications.

Methods: Retinal Nerve Fiber Layer (RNFL) and Ganglion Cell Layer (GCL) are measured by Optical Coherence Tomography in 61 ALS patients and 12 healthy controls. Visual evoked potentials testing and cognitive assessment of ALS subjects are conducted concurrently, together with clinical examination, disease history collection, ALS-Functional Rating Scale (ALS-FRS) administration and blood collection for neurofilament (Nfl) levels determination. All tests are repeated after 12 months to detect progression. The latest available vital status information is used for analysis.

Results: When compared with controls, ALS subjects show lower mean GCL thickness in both eyes (right/left: 78,24/77,13 vs 83,5/83 µm – p 0,052/0,047) and global minimum GCL thickness (68,15 vs 78,17 µm – p 0,026). RNFL also shows thinning, without reaching statistical significance (right/left: 89,39/89,57 vs 94,66/95,41 µm – p 0,116/0,084). Preliminary longitudinal analysis on 15 subjects reassessed after 12 months only shows left-eye GCL thinning (mean/minimum 78,67/71,73 vs 74,47/69,90 µm – p 0,014/0,077).

Conclusion: We detected GCL thinning transversally and longitudinally, confirming retinal degeneration as a neurodegeneration marker. Broader analysis, including additional follow-up data, will explore the relationships between such phenomenon and different motor and cognitive involvement patterns, progression rate and Nfl levels.

Disclosure: The authors declare no competing interests. This work was supported by grants of the Italian Ministry of Health to Luca Diamanti (2021-2022).

EPO-410

Validity and Reliability of a New Clinical Myotonia Rating Scale for Non-Dystrophic Myotonia

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Background and aims: The severity of myotonia is difficult to assess without the use of a standardized and validated tool.
Methods: The Clinical Myotonia Rating Scale (CMRS) was evaluated in Myotonia Congenita (MC) and Paramyotonia Congenita (PMC) patients during the randomised cross-over double-blind mexiletine vs placebo MYOMEX trial. The CMRS comprises two consecutive sections: a myotonia severity scale rated on the patient's clinical exam and a disability scale rated on the patient's opinion on daily activities. The CMRS was assessed by two different investigators at baseline and by one of them (always the same for each patient) at the end of each treatment period. Interrater reliability was estimated by weighted Kappa coefficients. Intraclass correlation coefficients (ICC) were calculated for the global scores (GS). Bland & Altman methods were also used. Spearman correlation coefficients were estimated for correlations with the stiffness score using visual analogue scale (VAS) and the Individualized Neuromuscular Quality of Life (INQoL) self-questionnaire.
Results: 13 MC patients and 12 PMC patients were evaluated at six centres. Kappa ranged between -0.02 and 0.82. The highest interrater agreement was for eyelid blinking frequency and respiratory muscle intensity items (0.73 95%confidence interval [0.54;0.91] and 0.72 [0.45;0.98] respectively) as well as for hygiene and getting dressed (0.82 [0.59;1.00] and 0.73 [0.45;0.98] respectively). The ICC severity score was 0.54 and the ICC disability score - 0.65. The severity GS was strongly correlated with both the VAS (0.70, $p \leq 0.001$) and the INQoL (0.67, $p \leq 0.001$).
Conclusion: The CMRS is a promising scale and requires further validation in myotonic disorders.
Disclosure: Savine Vicart, Yann Pereon, Sabrina Sacconi and Bertrand Fontaine have received consulting fees from Lupin for other initiatives.

EPO-411

Expert group recommendations for cardiac assessment of non-dystrophic myotonic adult patients treated with mexiletine

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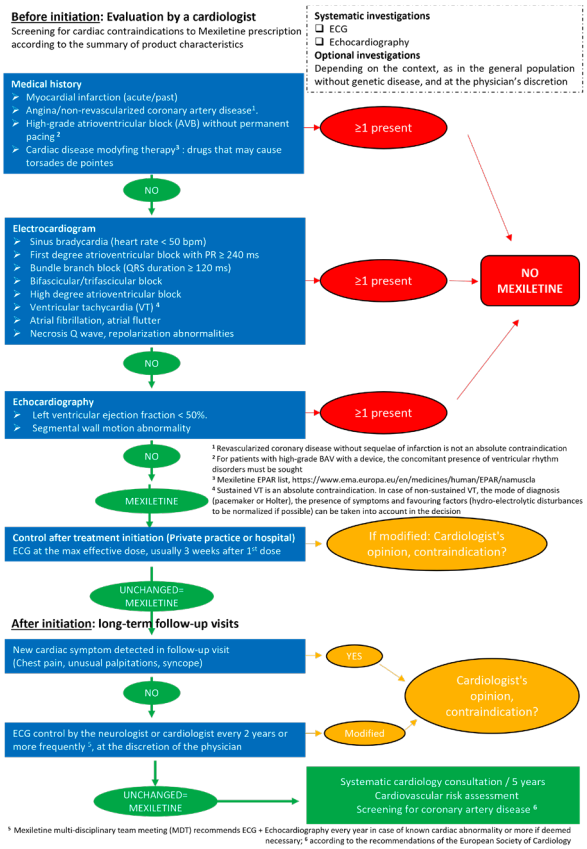
Background and aims: Mexiletine (NaMuscla™) is indicated for the symptomatic treatment of myotonia in adults with non-dystrophic myotonia (NDM). A cardiac assessment is required as mexiletine may have a pro-arrhythmic effect. Long-term safety data supporting use of mexiletine in patients with NDM combined with the extensive clinical experience of an expert group resulted in creation of an algorithm for cardiac monitoring of NDM patients treated with Mexiletine.
Methods: To define the treatment algorithm, several workshops with experts including 3 neurologists and 5 cardiologists from different French neuromuscular reference centres were set up. These workshops aimed to define the screening and surveillance tools required to avoid cardiac

events in mexiletine-treated patients. The recommendations are based on the summary of product characteristics (SmPC), a review of the literature on the safety of mexiletine-treated NDM patients and on the expertise of the authors.

Results: The expert group concluded that the cardiac safety profile of mexiletine in NDM patients appears similar to that of the general population. Therefore, NDM patients treated with Mexiletine should be monitored as any patient treated with a class 1b anti-arrhythmic. Cardiac assessment should be performed before initiation of mexiletine and at least every 2 years under treatment (Figure 1).



Mexiletine prescription algorithm in patients with NDM

Conclusion: An algorithm for cardiac safety monitoring in patients with NDM treated with mexiletine has been developed to assist the neurologists and cardiologists managing these patients.

Disclosure: All authors declare consulting fees from Lupin.

EPO-412

Rozanolixizumab responder and minimal symptom expression rates in generalised MG: Pooled Phase 3 and extension studies

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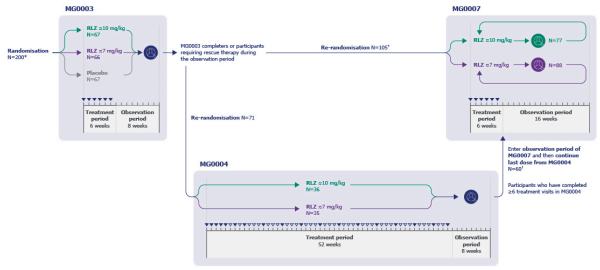
Background and aims: The Phase 3 MycarinG (MG0003/NCT03971422) trial demonstrated efficacy of one 6-week cycle of rozanolixizumab in generalised myasthenia gravis (gMG). We assessed consistency of cyclical rozanolixizumab efficacy and safety over time.

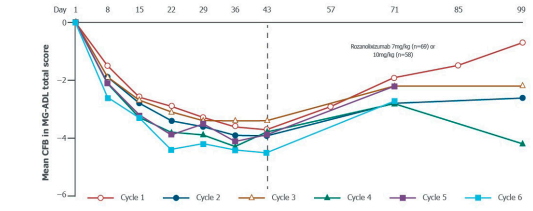
Methods: After 6 weeks of weekly rozanolixizumab/placebo in MycarinG, patients entered MG0004 (NCT04124965: ≤52 weeks of weekly rozanolixizumab) or MG0007 (NCT04650854: initial 6-week cycle; subsequent cycles administered on symptom worsening as determined by investigator's discretion, e.g. Myasthenia Gravis Activities of Daily Living [MG-ADL] increase ≥2/Quantitative Myasthenia Gravis [QMG] increase ≥3; "symptom-driven cycles") (Figure 1). Efficacy pool: data for patients with ≥2 symptom-driven cycles pooled across MycarinG, MG0004 (first 6 weeks) and MG0007 (interim analysis); safety pool: data for patients with ≥1 cycle across MycarinG (symptom-driven) and MG0007 (fixed/symptom-driven).

Results: 127 patients received ≥2 symptom-driven cycles of rozanolixizumab 7mg/kg (initial dose, n=69) or 10mg/kg (initial dose, n=58). MG-ADL change from baseline to Day 43, responder rates at Day 43 for MG-ADL, Myasthenia Gravis Composite and QMG and minimal symptom expression at any visit were consistent across cycles (Figure 2, Table). Treatment-free intervals (time from previous dose to first dose in symptom-driven cycle 1) were <4 weeks for 9.0%, 4–13 weeks for 59.3%, 13–26 weeks for 13.8% and ≥26 weeks for 4.2% of patients, with similar proportions at the next cycle. Treatment-emergent adverse events (most mild to moderate) occurred in 77.4% and 91.6% of patients receiving ≥1 cycle of rozanolixizumab 7mg/kg and 10mg/kg.



*127 patients who received ≥2 symptom-driven treatment cycles across the three studies were included in the primary efficacy pool.
†165 participants entered MG0007. Dose modifications during MG0007 from 10 mg/kg to 7 mg/kg and vice versa were permitted after the first cycle, at the beginning of each treatment cycle at the investigator's discretion, and provided the benefit-risk remains favourable for the participant. Worsening of generalised myasthenia gravis symptoms was assessed by the investigator with guidance to consider an increase of ≥2.0 points on the Myasthenia Gravis Activities of Daily Living scale or ≥3.0 points on the Quantitative Myasthenia Gravis scale.
RLZ, rozanolixizumab.

Figure 1. Pooled analysis design



Cycle	Day 1	8	15	22	29	36	43	57	71	85	99
Cycle 1, n	127	120	117	118	123	117	127	80	85	57	94
Cycle 2, n	127	108	112	110	125	112	127	-	66	-	39
Cycle 3, n	98	94	95	97	97	95	98	-	48	-	21
Cycle 4, n	75	75	74	70	72	73	75	-	30	-	5
Cycle 5, n	51	48	49	50	48	48	51	-	13	-	1
Cycle 6, n	32	30	32	30	32	32	32	-	7	-	-

CFB, change from baseline; MG-ADL, Myasthenia Gravis Activities of Daily Living.

Figure 2: Mean CFB in MG-ADL score per cycle, in patients who received ≥2 symptom-driven cycles of rozanolixizumab

Proportion of MG-ADL, MGC and QMG responders and proportion achieving MSE in patients who received ≥2 symptom-driven cycles of rozanolixizumab

	Cycle 1 n/N (%)	Cycle 2 n/N (%)	Cycle 3 n/N (%)	Cycle 4 n/N (%)	Cycle 5 n/N (%)	Cycle 6 n/N (%)
DL responders*	**94/127** (74.0)	**95/127** (74.8)	**63/98** (64.3)	**55/75** (73.3)	**40/51** (78.4)	**23/32** (71.9)
esponders†	**93/127** (73.2)	**95/127** (74.8)	**68/98** (69.4)	**55/75** (73.3)	**35/50** (70.0)	**22/31** (71.0)
esponders‡	**87/127** (68.5)	**78/125** (62.4)	**63/97** (64.9)	**51/74** (68.9)	**30/51** (58.8)	**21/32** (65.6)
	35/127 (27.6)	**34/127** (26.8)	**25/98** (25.5)	**24/75** (32.0)	**17/51** (33.3)	**13/32** (40.6)

nber of patients decreased over cycles as the number of symptom-driven treatment cycles varied between patients.
int improvement at Day 43.
oint improvement at Day 43.
ll, score of 0 or 1 at any visit.
L, Myasthenia Gravis Activities of Daily Living; MGC, Myasthenia Gravis Composite; MSE, minimal symptom expression; QMG, Quantitative Myasthenia Gravis.

Table: Proportion of MG-ADL, MGC and QMG responders and proportion achieving MSE in patients who received ≥2 symptom-driven cycles of rozanolixizumab

Conclusion: Rozanolixizumab efficacy was maintained over symptom-driven cyclical treatment and multiple endpoints. Funding: UCB Pharma.

Disclosure: This study was funded by UCB Pharma. Detailed author disclosures will be provided in the oral/poster presentation

EPO-413

Attenuated total reflection-Fourier transform infrared spectroscopy (ATR-FTIR) in muscle diseases

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Background and aims: Inherited muscle diseases are a heterogeneous group of clinical conditions, characterized by histological and functional abnormalities of skeletal muscle. Attenuated Total Reflectance (ATR) is one of the sampling technologies used for infrared spectroscopy and, as a rapid and non-destructive technique, it is increasingly used in different biological applications. The aim of this study was to evaluate whether the biochemical profile determined by the ATR-Fourier transform infrared (FTIR) spectroscopic technique would allow to distinguish patients affected by late-onset Pompe disease (LOPD), Becker muscular dystrophy (BMD), limb-girdle muscular dystrophies (LGMD), and healthy subjects (HS).
Methods: A total of 40 participants were included: 11 LOPD, 10 BMD, 10 LGMD, 9 HS. For ATR-FTIR, muscle samples were cut at 10 µm in cross-section and placed onto diamond/ZnSe crystal for spectral analysis.
Results: The results obtained show that the spectroscopic fingerprint embeds sufficient information to allow a correct classification of the majority of participants in three groups: dystrophic (BMD and LGMD) and metabolic (LOPD) myopathies, healthy subjects (accuracy 88.4±7.1%). The ATR-FTIR analysis was also effective in classification rates using a two-class model: LOPD vs LGMD (accuracy 95.7±3.2%), LOPD vs BMD (accuracy 82.9±4.6%) and LOPD vs BMD+LGMD (accuracy 93.4±3.0%).
Conclusion: In conclusion, our data suggest that ATR-FTIR profile is a reliable diagnostic biomarker for LOPD, BMD and LGMD. Future directions will include evaluating its role as a prognostic biomarker in these genetic diseases, also analyzing biofluids, and the ability of this technique to shed light on the underlying pathogenic mechanisms.
Disclosure: The authors declare no conflict of interest.

EPO-414

A case of late-onset Congenital Myasthenic Syndrome associated to PREPL heterozygotic mutation

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Background and aims: We report the first case of a late-onset CMS associated with a heterozygous missense variant in Prolyl-Endopeptidase-Like (PREPL) gene.

Methods: Biochemical tests, muscle MRI, electrodiagnostic testing, muscle biopsy and NGS.
Results: A short 52-years-old Italian male with clinical onset in the first decade with impaired ocular motility and diplopia. From third decade he developed bilateral eyelid ptosis, slowly progressive fatigability and weakness in the upper and lower limbs. Neurological examination showed bilateral ophthalmoparesis, shoulder-girdle hypotrophy and weakness, mild weakness of iliopsoas, rectus femoris and hamstring muscles and reduced ROTs. Fatigability tests were positive. CPK was normal. Electrodiagnostic testing showed a pathological repetitive nerve stimulation, a pathological single fiber EMG finding and a myopathic pattern on EMG with normal nerve conductions. The dosage of anti-AChR-Abs, anti-MuSK-Abs and anti-LRP4-Abs resulted negative and also the chest CT. Muscle MRI showed no significant changes. Muscle biopsy showed a slight myopathic changes (marked variability in size, nuclear centralizations and a prevalence of type I fibers). CMS was suspected and we started Pyridostigmine with benefit. We performed whole-exome sequencing and found a heterozygous missense variant in the PREPL gene: c.473T>C (p.Ile158Thr).
Conclusion: PREPL deficiency is a rare autosomal recessive inherited congenital myasthenic syndrome characterized by neonatal hypotonia, feeding problems, neuromuscular symptoms and growth deficit. In almost all cases is caused by biallelic deletion/duplication in PREPL gene. However, the function of this gene remains unknown. In our patient we found only one PREPL mutation, which might explain his clinical picture of CMS with a milder and later clinical expression.
Disclosure: Nothing to disclose.

Headache 3

EPO-415

Patients with Suspected Idiopathic Intracranial Hypertension: Is there a Reliable Score to Predict the Opening Pressure?

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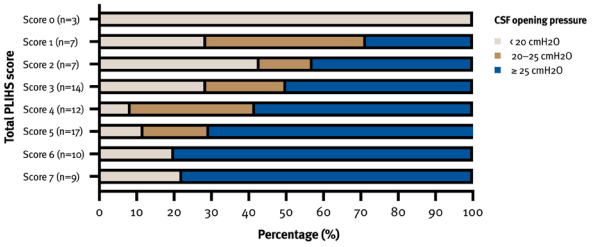
Background and aims: The Pre-Lumbar Puncture Intracranial Hypertension Scale (PLIHS) was reported to identify patients with suspected idiopathic intracranial hypertension (IIH) and high likelihood of pathologically raised opening pressure (≥25cmH2O). However, external validation is missing.
Methods: Patients from the Vienna IIH database who underwent diagnostic lumbar puncture for suspected IIH were applied the PLIHS (papilledema [Frisén grade II or higher], tinnitus, empty sella sign, distension of perioptic subarachnoid space, BMI ≥30; range 0–7; cut-off ≥3 points).
Results: We included 79 patients (87.3% female, mean age 36.0 years [12.2], median BMI 31.2 [27.5–37.1]), with 58.2% having opening pressure of ≥25cmH2O. Median PLIHS score was 4 (range 0–7), and it differed between patients above and below 25cmH2O (5 [1–7] vs. 3 [0–7]; p=0.001). AUC for predicting opening pressure ≥25cmH2O was 0.71 (95% CI 0.60–0.83) and did not differ from the reported one (0.84, 95% CI 0.78–0.90)1. Observed and reported sensitivities (89.1% vs. 87.4%), NPV (70.6% vs. 78.6%) and PPV (66.1% vs. 76.4%) were comparable, whereas observed specificity was lower (36.4% vs. 61.7%; p=0.029). PLIHS ≥3 points was associated with a nearly 5-fold increased risk for ≥25cmH2O (OR 4.69; 95% CI 1.46, 15.07; p=0.010), while from single PLIHS parameters only papilledema (OR 5.08; 95% CI 1.93, 13.36; p<0.001) and BMI ≥30 (OR 3.40; 95% CI 1.32, 8.79; p=0.012) were associated with elevated opening pressure.



Distribution of total PLIHS score in relation to CSF opening pressure.

Conclusion: In patients with suspected IIH, the PLIHS displays only moderate diagnostic accuracy with low specificity. It could potentially be improved by adding quantitative measures (OCT, orbital ultrasonography).
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

EPO-416

CLUSTER HEADACHE DECREASES LIFE EXPECTANCY: A 40-YEAR LONGITUDINAL STUDY

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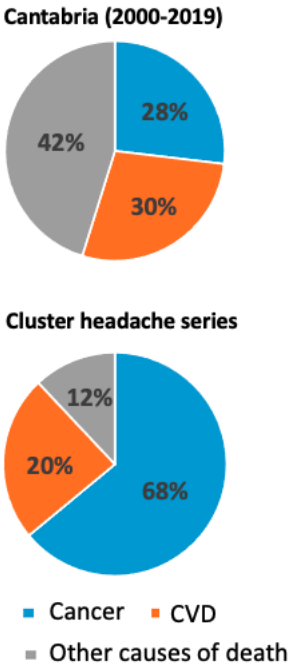
Background and aims: Cluster headache is the most frequent trigeminal-autonomic headache and one of the most disabling pains that exist. Patients affected by this entity frequently present unhealthy lifestyle habits. Given its relatively low prevalence, there are few data on the morbimortality associated with this pathology.
Methods: Our aim was to assess the morbimortality of cluster headache by calculating years of potential life lost (YPLL) in the patients included in a cluster headache registry of a tertiary hospital in Spain since 1974. Data were compared with those expected for the adjusted general population of our region according to the "Encuesta Nacional de Salud".
Results: There were 25 deaths among the 162 patients included. 21 of them (84%) lived fewer years than the expected mean for their sex and year of death, with a mean of 13.7 YPLL (SD 9.3).Cancer was the most frequent cause of death, and it was significantly more frequent among individuals with cluster headache than in the general population of our region (68% vs 28.5% p<0.001). Cardiovascular diseases were the second reason for death in this series. The percentage of male smokers was significantly higher among individuals with cluster headache than in the general population or our region (p=0.0095).

Subject	Age of death	YPLL	Cause of death
1	74	6	Cancer
2	78	2	Cancer
3	63	12	Cancer
4	72	8	Cancer
5	64	16	Suicide
6	69	11	Cancer
7	63	17	Cancer
8	72	8	Cancer
9	76	4	Cancer
10	56	24	Cancer
11	66	14	Cancer
12	77	8	Cancer
13	62	18	Cancer
14	75	10	Cardiovascular disease
15	69	11	Cancer
16	43	37	Drugs
17	50	30	Cancer
18	63	17	Cancer
19	76	4	Cancer
20	76	4	Cancer
21	59	26	Cardiovascular disease

YPLL and cause of death of patients who died prematurely in our series



Causes of death in our region (Cantabria) and ir our cluster headache series

Conclusion: Cluster headache patients who died of our series presented an average of almost 14 YPLL, mostly due to cancer followed by cardiovascular disorders. Tobacco could play an essential causal role, so it is essential to establish measures aimed at controlling unhealthy lifestyle habits in this population since the time of diagnosis.
Disclosure: Nothing to disclose.

EPO-417

Clinical predictors of good outcome in refractory chronic cluster headache treated with occipital nerve stimulation

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Background and aims: Occipital nerve stimulation (ONS) is a surgical treatment with good clinical evidence for the treatment of refractory chronic cluster headache (rCCH). However, the irregular response rate reported in different studies, and the associated cost make it necessary to investigate predictors of response.
Methods: We conducted a cross-sectional study through a review of the medical records of rCCH patients in our Headache Clinic. Epidemiological, clinical, and outcome variables were described.
Results: Twenty rCCH patients were treated with ONS. A good clinical outcome (at least three severe attacks per week that impact quality of life despite preventive or symptomatic treatment) was observed in 35.0% (7/20). Headache comorbidity, history of alcohol consumption or opioid use, and comorbid psychiatric disorders did not differ between patients with good and poor outcome after surgery. Age of onset, diagnostic delay, and time to surgery was also similar. Patients with good outcome presented less frequently a sense of restlessness or agitation (71.4% vs 100%, p=0.042), seasonal exacerbations (0.0% vs 61.5%, p=0.005), active tobacco use (50.0% vs 100%, p=0.021) and comorbid pain conditions such as fibromyalgia or chronic pain of traumatological origin (0.0% vs 46.2%, p=0.032).
Conclusion: Some clinical characteristics such as the absence of ictal restlessness and seasonal exacerbations may be related to a good outcome after ONS surgery in rCCH patients. Comorbid chronic pain conditions could be related to poor outcome, such as active tobacco use. Comorbidity with other headache disorders, opioid abuse, and diagnostic delay were not associated with poor outcome.
Disclosure: JA Membrilla has received honoraria as a consultant and speaker for TEVA and Novartis. Lilly, TEVA and Novartis have funded JA Membrilla's research and teaching activities. Boston Scientific, Lilly and TEVA have collaborated with JA Membrilla for his registration at scientific meetings.

EPO-418

Chronic cluster headache: description of epidemiology, clinical features, and treatment in a tertiary hospital

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Background and aims: Cluster headache (CH) is a relatively rare primary headache disorder in which large series of the chronic form are lacking. In this study, we aimed to describe the characteristics of chronic CH (CCH) patients.
Methods: We conducted a cross-sectional study through a review of the medical records of CCH patients in our Headache Clinic. Epidemiological, clinical, treatment, and outcome variables were described.
Results: From a series of 87 CH patients, 34 (39.1%) had CCH. Women represented 35.3% (12/34). Diagnostic criteria of refractory CCH (as defined by the European Headache Federation Consensus statement) were met in 76.5% (26/34). The mean age at diagnosis was 38.0 (SD 11.8), with a median diagnostic delay of 4.5 years (1.0-9.5). All patients underwent verapamil and topiramate treatment, being discontinued in 50.0% (17/34) in both cases. Lithium was used in 67.7% (23/34) and discontinued in 78.3% (18/23). OnabotulinumtoxinA was initiated in 85.3% (32/34) but discontinued in 46.9% (15/32). Most treatment discontinuations were due to inefficacy. Occipital nerve stimulation (ONS) was implanted in 58.8% (20/34), with 45.0% (9/20) remaining active. Further data on pharmacological and neurosurgical therapies are described. At the date this work was conducted, 55.9% (19/34) had poor clinical outcomes (having at least three severe attacks per week). In the remaining 44.1% (15/34), ONS was the treatment that achieved improvement in most cases (46.7%, 7/15).
Conclusion: CCH is not uncommon in some Headache Clinics, meeting refractoriness criteria in most cases. Half of the patients have poor prognosis, with ONS being the treatment with the best outcomes.
Disclosure: JA Membrilla has received honoraria as a consultant and speaker for TEVA and Novartis. Lilly, TEVA and Novartis have funded JA Membrilla's research and teaching activities. Boston Scientific, Lilly and TEVA have collaborated with JA Membrilla for his registration at scientific meetings.

EPO-419

Neck pain and migraine: clinical characterization of an often overlooked symptom

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Background and aims: Neck pain is increasingly recognized as a symptom which often accompanies migraine attacks. It is, however, rarely listed among the classical migraine symptoms. We aim to describe the relationship between migraine and neck pain: its prevalence, timing within the attack, severity relatively to other symptoms, and efficaciousness of abortive medications in treating this symptom.
Methods: Questionnaires were distributed in a headache clinic after informed consent was obtained. All patients were 18 years old or older and had a diagnosis of episodic or chronic migraine with or without aura according to ICHD-III. Demographic and clinical information was collected. Standard descriptive and inferential statistics were employed.

Results: Fifty patients were included, 86.0% female, with a mean age of 44.7 ± 12.7 years, 38.0% of which fulfilled criteria for migraine with aura. Average number of migraine attacks per month was 9.4 ± 7.2 days and 64,0% used some preventive treatment. 60.0% of all patients reported neck pain as one of their symptoms. Of these, 50.0% rated it as one of their three most bothersome symptoms, 53.3% reported neck pain onset to be simultaneous with headache and 73.3% noticed an improvement when using abortive medication. Neck pain prevalence did not differ between the groups diagnosed with migraine with and without aura (68.4% vs 54.8%, p=0.341).
Conclusion: Neck pain is a frequent and bothersome symptom of migraine, even if often overlooked by physicians. Direct inquiry about this symptom may help us to better understand the migraine burden and improve the quality of life of patients.
Disclosure: Nothing to disclose.

EPO-420

HEADWORK a tool for monitoring MABs efficacy on work disability in migraine patients

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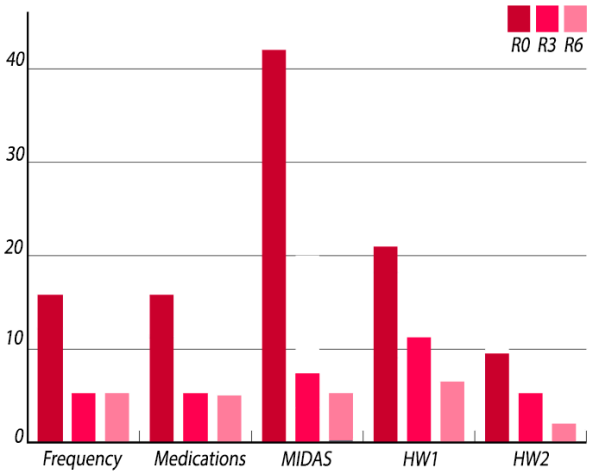
Background and aims: The efficacy of Monoclonal antibodies (MABs) is generally assessed with disease related metrics, but is crucial to evaluate the impact on the global burden of migraine. HEADWORK (HW) is a tool, developed to assess the work disability of migraineurs. Aim of this study was to test HW on migraine patients treated with MABs.
Methods: We enrolled 69 patients treated with MABs at the Headache Centres of "C.Besta" (Milan) and "C.Mondino" (Pavia). They were assessed with the HW questionnaire at baseline and at the 3rd (M3) and 6th month (M6) of treatment. HW questionnaire consists: "Work-related difficulties" (HW1); "Factors contributing to work-related difficulties" (HW2).
Results: Population: 15 M and 54 F, mean age (49.5y±8.6), mean age at onset of disease (18y±7), mean duration of disease (34y±11.6). We observed a marked and consistent reduction in 'classical' indicators: monthly migraine days (15±5.7 at baseline, 5±5.8 at M3, 6±6.2 at M6), medications per month (15±8.7 at baseline, 5±12.1 at M3, 6±6.6 at M6), MIDAS (41±43.2 at baseline, 6.5±11.3 at M3, 5±13 at M6), HIT-6 (66±2.8 at baseline, 59±8.7 at M3, 59±8.2 at M6). HW scores paralleled: HW1 (20±8.1 at baseline, 11±9 at M3, 7±8.2 at M6), HW2 (9±6 at baseline, 5±4.8 at M3, 3±3.8 at M6).



Results

Conclusion: Our data show that HW reveals a trend parallel to classic clinical indicators during MABs treatment. HW appears a suitable tool to assess migraine-related work disability in these patients.
Disclosure: Nothing to disclose.

EPO-421

Migraine patients need increased amounts of sleep during attacks to maintain neurological functioning

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Background and aims: There is a clear, but unexplained association between migraine and sleep. Migraine patients frequently describe increased sleep need during migraine attacks, and that sleep can ease the attack. In this study we investigated the effect of insufficient sleep in migraine, in order to explain why migraine patients have increased need for sleep during attacks.
Methods: Fifty-four migraine patients were examined both after two nights of eight-hour habitual sleep and two nights of four-hour restricted sleep. We recorded short interval intracortical inhibition (SICI), intracortical facilitation (ICF), and beta event related desynchronisation (beta-ERD) and synchronisation (beta-ERS). The effect of sleep condition and time after attack end or postictal versus interictal phase were evaluated in linear mixed models.
Results: SICI ($p = 0.041$) and beta-ERS ($p < 0.001$) were more reduced, and beta-ERD ($p = 0.002$) more increased after sleep restriction the shorter time that had elapsed since the previous attack. For the postictal phase within 24 hours after attack end specifically, SICI ($p = 0.013$) was more reduced and ICF (ICF 8, $p = 0.003$; ICF 10, $p = 0.021$) more increased after sleep restriction.

Conclusion: Insufficient sleep during or shortly after migraine attacks result in a dysfunction in GABAergic inhibition. This inhibitory alteration resembles that previously described in healthy subjects after total sleep deprivation. Thus, migraine patients have increased need for sleep during migraine attacks to maintain normal neurological functioning.

Disclosure: The authors declare that there is no conflict of interest relevant to this abstract.

EPO-422

Migraine-related stigma and its association with seeking care and migraine disability: Results from OVERCOME (EU) Study

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Background and aims: Migraine is a debilitating neurological disease associated with several consequences including migraine-related stigma. Here, we describe the frequency of migraine-related stigma and its association with seeking care, quality of life (QoL) and migraine-related disability.

Methods: The ObserVational survey of the Epidemiology, tReatment and Care Of MigrainE Europe [OVERCOME (EU)], is a cross-sectional, population-based survey (Oct-2020 to Feb-2021), conducted in Germany and Spain, as part of an overarching study program including the US and Japan. As part of the survey, patients reported their experiences with migraine-related stigma and were categorised, based on responses, to yes (sometimes/often/very often) or no (rarely/never). Results are summarised with descriptive statistics.

Results: OVERCOME (EU) respondents (N=20,756) had a mean age of 40.4 years, 60.3% were female. Migraine-related stigma was experienced by 32.6% (n=6760; Fig.1A). This cohort were more likely to hesitate seeking care (48.3%) than those who rarely/never experienced migraine-related stigma (30%; Fig.1B). Experiencing migraine-related stigma was associated with poorer QoL (MSQ-role function-restrictive 52.3[20.3] vs 68.0[20.6]) and higher headache days/month (HDs/M; mean[SD]=4.7[5.5] vs 3.5[4.5]; Figs.2). A greater proportion of those with migraine-related stigma compared to those without reported 15+ HDs/M (7.2% vs 4.1%), severe disability (MIDAS IV score=21+: 34.9% vs 16.0%) and severe interictal burden (MIBS Score=5+: 66.8% vs 34.2%; Figs.1B, 3).

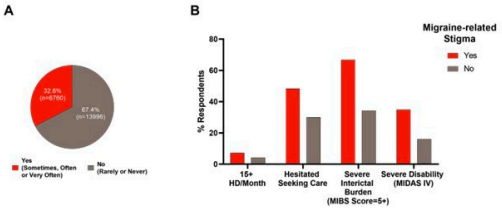

Figure 1. Proportion of respondents who experienced migraine-related stigma (A) and associated migraine characteristics (B). N=20,756. HD/month: headache days per month; MIBS: Migraine Interictal Burden Scale; MIDAS: Migraine Disability Assessment Score; N: number of total respondents; n: number of respondents per group.

Figure 1. Proportion of respondents who experienced migraine-related stigma (A) and associated migraine characteristics (B).

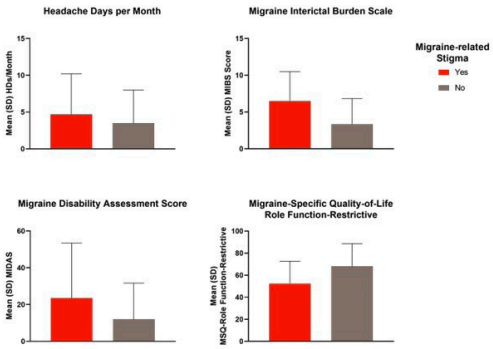

Figure 2. Migraine characteristics of OVERCOME (EU) survey respondents categorised based on experience of migraine-related stigma (yes or no). MIBS: Migraine Interictal Burden Scale – Score 0 = None; Score 1-2 = Mild; Score 3-4 = Moderate; Score 5+ = Severe. MIDAS: Migraine Disability Assessment Score – MIDAS I (score 0-5) = Little or No Disability; MIDAS II (score 6-10) = mild disability; MIDAS III (score 11-20) = moderate disability; MIDAS IV (score 21+) = severe disability; HD/Month: headache days per month. MSQ-RFR: Migraine-Specific Quality of Life Questionnaire-Role Function-Restrictive - Scale=0-100, where scores approaching 100 indicated better quality of life.

Figure 2. Migraine characteristics of OVERCOME (EU) survey respondents categorised based on experience of migraine-related stigma (yes or no).

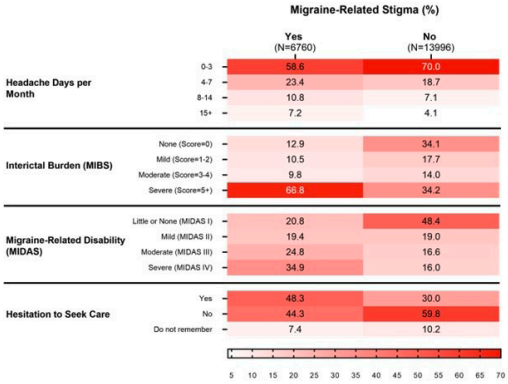

Figure 3. Distribution of respondents within migraine characteristic groups based on experience of migraine-related stigma. Heatmap displays percentage of respondents who experienced migraine-related stigma (yes) or rarely/never experienced migraine-related stigma (no) within specified groups relating to migraine characteristics. MIBS: Migraine Interictal Burden Scale; MIDAS: Migraine Disability Assessment Score; N: total number of respondents.

Figure 3. Distribution of respondents within migraine characteristic groups based on experience of migraine-related stigma.

Conclusion: In OVERCOME (EU), experiencing migraine-related stigma was associated with hesitation seeking care, higher HDs/M, poorer QoL and severe disability – specifically interictal burden. Migraine-related stigma remains a prevalent issue, further understanding and action are required to reduce its occurrence and improve patient QoL.
Disclosure: DN, AZ, SG and GD are employees and minor shareholders of Eli Lilly and Company. JP reports: serving on advisory boards for Allergan-Abbvie, Amgen-Novartis, Lilly, and TEVA; serving as speaker / on speaker boards for Allergan-Abbvie, Amgen-Novartis, Eli Lilly and Company, and TEVA; grant support for research or education from Allergan and Lilly; and serving on the editorial board for Headache. SE reports: grant support from Novartis, Teva, Perfood, Lilly and Lundbeck; serving as speaker / on advisory boards for Lilly, Lundbeck, Novartis, Perfood and Teva.

EPO-423

Evolution of migraine attack duration

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Background and aims: Migraine is a prevalent neurological disorder characterized by disabling headache attacks. Although headache days/per month is well studied among migraine patients; evolution of attack duration (hours) along in years is not fully investigated to our knowledge. There is lack of study investigated attack duration related factors and tendencies particularly among adults.
Methods: We hypothesized that due to accumulated attacks through years and decades, migraine attack duration could be prolonged. We grouped patients according to attack duration (short (4-12 hours), medium duration (13-24 hours) and long duration (>24 hours)) and evaluated related factors and tendencies.
Results: The study group consisted 694 patients. Long attack duration (>24 hours) group were significantly older ($p<0.001$). We observed a significant lineer association with increasing age and attack duration. Longer attacks observed more common at females ($p=0.007$). Headache days frequency per month were similar between groups. Headache history (for months) were significantly differed for long attack group ($p<0.001$). This feature also showed a lineer association similar to age of patients (median values for groups 60, 72, 120 moths respectively). The long attack groups' pain intensity was significantly higher than others ($p<0.001$).
Conclusion: This study reveals migraine attack duration is significantly changing with age of sufferer and disease course. This novel finding supports attack duration evolution throughout the life. This is the first study explicitly reveals attack duration's association with patient age and disease duration among adults.
Disclosure: This study reveals headache attack duration is evolutioning with accumulated attacks. This promising finding could lead to new studies and further studies are needed.

EPO-424

Effectiveness and safety of CGRP-mAbs in migraine related to mitochondrial diseases

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Background and aims: Migraine affects nearly 55% of patients with mitochondrial disease (MD), with attacks which are difficult to treat compared to other migraine patients. Migraine mechanisms, characterized by the imbalance between brain demand and energy resources, may be shared also by patients with MD, where dysfunctional glucose metabolism works as a key pathophysiological substrate for migraine attacks. To date, migraine response to monoclonal antibodies acting on CGRP (CGRP-mAbs) in patients with MD is unknown.
Methods: Monthly subcutaneous galcanezumab 120 mg have been administered as preventive treatment in two women with genetically proven neuropathy, ataxia, and retinitis pigmentosa syndrome (NARP) and progressive external ophthalmoplegia (PEO), suffering from chronic migraine, respectively without and with medication overuse. Patients underwent a monthly follow-up for six months to assess galcanezumab effectiveness, safety and tolerability.
Results: After the third Galcanezumab administration, both reported a significant improvement in monthly migraine days (from an average of 20 to 2 migraine, and from an average of 22 to 14 respectively in the patient with NARP and PEO), headache intensity, number of pain-killers intake and pain-killers response. We cannot exclude that CGRP-mAbs may act not only peripherally modulating CGRP-induced meningeal vessels vasodilation and neurogenic inflammation but also within the trigeminal ganglion, modulating, through CGRP pathway inhibition, the dysfunctional neuronal glycolytic metabolism.
Conclusion: CGRP-mAbs could represent an effective and safe preventive therapeutic strategy in patients with genetically proven mitochondrial disease complaining migraine attacks. Future studies with a larger sample of patients will further support our observations.
Disclosure: Nothing to disclose.

EPO-425

Serum alpha and beta-CGRP levels in chronic migraine patients before and after CGRP monoclonal antibodies

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Background and aims: To analyse the evolution of alpha and beta-CGRP circulating levels throughout the treatment with CGRP monoclonal antibodies (mAb) in chronic migraine (CM) patients.
Methods: We recruited CM patients beginning mAb treatment along with sex and age paired healthy controls (HC). Blood was extracted before initiation of mAb, at two-weeks (M0.5) and three months (M3) after first dose in CM, always in migraine-free periods, and once for HC. Determinations of alpha and beta-CGRP serum content were carried out using ELISA kits specific for detection of each isoforms.
Results: We assessed 96 CM and 78 HC. Baseline alpha-CGRP levels were significantly (p=0.019) elevated in CM (54.6±32.5 pg/mL) compared to HC (45.2±27.5 pg/mL) and normalized over the course of mAb treatment (M0.5: 47.4±27.8 pg/mL; M3: 46.0±29.0 pg/mL) (Fig. 1). Absolute decrease of alpha-CGRP throughout the treatment significantly correlated with the decrease in monthly headache days (p=0.02) (Fig. 2). Negative modulation of alpha-CGRP significantly associated with positive treatment outcome scores at the Patient Global Impression of Change scale (p<0.01) (Fig. 3) and with stop fulfilling analgesic overuse criteria (p<0.01). Beta-CGRP levels did not differ at baseline between CM patients (4.6±3.5 pg/mL) and HCs (4.5±2.6 pg/mL) nor was modulated by mAb treatment (M0.5: 4.6±3.1 pg/mL; M3; 4.5±2.9 pg/mL).

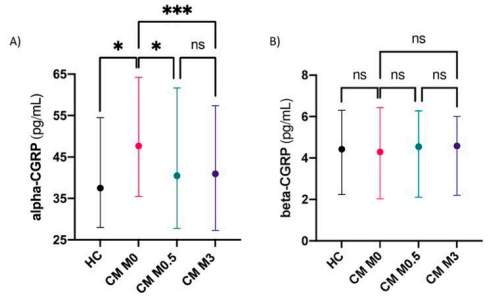

Figure 1.. Circulating levels of A) alpha-CGRP and B) beta-CGRP in healthy controls (HC) and patients with CM at baseline (CM M0), at two-weeks (CM M0.5) and at three-months (CM M3) after first dose of mAb treatment.

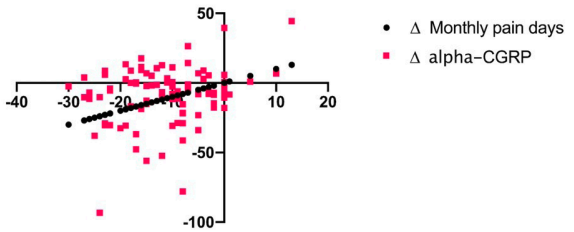

Fig. 2. XY plot showing the correlation between Δ monthly pain days (x axis) and Δ alpha-CGRP in pg/mL (y axis)

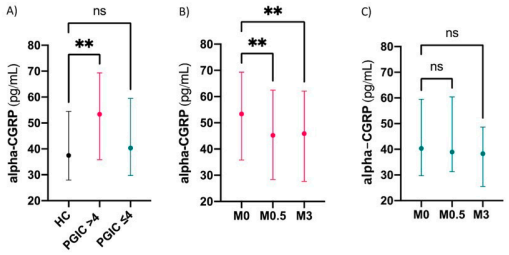

Fig. 3. Circulating levels of alpha-CGRP in: A) healthy controls (HC), patients with CM with a PGIC score >4 (PGIC>4) and those with a score >4 (PGIC>4) at baseline. B) patients with CM with PGIC score >4 at baseline (CM M0), at two-weeks (CM M0.5)

Conclusion: Treatment with mAB, regardless of its target, is able to progressively normalize basally increased alpha-CGRP levels in CM and this effect correlates with efficacy measures, which supports a role of this neuropeptide as the first CM biomarker.
Disclosure: This work was supported by grants from the Instituto de Salud Carlos III (PI20/01358), IDIVAL (INNVAL 20/25) and Lilly grant I5Q-NS-O002.

EPO-426

Clinical phenotypes in chronic migraine: Principal component analysis in the Italian National Headache Registry (RICe)

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Background and aims: The clinical heterogeneity of migraine raises the need of phenotypical classification to support the diagnostic-therapeutic process. This could be particularly important when considering chronic migraine (CM) and medication overuse headache (MOH) due to their high socio-economic impact. Migraine diagnostic criteria (ICHD-3) mainly focus on attack characteristics; this study aims to use a nationwide database to refine the characterization of patients subgroups.
Methods: A principal component analysis (PCA) was performed on 1238 patients diagnosed with migraine with or without aura, CM or MOH and included in the Italian Registry of Headaches (RICe Study) between April 2020 and March 2021.
Results: We extracted 3 components from categorical variables: the first inversely correlated the diagnosis of CM and MOH with the presence of migraine diagnostic criteria, while in the second one they were directly correlated, describing a group of "typical" patients; the initial localization of pain and the presence of high pain intensity and allodynia were associated in the third one. Considering

the quantitative variables, 2 components were extracted: the first related to age, BMI and monthly migraine days (MMD); the second was correlated with pain intensity.
Conclusion: A group of patients suffering from CM or MOH would be less identifiable through the migraine diagnostic characteristics, resulting in problems of underdiagnosis. Another group presents a significant association between BMI, age, and MMD, thus revealing possible risk factors for chronification. Further studies could evaluate the association between these phenotypes and other relevant characteristics (impact on daily life and on therapeutic efficacy).
Disclosure: No disclosures to declare.

EPO-427

Patient-reported outcomes and burden in resistant and refractory migraine: results from the REFINE study

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Background and aims: We assessed the burden of resistant (RES) and refractory (REF) migraine – defined according to the 2020 European Headache Federation criteria – in a real-world setting, according to patient-reported outcomes (PROMs).
Methods: The REFINE study is an observational, multicenter, international study which aim is to compare baseline characteristics, comorbidities, and PROMs of patients with RES, REF, and non-resistant and non-refractory migraine (NRNR).
Results: We included 612 patients with a median age of 46 years (IQR=37-55), of which 340 (55.6%) with NRNR migraine, 228 (37.3%) with RES, 44 (7.2%) with REF. Individuals with RES and REF migraine reported higher number of monthly migraine days compared with those with NRNR (median=10, IQR=5-16 vs. median=15 IQR=10-20 and median=16, IQR=10.5-25; p<0.001). In RES and REF groups, PROMs also revealed higher presence of anxiety (HADS_A scale; p<0.001) and depression (HADS_D scale; p<0.001) symptoms and poorer sleep quality (ISI score; p<0.001) compared with NRNR. RES and REF individuals reported higher impact of migraine on daily life (HALT score; p≤0.001) when compared to NRNR subjects (table1).
Conclusion: RES and REF are associated with relevant migraine burden, confirmed by the migraine frequency and PROM scores.
Disclosure: Nothing to disclose.

	Total (n = 612)	Non-resistant and non-refractory migraine (n = 340; 55.6%)	Resistant migraine (n = 228; 37,3%)	Refractory migraine (n = 44; 7.2%)	p-value
HIT-6 score, median (IQR)	62 (57-66)	62 (57-66)	65 (61-68)	66 (61-70)	≤0,001
HALT score, median (IQR)	31 (13-65)	20 (7-46)	50 (23-81)	60 (31-115)	≤0,001
HADS score - anxiety symptoms, median (IQR)	8 (5-11)	7 (4-10)	9 (5-12)	9 (5-12)	≤0,001
HADS score - depression symptoms, median (IQR)	6 (3-9)	5 (2-8)	8 (4-10)	10 (6-13)	≤0,001
ISI score, median (IQR)	9 (4-15)	8 (3-13)	11.5 (4-16)	13 (7-17)	0,006

Table 1. Patients reported outcomes measures (PROMs) scores reported as medians (IQR).

Neuroimmunology 3

EPO-428

Antineuronal antibodies of unknown significance: assesing risk of cancer in a Spanish reference laboratory cohort

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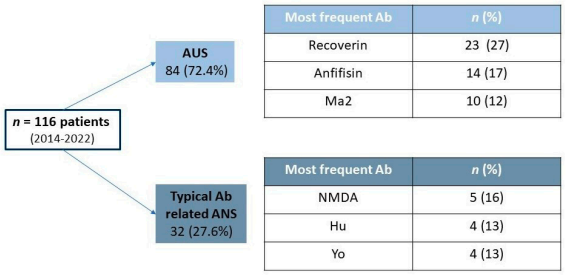
Background and aims: Widespread use of commercial assays has increased the detection of autoantibodies (Ab) related to autoimmune neurological syndromes (ANS). However, they also often reveal antibodies of unknown significance (AUS), apparently not related to a suspected ANS. We aim to describe the oncological risk of these cases.

Methods: Retrospective study including patients with positive results for intracellular or cell surface Ab detected in serum and/or cerebrospinal fluid in a reference laboratory of a Spanish tertiary hospital between 2014-2022. AUS were defined as the presence of Ab in the absence of a concordant ANS. Ab were classified into high/intermediate/low-risk of paraneoplastic neurological syndromes (PNSs) according to updated Graus criteria. Clinical records were reviewed for any tumour detection at acute phase and after two-year follow-up. We compared tumour detection rate between patients with AUS and those with typical Ab-mediated neurological syndromes.

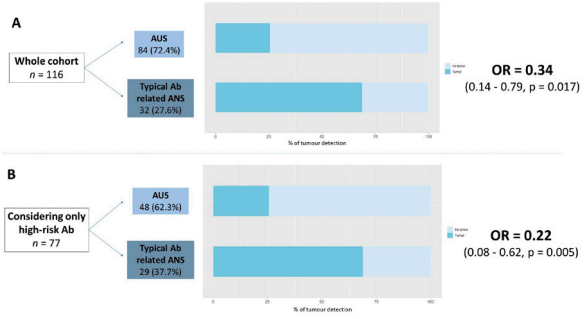
Results: We included 116 patients (54.3% men, 61.6±17.5 years). The most frequent Ab was anti-Recoverin (20.7%). Fifty-eight patients (50%) had a high-risk Ab. The most frequent syndrome was autoimmune encephalitis (9.5%). Twelve patients (10.3%) had a high paraneoplastic-risk syndrome, and 77 (66.4%) low-risk or non-autoimmune disorders. We identified 83 (71.6%) patients with AUS. A novel cancer was detected in 37.9% of patients, being less frequent in patients with AUS (OR=0.34, p=0.017). When only high-risk Ab were considered, AUS also presented less tumour association than remaining Ab (OR=0.22, p=0.005).

Paraneoplastic risk	Type of antibody	Total (*n*)
High	Yo	9
	Sox1	3
	Tr	3
	Hu	6
	CV2	9
	Anfifisin	15
	Ma2	12
	Ri	1
Intermedium	NMDA	6
Low	CASPR2	2
	GAD65	7
	LGI1	5
Undetermined (not included in Graus criteria)	Recoverin	24
	Titin	9
	Zic4	5

Distribution of antibodies in our cohort, classified according to Graus criteria into high risk for paraneoplastic neurological syndromes (>70% with an underlying malignancy), intermedium (30-70%), and low risk (<30%).



Most frequent antibodies found in each group. AUS: antibodies of unknown significance. Ab: antibody. ANS: autoinmune neurological syndromes.



Tumour detection rate in each group: in the whole cohort (A), and considering only high-risk antibodies (B).

Conclusion: In our cohort, AUS were less likely to be related to cancer development. Ab testing should be directed by clinical presentation to avoid misdiagnosis.

Disclosure: Nothing to disclose.

EPO-429

Epigenetic characterization of monocyte-derived microglia (MDMi) differentiation and ATP-driven innate immune memory

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Background and aims: Microglia are the brain's immune regulators. The dysregulated microglia activation observed across neurologic diseases may result from consecutive stimuli, in which a previous insult would pre-condition subsequent responses. Purinergic signalling is considered to be implicated in neuropathology and high ATP levels have been shown in settings like epilepsy. The functional characterization of human microglia is ethical and technically challenging. The MDMi in vitro model is promising due to its speed, scalability, low-cost, and replication of main microglial features. We developed an MDMi culture and investigated ATP-driven preconditioning in microglia activation.

Methods: Peripheral blood monocytes were from healthy donors using CD14+ microbeads. MDMi cells were obtained by incubating monocytes in serum-free conditions supplemented with cytokine cocktail. MDMi were treated with ATP and posteriorly LPS. Cells were characterized by optic microscopy, flow cytometry, RT-PCR, ELISA and DNA methylation using Infinium MethylationEPIC BeadChips.

Results: MDMi showed elongated and ramified morphology and upregulation of canonical markers at day 7. Differentially methylated positions (DMPs) between MDMi and monocytes were enriched for binding motifs of microglia lineage transcription factors, like PU.1 and IRF8. MDMi cells treated with LPS showed higher pro-inflammatory activation when previously conditioned with ATP. Such was accompanied by DNA methylation reprogramming of immune-related pathways, adrenergic receptor binding and nucleotide phosphorylation.

Conclusion: MDMi carry microglial epigenetic microglial traits, which validates it as a valuable model to study microglia. Unbalanced microglia activation may be modulated by an ATP-driven epigenetic reprogramming. A better characterization of these mechanisms would be a step forward in understanding microglia's role in neuropathology.

Disclosure: Nothing to disclose.

EPO-430

Prevalence, clinical profiles, and prognosis of Stiff-person syndrome in Japanese nationwide survey

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Background and aims: To elucidate epidemiological, clinical, immunological profiles, and treatment of stiff-person syndrome (SPS) in Japan.

Methods: A nationwide epidemiological survey was conducted using an established method. Data processing sheets were randomly sent to all specialist departments of internal medicine, neurology, pediatrics, psychiatry, and neurosurgery throughout Japan to identify patients with SPS who were seen between January 2015 and December 2017.

Results: The estimated number of patients with SPS was 257 (95% confidential interval [CI]: 161-354), and the prevalence was 0.2 per 100,000 (95% CI, 0.13-0.28). Detailed clinical profiles were available for 55 patients. The median age at onset was 51 years (range, 7–83 years) and 41 (75%) were female. Of these, 58% had Classic SPS, 25% had stiff-limb syndrome (SLS), and 18% had SPS-plus. Autoantibodies were positive in 68% patients; glutamic acid decarboxylase-65 (GAD65) antibodies in 44%, α1 subunit of glycine receptor antibodies in 20%, and γ-aminobutyric acid-B receptor antibodies in 4%. After immunotherapies, the median modified Rankin score (mRS) was 2 at the last visit. The coexistence of type 1 diabetes mellitus was independent risk factor for poor outcome (mRS $\geq$3) in GAD65 -positive patients (Odds ratio, 16.0, 95%CI 2.8–139.9, p=0.001).

Conclusion: This study provides current epidemiologic and clinical status of SPS in Japan. GAD65 antibodies were most frequent, however, their titers were not correlated with the response to therapies. The outcome of SPS was generally favorable, but more aggressive immunotherapies may be necessary for patients associated with type 1 diabetes.

Disclosure: All researchers report no disclosures.

EPO-431

White matter alterations in a mouse model of anti-NMDAR encephalitis by active immunization

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Background and aims: Anti-NMDA receptor (NMDAR) encephalitis is a neurological disorder that associates with neuropsychiatric manifestations caused by antibody-mediated internalization of the receptor. Studies with advanced imaging show extensive changes in white matter integrity in most patients. Antibodies from patients have been shown to alter NMDAR function in cultured oligodendrocytes. Here, we aim to explore the pathogenic mechanisms of white matter alterations by active immunization.
Methods: 8-week-old female C57BL/6J mice were immunized at days 1 and 28 with 200 µg of the GluN1 356-385 peptide or saline along with AddaVax adjuvant and Pertussis Toxin. NMDAR antibodies in serum and CSF were determined by cell-based assays, and the effects of the antibodies were assessed with confocal brain tissue immunohistochemistry. Behavioural alterations were assessed with a standard panel of tests: Novel Object Location test (memory), Pre-Pulse Inhibition (psychotic-like behaviour), and Tail Suspension Test (depressive-like behaviour).
Results: Compared with control mice, those immunized with GluN1 356-385, showed decreased Myelin Basic Protein (MBP) clusters in the corpus callosum, as well as striatum and cerebellum white matter. These findings were associated with the presence of NMDAR antibodies and a significant decrease in synaptic NMDAR clusters in the brain. Accompanying symptoms included memory deficit, acute psychotic-like behaviour, and chronic depressive-like behaviour.
Conclusion: This model of active immunization causes alterations of the white matter and confirms previous studies with the model of passive transfer of patients' antibodies. The model will help to determine the immunobiology of the disease and how pharmacological interventions can be used as an adjuvant to immunotherapy.
Disclosure: J. D. receives royalties from Euroimmun for the use of NMDAR as an antibody test.

EPO-432

Immunomodulatory aspects of therapeutic plasma exchange in neurological disorders – a pilot study

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Background and aims: Plasma exchange (PLEX) represents a rescue therapy for autoimmune disorders. While used for several neurological indications, investigations on the immunomodulatory effects of PLEX have been sparse. We aimed to explore changes in antibodies, cytokines and lymphocytes associated with therapeutic PLEX.
Methods: We included 10 patients (3 women, average age: 55 ± 19 years) that underwent PLEX for various neurological autoimmune disorders between 2020 and 2022. We assessed various pathogen-specific antibodies, total immunoglobulin levels (IgM, IgA, IgG; IgG1/2/3/4), interleukin-6 concentrations (IL-6, pg/mL) and main lymphocyte subset counts (cells/µL) prior to PLEX (pre-PLEX), immediately after PLEX (post-PLEX) and four weeks later (follow-up/4wk). We calculated proportional changes of pathogen-specific antibody levels and absolute changes of total immunoglobulins, IL-6 and lymphocyte subsets referenced by their respective pre-PLEX baseline values.
Results: Pathogen-specific antibody levels were reduced by 86% ($p < 0.05$) post-PLEX and recovered to 55% ($p < 0.05$) at follow-up/4wk. Similar, total IgG (and subclasses 1-4), IgA and IgM were reduced by 86% ($p < 0.05$) post-PLEX and recovered to 80% ($p < 0.05$) after 4 weeks. We found no effects on B- and T-cell counts. The average IL-6 increased from 4.0 pg/ml (95% CI, 0.5 – 7.7) to 18.9 pg/ml (95% CI, 2.9 – 34.9, $p = 0.071$) at post-PLEX.

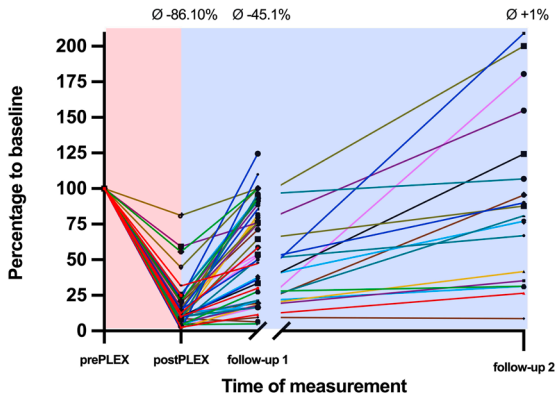

Fig. 1. Impact of PLEX on pathogen-specific antibody levels

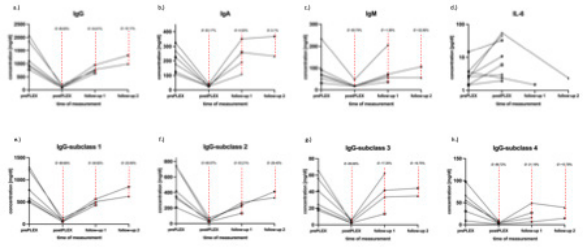

Fig. 2: Impact of PLEX on immunoglobulins IgA/IgM/IgG

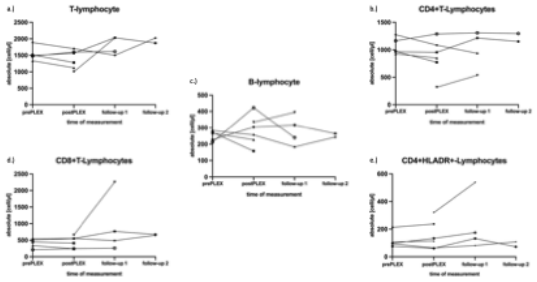

Fig. 3 Impact of PLEX on main lymphocyte subsets

Conclusion: PLEX effects a profound but transient reduction of circulating antibodies. While this indicates no loss of control for pathogens, it has also implications on the treatment strategy of the underlying autoimmune disorder. The impact on IL-6 needs further investigation.
Disclosure: Nothing to disclose.

EPO-433

Autoimmune Encephalitis and Long-Term Cognitive and Functional Outcomes

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Background and aims: Autoimmune encephalitis (AE) comprises a heterogeneous group of inflammatory brain diseases. The extent of dysfunction varies, and it may persist in the long-term. However, few studies have detailed the cognitive and functional outcomes of these patients.
Methods: We carried a single-centre observational cross-sectional study, including ≥18-yo patients diagnosed with EA both with autoantibodies and with definite seronegative limbic encephalitis, at a Portuguese tertiary centre (January 2007-December 2021). A neuropsychological evaluation and questionnaires to assess functional status were applied in a scheduled appointment. For cognitive scales, impairment was considered below 1.5sd from normative values.
Results: All 13 patients were independent according to the modified Rankin Scale, however, Functional Assessment Inventory in Adults and the Elderly identified functional impairment in 5 (38.5%). Only 4 patients (30.8%) had an entirely normal neuropsychological evaluation. Five patients (41.7%) showed cognitive impairment on MoCA. Seven patients (58.3%) showed impairment in at least one memory test; the same holds for executive functions. Older age at disease onset correlated with higher functional disability, lower MoCA, and higher verbal memory and executive impairment. Also, higher CSF protein counts correlated with impaired verbal memory and executive functioning tasks.
Conclusion: Although most times subtle, we found frequent multimodal impairment in this AE population, especially in older individuals. Disability and cognition ought to be systematically screened in this setting.
Disclosure: The authors declare no conflict of interest.

EPO-434

Characterization of Subclinical Spinal Cord and Optic Nerve MRI Lesions in the N-Momentum Trial

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Background and aims: Neuromyelitis optica spectrum disorder (NMOSD) causes inflammatory attacks on the optic nerve (ON), spinal cord (SC), and brain/brainstem. Subclinical MRI findings have unknown significance therefore we evaluated the frequency, prognosis, and response to inebilizumab (INEB).
Methods: Gadolinium-enhancing (Gd+)T1 and T2 weighted MRI of SC, ON, and brain/brainstem were performed at baseline and RCP end (Week 28) in participants without NMOSD attack. Serum glial fibrillary acidic protein (sGFAP) concentrations were determined using single-molecule array assay.

Results: 134 participants with full neuroaxis MRI and no NMOSD symptoms at RCP end, 20(15%) had asymptomatic Gd+T1-SC lesions, and 65(49%) had asymptomatic Gd+T1-ON lesions. Subclinical Gd+T1 lesions in the SC/ON were shorter in length(mm) than attack-related lesions: SC p=0.08, ON p<0.001. Total Gd+T1 and T2 subclinical SC-lesions were less frequent with INEB than Placebo at RCP end; mean(±SE): Placebo=0.74(0.50,1.09), INEB=0.27(0.20,0.35). The frequency of new subclinical SC and ON lesion formation decreased with continued INEB over the open-label period. More participants with subclinical T2-lesions in the SC (but not ON) had a 2-fold change increase in sGFAP from baseline vs. those without lesions, p<0.001. Subclinical Gd+T1 and T2 lesions in SC were associated with domain-specific attacks in the following year: Gd+T1, p<0.0001; T2, p=0.03.
Conclusion: Subclinical Gd+T1 ON lesions are more frequent than SC lesions. The total length of subclinical Gd+T1 ON/SC lesions was smaller than attack-associated lesions. The subclinical lesions predicted future attacks for the SC but not the ON. Both ON and SC lesion formation frequencies were reduced with repeated inebilizumab treatment.
Disclosure: FP Bayer, Biogen Idec, Merck Serono, Novartis, Sanofi Genzyme, Teva, Guthy-Jackson Char Found, German Res Council (DFG Exc 257), German Compet Network for MS, OCTIMS study comittee JLB MedImmune, Alexion, Antigenomycs, BeiGene, Chugai, Clene Nanomed, Genentech, Genzyme, Reistone, Roche, Imcyse, TG, Alexion, Novartis, NIH JJC Roche, UCB, Horizon HPH Bayer, Biogen Idec, Celgene Receptos, CSL Behring, GeNeuro, Genzyme, Horizon, MedDay, MedImmune, Merck Serono, Novartis, Roche, Sanofi, TG Thera HJK NRF of Korea, Aprilbio, Eisai, Alexion, Aprilbio, Altos Biologics, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll BioPharma, Handok, Horizon, Kolon LS, Medimmune, Merck Serono, Mitsubishi Tanabe, Novartis, Roche, Sanofi Genzyme, Teva-Handok, UCB KF AbbVie, Asahi Kasei, Biogen, Chugai, Eisai, Merck, Mitsubishi Tanabe, Novartis, Ono, Roche, Sumitomo Dainippon, Takeda, Teijin, UCB, Horizon, Ministry of Edu Sci and Tech of Japan, Ministry of Health, Welfare, Labour of Japan OA German Research Found (DFG), German Ministry of Edu and Res (BMBF), Bayer, Biogen, Genzyme, Horizon, Novartis, Teva, Almirall, MedImmune, Merck Serono, Roche BAC Alexion, Atara, Autobahn, Avotres, Biogen, Boston, EMD Serono, Gossamer, Hexal/Sandoz, Horizon, Immunic AG, Neuron23, Novartis, Sanofi, Siemens, TG Thera, Therini, Genentech DMC, KRP, MAS Horizon The study and analyses funded by Horizon.

EPO-435

Proteomic fingerprint to understand treatment response and long-term outcome in anti-NMDAR encephalitis

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Background and aims: Anti–N-Methyl-D-Aspartate receptor encephalitis (anti-NMDARE) is a neurological disorder caused by pathogenic antibodies affecting NMDA receptors. It is a life-threatening disease and many patients end up on the intensive care unit. Despite its severity, most patients ultimately improve with immunotherapy, albeit recovery is prolonged and often incomplete. Biomarkers to predict treatment response and outcome are scarce and their discriminative value is limited, making treatment decisions difficult and expert opinion only. We aim to 1) identify immunological pathways relevant in anti-NMDARE (apart from the antibodies), and 2) identify biomarkers to better predict treatment response and outcome.
Methods: We investigated the CSF proteome from 29 untreated anti-NMDARE patients using SomaScan, a proteomic platform able to detect ~1,350 proteins including low abundant proteins, and compared these to 15 healthy controls. Difference in expression was confirmed using Luminex. Pathway analysis was performed by String and Ingenuity.
Results: Preliminary results indicate that the expression of TNF sR-II and sL-Selectin was upregulated in anti-NMDARE (median 57,032 vs 17,487RFU and 106,482 vs 46,636RFU, respectively, both p<0.0001)), especially in those with a poor prognosis. Upregulation was confirmed by Luminex (median concentration 1,037 vs 135pg/ml and 11,600 vs 4,113pg/ml, respectively, both p<0.0001). This upregulation was joined by alterations in related pro-inflammatory cytokines (e.g. IL6) and chemokines (e.g. CXCL8) in anti-NMDARE patients.
Conclusion: The proteomic footprint identified pathways involved in the pathophysiology of anti-NMDARE, allowing testing of targeted biomarkers by easier, high-throughput methods. This proof-of-principle study opens the road towards better understanding of anti-NMDARE and development of tailored treatments for anti-NMDARE patients.
Disclosure: I do not have a conflict of interest.

EPO-436

Immunomodulatory effects of diroximel fumarate on T cells subsets during experimental autoimmune neuritis in Lewis rats

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Background and aims: Diroximel fumarate is an immunomodulatory drug, approved for the treatment of multiple sclerosis. In view of the limited therapeutic options for human polyneuritis, we used the animal model of experimental autoimmune neuritis(EAN) in the Lewis rat to study the effects of diroximel fumarate on autoimmune inflammation through T cells in the peripheral nervous system.
Methods: EAN was induced by immunization with the neuritogenic peptide (amino acids 53-78) of P2 myelin protein. Clinical course, nerve conduction studies, histological analyses of the peripheral nerves and the intestinal immune system as well as rt-PCR analyses were performed with a focus on pro inflammatory VLA-4 / CXCR4 and TGFb / Smad 7 axes.
Results: Preventive treatment beginning at the day of immunization with DRF given at 90 mg/kg twice daily by oral gavage significantly ameliorated clinical neuritis by reducing demyelination and axonal degeneration in the nerve conduction studies. Histology revealed a significantly lower degree of inflammatory infiltrates in the sciatic nerves. Furthermore VLA-4 / CXCR4 and TGFb / Smad 7 axes, which become activated through the early EAN phase are both modulated through DRF both in the peripheral nerve and the intestinal immune system (jejunum), thereby mediating its immunomodulatory properties.
Conclusion: We conclude that DRF modulates the immune system in EAN through reduction of the proninflammatory properties of the VLA-4 / CXCR4 axis, which mediates inflammatory infiltration in the peripheral nerves and TGFb / Smad 7 axes, which increases proinflammatory potential of peripheral T cells both in the intestinal immune system and the peripheral nerves.
Disclosure: The authors report no disclosures.

EPO-437

Small fiber involvement and macrophage-dependent axonal pathology in the rat model of experimental autoimmune neuritis

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Background and aims: Experimental autoimmune neuritis (EAN) is a common animal model for acute human immune-mediated polyneuropathies. Although already established in 1955, a number of pathophysiological mechanisms in the peripheral nervous systems still remain unknown. We provide an extensive characterization of EAN progression in Lewis rats, including new insights into the integrity of small nerve fibers, neuropathic pain and macrophage activation.
Methods: Acute EAN was induced with P253-78 peptide and consequently investigated using the CatWalk XT, electrophysiological and histopathological analyses, qPCR, dorsal root ganglia outgrowth studies as well as the von Frey hair and Hargreaves test. For the longitudinal set up, rats were sacrificed at d10 (onset), d15 (peak), d26 (recovery), d29 (late recovery).
Results: We confirmed the classical T-cell and macrophage driven inflammation and the primarily demyelinating nature of the EAN. The dual role of macrophages in EAN is implicated by the high number of remaining macrophages throughout disease progression. Furthermore, different subpopulations of macrophages based on Cx3cr1, Pf4 and Mgl1 expression were identified. In addition, a modulation of the sensory system in EAN was detected. An outgrowth of small fibers in the plantar skin at onset and peak of the EAN went parallel to the development of an acute hyperalgesia mediated through transient receptor potential vanilloid 1 modulation.
Conclusion: Our data depict EAN as a primary demyelinating disease with implicated axonal damage, small unmyelinated fiber impairment throughout the disease progression course and the pivotal role of macrophages in the effector and during the recovery stage.
Disclosure: Nothing to disclose.

EPO-438

Meningeal carcinomatosis or neurological immune-related adverse event? A diagnostic challenge in the ICI-treated patient

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Background and aims: Immune Checkpoint Inhibitor drugs (ICIs) can be associated with neurological immune-related adverse events (n-irAEs) such as polyradiculoneuritis. Leptomeningeal carcinomatosis (LC), a rapidly fatal cancer

manifestation, can mimic polyradiculoneuritis by involving spinal roots. Here, we present two challenging cases of ICI-treated patients with polyradiculoneuritis and LC.
Methods: Data were collected from medical records. Cerebrospinal fluid (CSF) histology was performed by cytospin followed by May-Grunwald Giemsa staining.
Results: Case 1: 67 yo man with pulmonary adenocarcinoma treated with pembrolizumab presented with progressive numbness, weakness in his legs and cranial neuropathy. Spine MRI showed nerve roots contrast-enhancement with pseudonodular aspect. Case 2: 47 yo man with renal-cell carcinoma treated with nivolumab presented with distal painful dysesthesia in his legs. Spine MRI showed contrast enhancement of nerve roots at the cauda equina. Both patients showed a long disease course (14 and 2 months) and inflammatory signs on CSF (cells: 43 and 77 cells). Cytospin identified rare likely cancerous cells with increased cytoplasm-nucleus ratio and intense basophilia. Both patients were treated with high-dose steroids, with poor response, and restarted ICI-treatment. Patient 1 died after 3 months, while patient 2 is still on follow-up.
Conclusion: LC diagnosis is challenging. In our cases, the long disease duration could be explained by the effect of ICIs on LC, whereas the inflammatory signs detected in CSF likely reflect the ICI-increased immune response against the tumor localized into the spinal roots. In this scenario, continuation of ICIs is crucial to support the anti-tumoral response.
Disclosure: I have no conflict of interest to declare.

EPO-439

Targeting the gut-brain axis to dampen neuroinflammation using a murine model of multiple sclerosis

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Background and aims: Multiple sclerosis (MS) and its animal model, the experimental autoimmune encephalomyelitis (EAE), are demyelinating diseases of the central nervous system (CNS). Both are mediated by auto-reactive CNS-specific T lymphocytes activated in the periphery. Gut microbiota is an emerging factor involved in MS pathogenesis that needs further characterization. We hypothesize that myelin-specific T lymphocytes, in particular Th17 subsets, acquire their encephalitogenic properties by interacting with the gut microbiota during colonic lamina propria infiltration in the EAE adoptive transfer model.
Methods: We used a broad-spectrum antibiotic cocktail to unravel the impact of gut microbiota in the EAE Th17 cell adoptive transfer murine model and characterized immune cells from the colon by flow cytometry and RNA sequencing. Next, we treated myelin-specific Th17 cells with microbiota-derived metabolites from mouse fecal filtrates to decipher their impact on Th17 cells using flow cytometry. Feces were characterized for metabolomics by UPLC-MS/MS.
Results: Antibiotic treatment attenuates EAE adoptive Th17 cell transfer disease and reduces CNS-specific Th17 cell infiltration in the CNS. It decreases their pathogenic signature and their pro-inflammatory cytokine and chemokine receptor expression. Gut-derived fecal filtrates treatment of myelin-specific Th17 cells enhances their pathogenicity in a microbiota-dependent manner. Furthermore, adoptive transfer of Th17 cells exposed to fecal filtrates increases EAE disease severity.
Conclusion: We propose that the interaction between adoptively transferred Th17 cells and microbiota-derived metabolites induces a pathogenic switch in the colon and enhances their migratory abilities leading to increase neurological disease severity.
Disclosure: CP has participate to advisory boards for Biogen, Merck, Novartis, Roche none related to this work Author Details

EPO-440

Etiology of optic neuritis (ON) in the tropics.

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Background and aims: ON, an inflammatory demyelinating optic neuropathy, has heterogeneous etiologies, which include CNS inflammatory demyelinating disorders such as multiple sclerosis (S, NMOSD and myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD), systemic autoimmune diseases (SLE, Sjogren's), post viral demyelination (post viral ON and ADEM) as well as infections such as tuberculosis and viruses. The purpose of this study was to evaluate the causes of ON in the tropics.
Methods: Clinical, radiological data, immunological tests performed, cerebrospinal fluid analysis, visual evoked potentials (VEPs) and results of all relevant tests of patients presenting with ON was prospectively collected. Patients were categorised according to the final diagnosis.
Results: The final diagnosis in 131 patients who presented with ON was as follows: MS-22, NMOSD-24, MOGAD-20, idiopathic ON-39, post-viral ON-3, ADEM-1, recurrent ON (with negative aquaporin-4 and MOG antibody)-2, idiopathic neuroretinitis-6, chronic relapsing inflammatory optic neuropathy (CRION)-7, Vogt Koyanagi Harada syndrome-1 and infection in 6 (tubercular meningitis-4 and

dengue-2) patients. Along with post-viral ON, six patients with CNS inflammatory disorders (2 each with MS, NMOSD and MOGAD) had prior history of viral infection. Mean age of MS, NMOSD and MOGAD patients was 26.8, 42 and 26.5 years respectively.
Conclusion: MS, NMOSD and MOGAD together formed a large proportion (50.4%) of ON whereas infection related (post-viral, ADEM and infectious ON) were just 10.6%. Preceding viral infection was seen even in 4.6% patients with CNS inflammatory disorders. Average age of patients with NMOSD was much higher than MS and MOGAD.
Disclosure: Nothing to disclose.

EPO-441

Nasal administration of anti-CD3 monoclonal antibody improves cognition in mouse models of Alzheimer's disease

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Background and aims: Alzheimer's disease (AD) is a neurodegenerative disorder in which microglial cells change from a homeostatic (M0) to a neurodegenerative (MGnD) phenotype and become activated, contributing to neuroinflammation and cognition decline. We have shown in several mouse models of central nervous system (CNS) inflammation that nasal administration of anti-CD3 monoclonal antibody localizes to the cervical lymph nodes where it induces IL-10-producing Treg cells that migrate to the CNS to control inflammation by inducing a MGnD phenotype. Here, we investigated whether nasal anti-CD3 would improve cognition in APP-PS1 and 3xTg mice, which are wildly used for evaluating the cognitive dysfunction.
Methods: Nasal anti-CD3 or isotype control were administered at a dose of 10mcg/mouse, 3x/week for 2 months (APP-PS1) or 5 months (3xTg) and then tested for cognition using the Y-maze and the Morris water maze. Mice were then euthanized, and brains removed for microglial cell sorting and transcriptomeic analysis.
Results: We found that nasal anti-CD3 improved short-term memory in 10-month-old APP-PS1 mice and both short- and long-term memory in 6-month-old 3xTg mice compared to isotype control treated groups. Improvement in cognition was associated with a downregulation of microglial genes associated with neurodegeneration and an upregulation of microglial homeostatic genes. In addition, CD4+ T cells were detected in the AD mouse brains by flow cytometry and immunohistochemistry.
Conclusion: To conclude, our results suggested that nasal anti-CD3 may constitute a novel microglial modulating immunotherapy to treat AD.
Disclosure: Nothing to disclose.

EPO-442

PERIPHERAL NERVOUS SYSTEM ADVERSE EVENTS ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS

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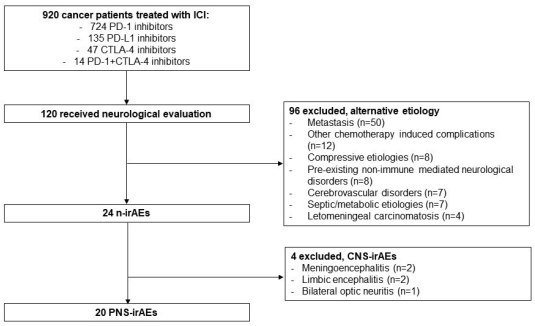
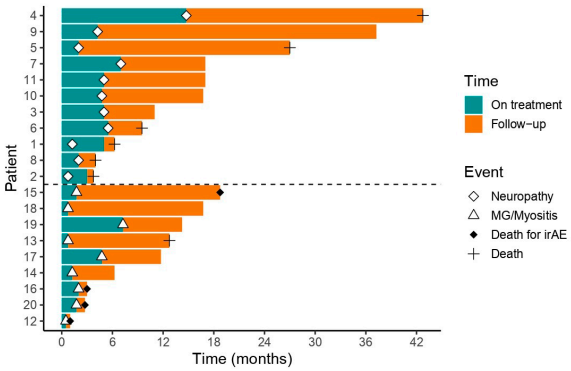
Background and aims: Immune checkpoint inhibitors (ICIs) represent an effective cancer immunotherapy yet are associated with immune-related adverse events (irAEs). The aim of this study was to characterize irAEs involving the peripheral nervous system (PNS-irAEs) in a real-world cohort of ICI-treated patients.
Methods: Cancer patients treated with ICIs between January 2014 and March 2022 were included. Patients with PNS-irAEs were identified and divided into two groups: (1) cranial/peripheral neuropathies and (2) myasthenia gravis (MG) and/or myositis. Clinical characteristics and outcomes, measured with the modified Rankin Scale (mRS), were compared among the two groups.
Results: Among 920 ICI-treated patients, 20 patients (2.17%) developed a PNS-irAEs. The median latency from ICI exposure was 8.8 weeks. Eleven patients developed a neuropathy: polyneuropathy (n=4), cranial neuropathy (n=3), small-fiber neuropathy (n=3), brachial plexopathy (n=1). Nine patients presented MG and/or myositis: concomitant MG and myositis (n=6), isolated myositis (n=2), exacerbation of MG (n=1). Immunosuppressive treatment and/or ICI withdrawal determined a significant clinical improvement, expressed by a mRS reduction, in the neuropathy group (p=0.004), but not in the MG/myositis group (p=0.11). Overall, death due to irAEs occurred in four patients (20%), all with MG/myositis. Compared to patients with neuropathies, those with MG/myositis had a shorter latency onset (p=0.036), developed more frequently concomitant non-neurologic irAEs (p=0.028) and showed a higher mortality rate (p=0.026).
Conclusion: In our large cohort of ICI-treated patients, 2.17% developed PNS-irAEs. Compared to patients with neuropathies, those with MG/myositis had a more aggressive clinical course, characterized by earlier onset, worse response to treatment, and higher mortality.



Patients' selection. CNS-irAEs: central nervous system immune-related adverse events; CTLA-4: cytotoxic T-lymphocyte antigen 4; ICI: immune checkpoint inhibitor; n-irAEs: neurological immune-related adverse events; PD-1: programmed cell death 1; PD-L1 pro



Swimmer plot graph that shows the duration of ICI treatment (blue part of the bar) and total follow-up time (orange part of the bar) in patients with ir-neuropathies (above the dotted line) and ir-MG/myositis (under the dotted line). The onset of the PNS-

Disclosure: Funding: the present study has no funding sources. Conflict of Interest: Prof. Andrea Ardizzoni reports research grants from Celgene, BMS, Ipsen, Roche; honoraria for advisory board participation from BMS, MSD, ROCHE, AstraZeneca, Eli-Lilly. Dr. Francesco Gelsomino reports personal fees from AstraZeneca and honoraria for advisory board participation from Eli-Lilly. The other authors have no conflict of interest to declare.

Clinical neurophysiology; Neurological manifestation of systemic diseases; Neuro-ophthalmology/neuro-otology

EPO-443

"All Tibial Foot": an integrative neurophysiological and neuroradiological study.

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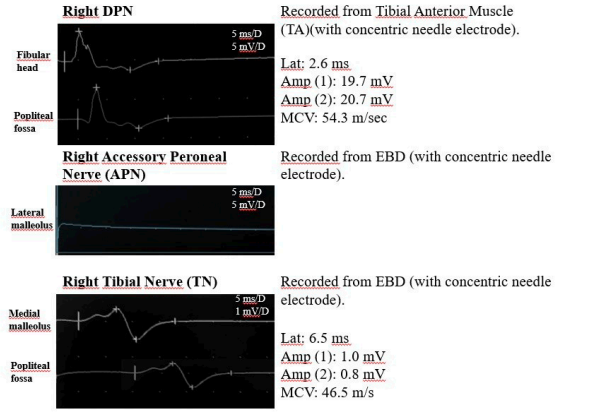
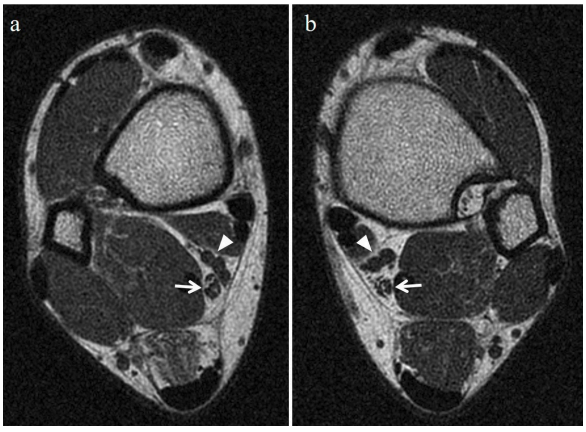
Background and aims: A highly rare anatomic variant is here reported. We presented the case of a patient with the right foot totally innervated by TN. This condition is known as "All Tibial Foot" and it has been reported in only three cases.

Methods: Our study is the first to analyze "All Tibial Foot" with concentric needle electrode nerve conduction study, avoiding the hypothesis of a volume conducted potential mimicking a CMAP response. Neuroradiological study of this rare anatomic variant has not previously been performed.

Results: A 39-year-old man was admitted to our department. Neurological examination showed right gastrocnemius hypertrophy. Patients underwent EMG and nerve conduction study, which was performed with needle electrodes. The absence of right DPN CMAP recorded on EDB was observed. Nevertheless, normal CMAPs were found stimulating DPN recorded on Tibial Anterior (TA) muscle at fibular head and at popliteal fossa. A needle nerve conduction study excluded the presence of APN. A normal DPN CMAP was obtained stimulating TN at ankle and at popliteal fossa and recording on EBD. DPN Sensory Nerve Action Potentials (SNAP) recorded between first and second toes and Sural SNAPS were also normal. Neuroimaging studies (MRI and ultrasound evaluation) confirmed right gastrocnemius hypertrophy, showing a normal representation of DPN and TN nerves and of TA and EDB muscles bilaterally. A diagnosis of right "All Tibial foot" was made.



The ENG study that highlights a Tibial Foot pattern of motori innervation.



Axial T1-weighted turbo spin-echo images of the right (a) and left (b) ankle. The TN (white arrows) located behind the posterior tibial artery and vein (white arrowheads). Normal morphology of EBD muscles (red arrowheads).

Conclusion: Clinicians should considerate "All tibial foot" variant, in addition to APN variant or EBD aplasia, when DPN CMAP is not recorded from EBD.

Author and year	Admission diagnosis	Age	Sex	DPN stim. at ankle; rec from EDB	DPN stim at fibular head; rec from EDB	DPN stim at popliteal fossa; rec from EDB	APN stim at lateral malleolus; rec from EDB	DPN stim at fibular head; rec from TA	TN stim at ankle; rec from EDB	TN stim at popliteal fossa; rec from EDB	DPN sensitive stim at ankle; rec between first and second toes	SPN stim at lateral calf; rec from lateral malleolus	SN stim at lateral calf; rec from posterior lateral malleolus	Other EMG/ENG evidence
Yamashita et al. [1994][1]	Encephalitis	23	M	Not recorded*	Not recorded*	Not recorded*	Not recorded*	Normal CMAP*	Normal CMAP*	Normal CMAP*	Normal SNAP*	Normal SNAP*	Normal SNAP*	None
Lindes et al. (1994)[2]	Erectile disfunction	62	M	Not recorded*	Not recorded*	----	Not recorded*	Normal CMAP*	Normal CMAP*	Normal CMAP*	----	----	----	Martin Gruber anastomosis
Glocker et al. [1995][3]	Traumatic lesion of common peroneal nerve	19	F	Small CMAP*	Small CMAP*	----	Not recorded*	----	Normal CMAP*	Normal CMAP*	----	----	----	Denervation in TA
Battiato et al. [2022]	Transient ischemic attack	39	M	Not recorded*	Not recorded*	Not recorded*	Not recorded*	Normal CMAP*	Normal CMAP*, Small CMAP*	Small CMAP*	Normal SNAP#	Normal SNAP#	Normal SNAP*	None

Legend: DPN: Deep Peroneal Nerve; APN: Accessory Peroneal Nerve; TN: Tibial Nerve; SPN: Superficial Peroneal Nerve; SN: Sural Nerve; EDB: Extensor Digitorum Brevis (EDB) muscle; TA: Tibial Anterior muscle; CMAP: compound motor action potential; SNAP: sensory nerve action potential. *recorded with surface electrode; #recorded with concentric needle electrode.

Nerve conduction studies of "All Tibial Foot" in four reported cases, from 1994 to 2022.

Disclosure: In the interest of transparency, i declare the absence of relationships/activities/interests related to the manuscript.

EPO-444

Is there any effect of migraine on the symptoms and recovery of BPPV?

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Background and aims: The purpose of our study was to determine whether migraine has any influence on the severity of vertigo and dizziness, as well as the quality of life, in patients with BPPV.
Methods: A total of 128 BPPV patients were recruited for this prospective cohort study, 64 of whom had migraine (39.1 (10.2) years; 55 females, 9 males) and 64 without migraine (44.6 (9.5) years; 36 females, 28 males). At baseline, the participants filled out a sociodemographic form, Vertigo Symptom Scale(VSS), Vertigo Dizziness Imbalance Symptom Scale(VDI-SS) and Health related quality of life scale(VDI-HRQoLS), Beck Depression Inventory(BDI), Beck Anxiety Inventory(BAI), Motion Sickness Severity Scale, Headache Impact Test(HIT-6), Migraine Disability Assessment Scale(MIDAS). All patients were asked to complete the clinical scales again at the one-month follow-up visit.
Results: The VSS scores were higher in migraine group both at the baseline (19.5(10.7) vs. 11.3(8.5); p<0.001) and 1 month follow-up (10.9(9.3) vs. 2.2(2.7); p<0.001). The VDI-SS scores indicates that the migraine group had higher dizziness levels of dizziness at the baseline (61.9% vs. 77.3%; p<0.001) and one month later (78.9% vs. 93.7%; p<0.001). According to the VDI-HRQoLS scores, the quality of life was impaired in patients with migraine at the baseline (77.4% vs. 91.8%; p<0.001) and one month after (86.3% vs. 97.6%; p<0.001).
Conclusion: Patients with both BPPV and migraine tend to experience more severe vertigo and dizziness and have a greater impact on their quality of life compared to those with BPPV alone.
Disclosure: Clinicians are recommended to inquire migraine when they are taking a history from the patient with BPPV. Patients with both migraine and BPPV may require special attention during their treatments.

EPO-445

Dissociation between the blink-to-visual-threat reflex and the visual field

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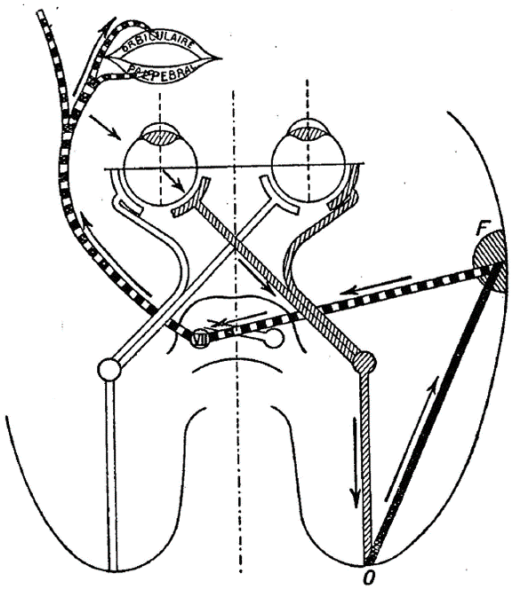
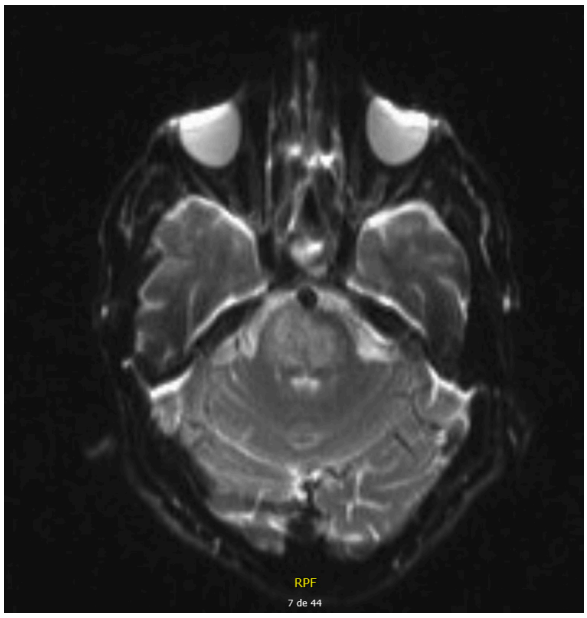
Background and aims: The blink-to-visual-threat reflex is a neurological examination maneuver often used to roughly assess visual fields in patients unable to communicate. However, its reflex arc is long and complex, and it includes not only visual pathways but also motor pathways, from the retina to the orbicularis oculi muscle. Thus, the absence of the blink-to-threat reflex doesn't always mean a visual field defect.

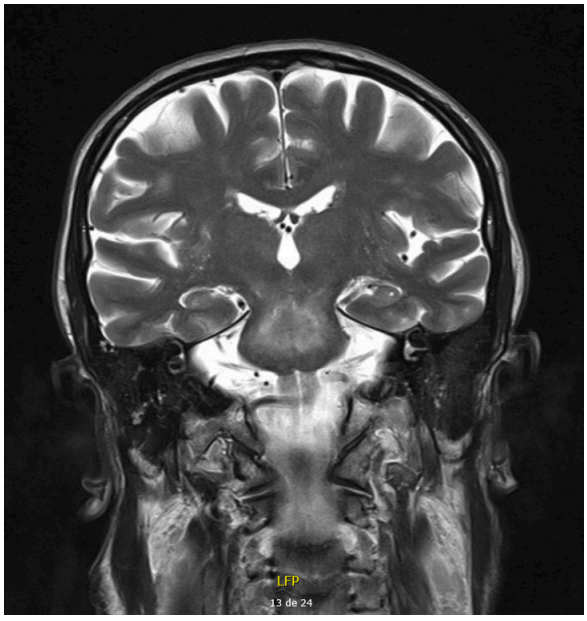


Schematic representation of the reflex arc of the blink reflex to visual threat (adapted from Rademaker and Garcin, 1934)

Methods:N/A
Results: A 69-year-old male was admitted to the ER for sudden onset of left hemiparesis and anarthria. CT scan and angio-CT had no acute lesions, but they documented a proximal occlusion of the basilar artery. The patient underwent mechanical thrombectomy with significant remaining stenosis. He was admitted to the ICU, intubated, and later tracheostomized. The patient recovered gradually, presenting with left hemiplegia, peripheric type left facial palsy, severe dysphagia, and blink-to-threat reflex absent bilaterally. He was still able to follow commands, even in response to visual stimuli. MRI imaging didn't document any occipital lesions, although it revealed acute ischemic lesions that covered nearly the entirety of the transversal section of the pons and right postero-lateral portion of the mesencephalon. These lesions, while not part of the visual pathways, resulted in a lesion of the efferent pathways of this reflex arc, which lead to its bilateral suppression.



MRI - DWI



MRI - T2

Conclusion: This case portrays a dissociation between the absence of blink-to-visual-threat reflex and visual field integrity, which must be taken into account. While useful, this reflex must be interpreted carefully in its clinical context.

Disclosure: Nothing to disclose.

EPO-446

Painful ophtalmoplegia and visual loss – when patients with acute rhinosinusitis see the neurologist

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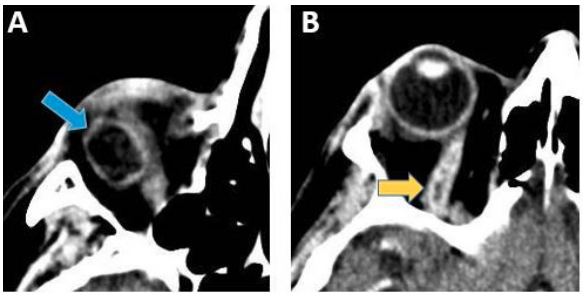
Background and aims: Orbital cellulitis is a complication of acute rhinosinusitis with the development of potentially severe neurological deficits such as opthtalmoplegia and loss of vision. Septic cavernous sinus thrombosis and intracranial dissemination are fearful evolutions.

Methods: We report two clinical cases of orbital cellulitis related to acute rhinosinusitis with subsequent extension of the infection in the cavernous sinus or intracranially.

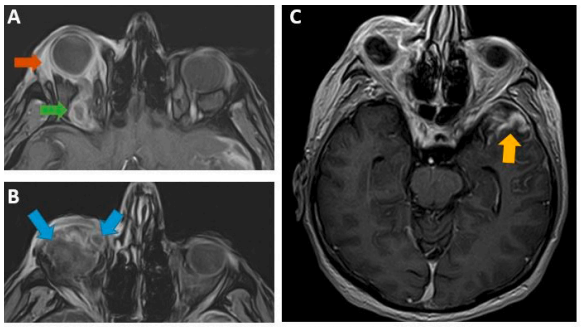
Results: Clinical case 1. A 62 year-old male patient presented to the hospital for periorbital pain, ptosis, and loss of vision in the right eye with sudden onset. Clinically, painful complete ophtalmoplegia, chemosis, proptosis and loss of vission were noticed. Contrast-enhanced CT scan revealed right orbital cellulitis with orbital abscesses, ophtalmic vein thrombosis and sphenoidal rhinosinusitis. MRI revealed multiple small left temporal and parietal abscesses. Intravenous antibiotic treatment and low-molecular-weight heparin were started. Clinical case 2. A 45 year-old male patient, with COVID and type 2 diabetes, presented for left facial pain followed by loss of vision and ptosis of the left eye. Clinically, left painful ophtalmoplegia, loss of vision, maxillary and ophtalmic trigeminal hypoesthesia were noticed. Contrast-enhanced CT scan and MRI revealed left orbital cellulitis with orbital abscesses, partial cavernous sinus thrombosis and pansinusitis. Surgery with drainage of the left paranasal sinuses was performed, intravenous antibiotics and anticoagulation were initiated. One month later, both patients did not clinically aggravate but ophtalmoplegia and visual loss persisted.

Conclusion: Rapid diagnosis and initiation of appropiate treatment are crucial to prevent devastating consequences in complicated acute rhinosinusitis.

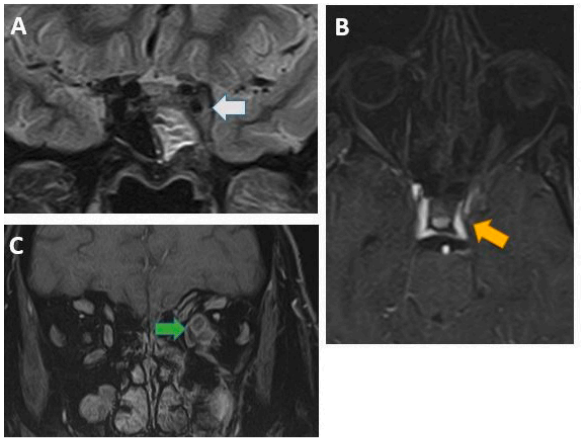
Disclosure: -



Patient 1 – Figure 1: Contrast-enhanced CT scan reveals orbital abscess with ring enhancement (image A, blue arrow) and superior ophthalmic vein thrombosis with filling defect (image B, yellow arrow).



atient 1 – Figure 2: Contrast-enhanced MRI reveals the superior ophthalmic vein thrombosis with filling defect and nlargement (image A - green arrow), orbital cellulitis with diffuse inflammation and proptosis (image A- brown rrow), multiple orbital abscesses with ring enhancement (image B - blue arrows) and parenchymal abscess in the emporal lobe with contrast enhancement (image C - yellow arrow)



Patient 2 – Figure 1: Brain MRI reveals the partial cavernous sinus thrombosis with thickening of the cavernous sinus (image A – white arrow), partial filling defect (image B – yellow arrow) and multiple orbital abscesses with ring enhancement (image C – green arrows).

EPO-447

Late-onset Fabry disease due to p.F113L mutation: clinical profile of the first Italian cluster

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[1]Department of Medical and Surgical Sciences, Magna Græcia University of Catanzaro, Catanzaro, Italy, [2]Regional Epilepsy Centre, Great Metropolitan "Bianchi-Melacrino-Morelli Hospital", Reggio Calabria, Italy, [3]Great Metropolitan Hospital "Bianchi-Melacrino-Morelli", Cardiology Department, Reggio Calabria, Italy

Background and aims: The GLA c.337T>C (p.F113L) is a known pathogenic mutation associated to late-onset Fabry disease (LOFD). A founder effect was demonstrated in a large cohort of predominantly cardiac LOFD in the Portuguese region of Guimarães. Herein we report an in-depth description of clinical and biochemical phenotype of a cluster of five Italian families living in Calabria, Southern Italy, with LOFD caused by p.F113L mutation.
Methods: Five index males with p.F113L mutation with at-risk relatives were identified and underwent biochemical and genetical screening test. Multidisciplinary clinical and instrumental evaluations were performed on mutation's carriers.
Results: Twenty-seven (12 M, 15 F) individuals with GLA mutation were identified (table). Sixteen (59.2%) subjects (M: 8/12; F: 8/15) had clinical or instrumental cardiac manifestations. Notably, myocardial fibrosis was found in 7/8 (87.5%) patients, of whom 2 under 40 years old. Seven patients (all females) complained of acroparesthesias. Renal manifestations occurred in 10 (37%) patients (M: 4/12; F: 6/15), angiokeratomas in 9 (33.3%) subjects (M: 2/12; F: 7/15). Stroke occurred in 4 (14.8%) patients (M: 3/12; F: 1/15). White matter lesions were detected in 12/19 (63.1%) patients (M: 4/7; F: 8/12) and occurred in 40% of subjects under 40 years old.

Demographical and clinical characteristics	All patients (n: 27)	Male (n: 12)	Female (n: 15)
Age at diagnosis (years; mean±SD)	53.8±19.1	53.8±19.9	53.8±19.0
Mean plasma Lyso-GB3[1] (ng/mL; mean±SD)	3.1±2.6	6.3±1.7	1.4±0.4
Cardiac manifestations	16 (59.2%)	8 (66.7%)	8 (53.3%)
Myocardial ischemic events (n, %)	2 (7.4%)	2 (16.7%)	0
Heart failure (n, %)	7 (25.9%)	5 (41.7%)	2 (13.3%)
LVH[2] (n, %)	12 (60%)	6 (66.7%)	6 (54.5%)
LGE[3] (n, %)	7 (87.5%)	2 (100.0%)	5 (83.3%)
Arrhythmia (n, %)	7 (25.9%)	3 (25%)	4 (26.7%)
Neurological and neuropsychiatric manifestations	14 (51.8%)	5 (28.3%)	9 (60%)
Stroke (n, %)	4 (14.8%)	3 (25%)	1 (6.7%)
WML[4] (n, %)	12 (63.1%)	4 (57.1%)	8 (66.6%)
Brain haemorrhage[4] (n, %)	1 (5.2%)	1 (14.3%)	0
Acroparesthesias (n, %)	7 (25.9%)	0	7 (46.7%)
Carpal tunnel syndrome[5] (n, %)	3 (15%)	0	3 (23.1%)
Polyneuropathy[5] (n, %)	2 (10%)	1 (14.3%)	1 (7.7%)
Dysautonomia (n, %)	6 (22.2%)	3 (25%)	3 (20%)
Anxiety/depression (n, %)	3 (11.1%)	0	3 (20%)
Renal manifestations	10 (37%)	4 (33.3%)	6 (40%)
Albuminuria/proteinuria (n, %)	10 (37%)	4 (33.3%)	6 (40%)
Kidney failure (n, %)	3 (11.1%)	0	3 (20%)
Angiokeratomas (n, %)	9 (33.3%)	2 (7.4%)	7 (46.7%)
Eye manifestations	4 (14.8%)	1 (8.3%)	3 (20%)
Cornea verticillata (n, %)	1 (3.7%)	0	1 (6.7%)
Cataracts (n, %)	3 (11.1%)	1 (8.3%)	2 (13.3%)
Sensorineural deafness (n, %)	3 (11.1%)	0	3 (20%)
Pulmonary manifestations (n, %)	2 (7.4%)	1 (8.3%)	1 (6.7%)
Gastrointestinal manifestations (n, %)	4 (14.8%)	1 (8.3%)	3 (20%)

LVH: left ventricular hypertrophy; LGE: late-gadolinium enhancement.
Performed 20/27 (7 M and 13 F); [2]cardiac imaging performed in 20/27 (9 M and 11 F); [3]cardiac MRI performed in 8/27 patients (2 M and 6 F); [4]brain imaging erformed in 19/27 patients (7 M and 12 F); [5]ENG performed in 20/27 patients (7 M and 13 F).

Demographical, clinical and instrumental features of subjects with the GLA p.F113L mutation.

Conclusion: This study demonstrates that GLA p.F113L mutation is also present in Southern Italy. Disease manifestations are frequent in both sexes and may occur early in life. Cardiac involvement represents a core manifestation in Portuguese families as well as in our cohort, while neurological and renal manifestations are more frequent in the Italian cluster.
Disclosure: All authors report no disclosure.

EPO-448

The Use Of Optical Coherence Tomography In Clinical And Subclinical Optic Neuritis

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Background and aims: Despite the high prevalence of clinical(CON) and subclinical(SON) optic neuritis in multiple sclerosis(MS), current diagnostic criteria do not consider optic neuritis as evidence for dissemination in space. Optical coherence tomography(OCT) may be a useful tool to confirm CON and detect SON, and therefore contribute to MS diagnosis.
Methods: Objectives: To sought the utility of OCT in confirming CON and detecting SON, and to compare OCT and clinical data between eyes with CON, SON and with no optic neuritis (NON). Methodology: Retrospective analysis of MS patients. Eyes were separated into 3 groups: CON(acute visual event with concordant exam, >6m apart from OCT), SON(retinal nerve fiber layer(RNFL) or ganglion cell layer(GCL) difference between eyes >6micron and/or significant RNFL and GCL loss on deviation/color maps in one or both eyes) and NON(none of the above).
Results: We included 125 patients(244 eyes)(mean age 37.97±11.73 years, 65.6% (n=82) females). OCT detected SON in 11.5% (n=28) of eyes and confirmed the presence of CON in all CON eyes(23.8% (n=58)). The remaining 158 (64.8%) eyes were NON. Disease duration, EDSS, and number of relapses in the last 2 years, were similar between groups. There were no differences in mean RNFL (p=0.91), and mean GCL (p=0.94) between CON and SON eyes. Mean RNFL thickness correlated inversely with disease duration (R=-0.161, p=0.012).
Conclusion: OCT confirmed the occurrence in all previous CON and further detected SON in 10% of eyes. There were no differences between CON and SON eyes, suggesting that the OCT criteria here used for classifying SON are probably picking real optic neuritis.
Disclosure: Nothing to disclose.

EPO-449

Neurosarcoidosis: a rare disease with many facets

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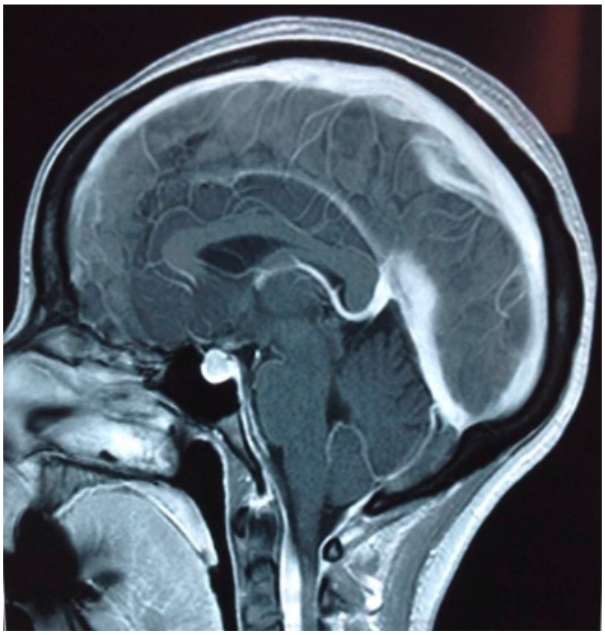
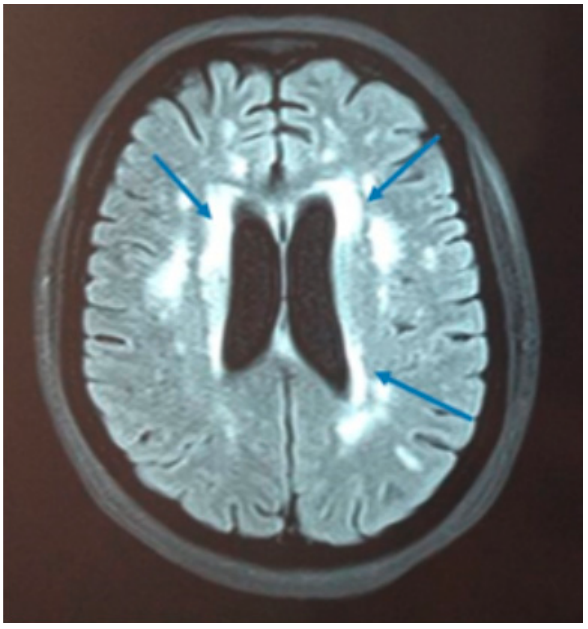
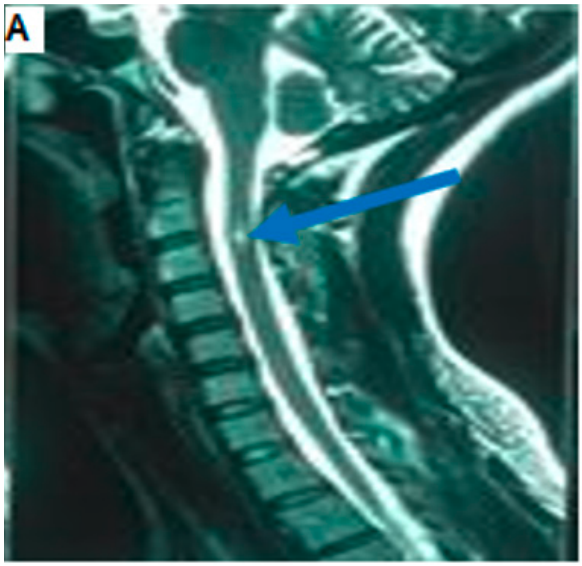
Background and aims: Sarcoidosis is an immune-mediated disease characterized by granulomatous inflammation. Neurosarcoidosis (NS)can involve the central nervous system or the peripheral nervous system or both. Our aim is to describe the clinical and radiological manifestations of NS in tunisian patients.
Methods: We conducted a descriptive and retrospective monocentric study of 38 patients with neurosarcoidosis, followed in the internal medicine and neurology departments at the Military Hospital of Tunis over a period of 20 years from 1997 to 2017.
Results: Thirty-eight patients met the inclusion criteria for NS , all patients underwent a magnetic resonance imaging (MRI) of the brain and spinal cord . Central neurological involvement was present in 33 patients (86.8%). Cranial nerve involvement was found in 10 patients (26.3%), the peripheral nervous system was affected in 5 patients (13.1%) , and ten patients had at least two types of involvement.







Conclusion: Although sarcoidosis commonly affects the lungs, eyes, liver and lymph nodes, neurological involvement can be observed and can sometimes be the only manifestation of the disease.
Disclosure: Nothing to disclose.

EPO-450

No effects of sleep deprivation on brain excitability in a threshold tracking TMS study

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Background and aims: Sleep deprivation was reported to increase the risk of epileptic seizures in healthy individuals, to have antidepressant effects and to influence cortical excitability explored using conventional transcranial magnetic stimulation (TMS). However, these studies included a limited number of TMS modalities and a limited number of inter-stimulus intervals (ISIs); moreover, no studies were performed using threshold tracking TMS (TT-TMS). This study aimed to investigate the effects of sleep deprivation on cortical excitability using TT-TMS and a wide range of ISIs.
Methods: 13 healthy subjects (age 24-59), sleep deprived for at least 24 hours, have been included. The local ethical committee approved the study (1-10-72-171-22). The following paired-pulse TT-TMS methodologies have been applied using the QtracS software and automated QTMSG-12 recording protocols: short- and long interval intracortical inhibition (SICI and LICI), short and long interval facilitation (SICF and ICF) and short-latency afferent inhibition (SAI). The recording was obtained from the abductor pollicis brevis (APB) muscle and using a MagStim/Bistim TMS device and a figure-of-eight coil.
Results: There was no significant difference in SICI, ICF, LICI or SAI at any of the ISIs. For the presentation results will be updated with further individuals.
Conclusion: At this stage, our results do not show any effect of sleep deprivation TMS cortical excitability measurements. As the automated TT-TMS reduces the intra- and inter-day variability better than conventional TMS measurements, this can explain the results of our study in comparison to the literature.
Disclosure: Nothing to disclose.

EPO-451

Dizziness in Postural Orthostatic Tachycardia Syndrome - is there a migrainous component?

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Background and aims: Postural tachycardia syndrome (PoTS) is a chronic condition characterised by increase in heart rate on prolonged standing. A variety of symptoms and comorbidities is recognised including dizziness and also migraine. Much of the dizziness in PoTS is likely due to direct orthostatic effects, however this study looked for evidence of other mechanisms for dizziness in this population.
Methods: This was a retrospective review of 85 patients with PoTS attending a tertiary Neuro-otology clinic undergoing standardised detailed assessments (validated symptom questionnaires, history/physical examination, neuro-otological diagnostics (pure tone audiometry PTA, video head impulse test VHIT, videonystagmography VNG and caloric testing).
Results: 85 patients were included (Mean age 35 years +/-12, 92% were female). 85% had migraine and 29% had a phenotype of vestibular migraine. Visual motion intolerance was present in 41% and 47% experienced true rotational vertigo. Physical examination was limited in a minority (23%) by comorbidity (chronic pain), or symptom provocation. PTA was abnormal in 36%, VHIT was abnormal in 2%, and 38% had abnormal caloric testing. 49% of cases were offered migraine management advice and 54% were offered vestibular rehabilitation.
Conclusion: Dizziness in patients with PoTS can be complex and multifactorial. There are likely to be multiple potential mechanisms including vestibular migraine and minor head injuries from syncope, and this may be a mechanism for some of the findings. Further prospective in a more representative population evaluation is recommended. Clinicians seeing patients with PoTS need a systematic approach to dizziness to identify and treat non-cardiac causes.
Disclosure: Nothing to disclose.

EPO-452

Efficacy and safety of tiomolibdate choline in Wilson disease: 96-week results from an ongoing phase 3 study

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Background and aims: Patients with Wilson disease (WD) in the open-label randomised phase III FoCus trial (NCT03403205) underwent 48 weeks (W) of treatment with the oral, copper-binding agent, tiomolibdate choline (INN: tiomolibdic acid; ALXN1840) or standard-of-care (SoC). All patients completing 48W were offered participation in an extension and were evaluated for copper mobilisation, neurologic signs/symptoms, and safety during 96W of tiomolibdate treatment.

Methods: At enrollment, 214 patients (aged >=12 years) were randomised to tiomolibdate (15mg every-other-day to 60mg daily) or SoC (penicillamine, trientine and/or zinc) for 48W. 178 patients enrolled in the extension (tiomolibdate only) were evaluated over 96W following the first dose of tiomolibdate (baseline). Prespecified endpoints were directly measured non-ceruloplasmin bound copper (dNCC) and Unified WD Rating Scale (UWDRS) Parts II and III. UWDRS scores were stratified by presence of baseline neurologic symptoms (score >0).

Results: At baseline, 123 (69.1%) patients had received SoC for >=18 months; 67 and 134 had total scores on UWDRS Part II >0 and Part III >0, respectively. dNCC remained stable between W48–96 (Figure 1). At W96, least squares mean changes from baseline in UWDRS Parts II and III were –1.0 (95% confidence interval: –1.4,–0.5) and –4.2 (–5.6,–2.9), respectively, and in patients with score >0, –2.6 (–3.8,–1.5) and –5.5 (–7.2,–3.7), respectively, suggesting improvement (Figure 2). Safety data are shown in Table 1; no deaths occurred in the extension.

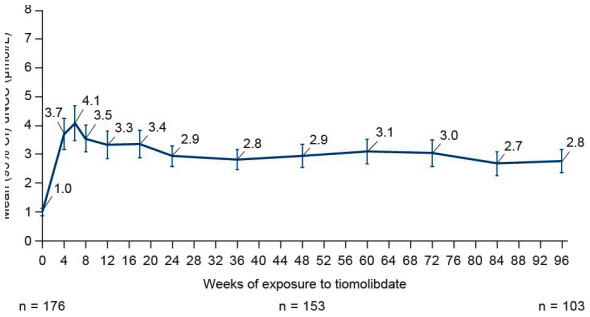

Figure 1. dNCC by week after initiation of tiomolibdate

	Patients enrolled in extension phase N = 178; PY = 349.5		
	n (%)	Number of events	Events per 100 PY
Any AE	156 (87.6)	999	44.6
Any SAE	35 (19.7)	63	10.0
Drug-related AE*	83 (46.6)	226	23.7
Drug-related SAE*	5 (2.8)	5	1.4
AE leading to withdrawal of study drug	10 (5.6)	12	2.9
Death†	0 (0.0)	0	0.0
AE by severity			
Grade 1	145 (81.5)	715	41.5
Grade 2	88 (49.4)	242	25.2
Grade 3	28 (15.7)	40	8.0
Grade 4	2 (1.1)	2	0.6
Grade 5	0 (0.0)	0	0.0
	Worst post-baseline laboratory value, by severity grade (CTCAE)		
	Grade 1, n (%)	Grade 2, n (%)	Grade 3, n (%)	Grade 4, n (%)
ALT (n=176)	64 (36.4)	11 (6.3)	14 (8.0)	3 (1.7)
GGT (n=176)	42 (23.9)	27 (15.3)	15 (8.5)	5 (2.8)
Triglycerides (n=174)	68 (39.1)	24 (13.8)	10 (5.7)	5 (2.9)
Cholesterol (n=174)	89 (51.1)	9 (5.2)	6 (3.4)	0
Neutrophils (n=174)	1 (0.6)	36 (20.7)	12 (6.9)	4 (2.3)

*Assessed as drug-related by investigator

† 2 patient deaths – both assessed by investigators as unrelated to study treatment – occurred during the primary evaluation period; these are not captured here because the analysis included only patients who entered the extension phase

AE: adverse event; ALT: alanine aminotransferase; CTCAE: Common Terminology Criteria for Adverse Events; GGT: gamma-glutamyltransferase; PY: person-years; SAE: serious adverse event.

Table 1. Safety – weeks 0–96 after first exposure to tiomolibdate

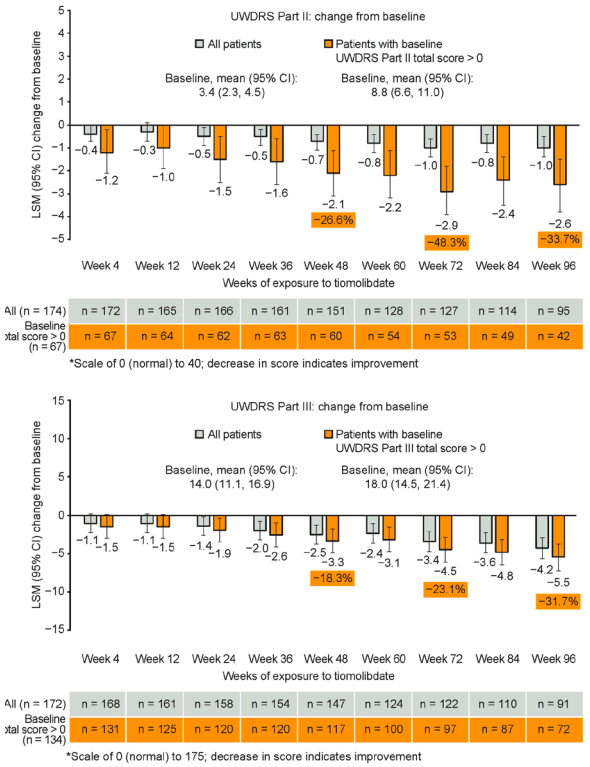

Figure 2. UWDRS Part II (patient/caregiver-assessed) and Part III (neurologist-assessed):* change from baseline

Conclusion: Treatment with tiomolibdate over 96W was generally safe and well-tolerated and was associated with sustained copper sequestration and improvement in neurologic symptoms.
Disclosure: This study was sponsored by Alexion, AstraZeneca Rare Disease.

EPO-453

A digital platform for neurovisual rehabilitation

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Background and aims: Rehabilitation of visual deficits is crucial for improving cognitive and motor functions and quality of life, however, the possible influence of visual-sensory and ocular motor disorders on the patient's outcome is often ignored in neurorehabilitation. Sensory and motor aspects of visual system may be the target of neurovisual rehabilitation.
Methods: A digital rehabilitative platform was designed to include specific tasks for each deficit: Saccadic tasks in patients with diplopia. Benton's line and antisaccade task are designed for peripheral visual field deficits and Unilateral Spatial Neglect (USN) rehabilitation. Visual search and visual sequential search tasks, visual recognition and identification of figures, 2-3D shapes, objects, facial expression recognition and colors (Stroop test) are designed for rehabilitation of visual perception, visual attention and visual agnosia. The platform is accessible to both clinical and remotely . A report of each rehabilitation cycle allows a constant monitoring of patient results but it is also used for different statistics and for addressing the work to each individual patient customizing its reports at various levels of difficulty.
Results: We tested 46 patients: 21 patients with central visual deficits: 9 patients with diplopia, 2 patients with USN, 3 patients with hemianopia and 7 patients with visual perception deficits. The results showed a significant improvement in subjective and objective visual functions.
Conclusion: Neurovisual rehabilitation platform represents a valid instrument for rehabilitation of visual deficits in neurological patients, allowing the clinician to personalize and monitor the treatment's progression and ensuring an easily accessible instrument for patients.
Disclosure: Nothing to disclose.

EPO-454

Effects of ageing on hand muscles

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Background and aims: Hand function decreases with age, due to a reduction in functional motor units, joint degeneration, and neural control. We aimed to investigate the effect of age on different hand muscles using compound muscle action potential (CMAP) amplitude and neurophysiological index (NI), which combines CMAP amplitude, distal motor latency (DML) and F-waves frequency.
Methods: We studied data from adult subjects without neuromuscular disorders. CMAP amplitude, DML and F-wave frequency were obtained for abductor pollicis brevis (APB), first dorsal interosseous muscle (FDI), and abductor digiti minimi (ADM). CMAP and NI from each muscle were analysed. Focal nerve lesion was excluded. Age groups were defined by median and interquantile ranges (IQRs). Lower limit values were defined by the 5th percentile. We used Kruskal–Wallis one-way analysis, Pearson correlation and linear regression for testing age-dependence measurements.
Results: We included 164 subjects; 85 (52%) were women with a median age of 56.0 years (IQR 41.0-72.8). No gender differences were observed, except for FDI CMAP amplitude (12.6 versus 11.1, $p<0.001$) and FDI NI (3.1 versus 2.8, $p=0.041$), which were higher in men. Median and lower limit cut-off values differed significantly between age groups for all neurophysiological measurements ($p<0.001$). APB, FDI and ADM CMAP amplitudes decreased around 0.07, 0.05 and 0.03mV/year, respectively. APB, FDI, and ADM NI decreased around 0.03, 0.02 and 0.01/year, respectively.
Conclusion: CMAP and NI are both age-dependent, confirming an age-related loss of motor units in hand muscles. However, age-dependent changes in APB and FDI are more markedly possibly related to a higher user-effect.
Disclosure: Nothing to disclose.

EPO-455

Dural arteriovenous fistula as the cause of intracranial hypertension

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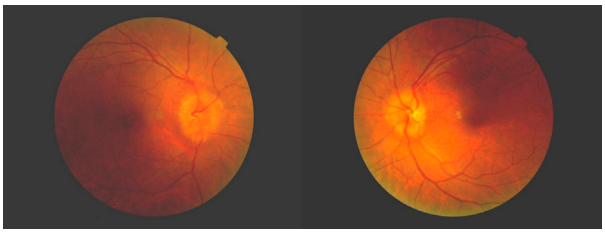
Background and aims: Dural arteriovenous fistula (DAVF) is an abnormal shunt between the arterial and venous systems located within the dura. Presenting symptoms of DAVF are variable and can develop intracranial hypertension in about 8% of that. We describe a patient with intracranial hypertension due to DAVF.

Methods: A 55-year-old female presented with a 5-month history of bilateral transient visual obscurations which occur with postural provocation.

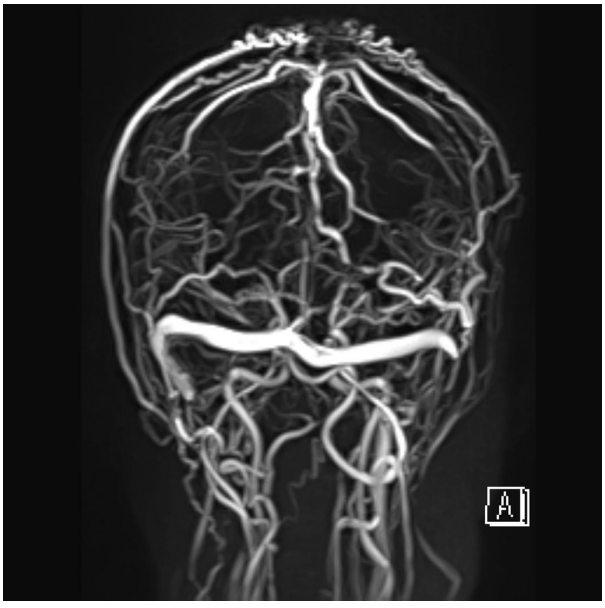
Results: Visual acuity was 20/20 in each eye, and visual field tests demonstrated enlarged blind spot with peripheral field constriction in the right eye. Fundus examinations showed bilateral papilledema with Frisen Grade 3. There was no mass-like lesion in brain computed tomography, and lumbar puncture showed an opening pressure of 380 mmH2O with normal CSF contents. Magnetic resonance venography showed stenosis of the left transverse sinus with a suspicious DAVF in the right transverse sinus. Transfemoral cerebral angiography (TFCA) confirmed a DAVF of the right transverse sinus with arterial supply from the posterior meningeal artery. The left transverse sinus was markedly narrowed. After Onyx embolization of a DAVF and venous stenting of the left transverse sinus, her symptoms was gradually improved. Bilateral papilledema also disappeared in a 1-month follow-up fundus examination.

Conclusion: Clinician should be aware of alternate causes of intracranial hypertension such as DAVF. Our case highlights a critical role of endovascular intervention in managing intracranial hypertension secondary to DAVF.

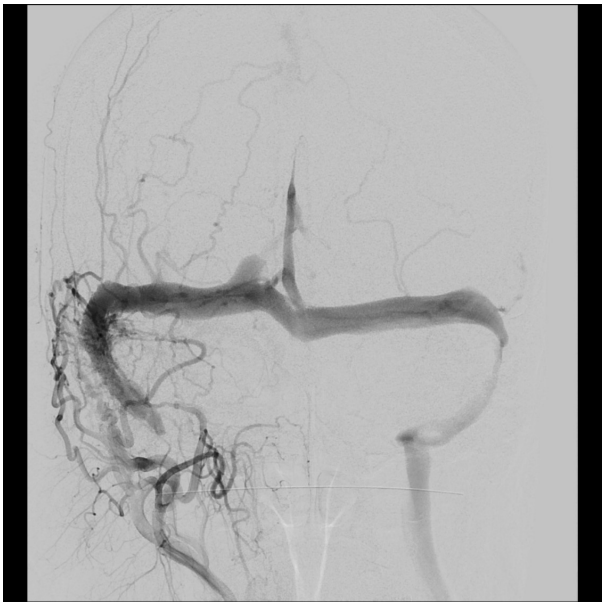
Disclosure: We have no disclosure of any competing interest.



Fundus photography disclosed bilateral papilledema with Frisen Grade 3.



Magnetic resonance venography showed stenosis of left transverse sinus with a suspicious dural arteriovenous fistula in the right transverse sinus.



Transfemoral cerebral angiography exhibited a dural arteriovenous fistula of the right transverse sinus with severe stenosis of left transverse sinus.

EPO-456

Ocular Neuromyotonia In Thyroid Eye Disease

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Background and aims: Ocular neuromyotonia (ONM) consists of abnormal tonic spasms of the extraocular muscles, manifesting as intermittent diplopia. While usually associated with chronic nerve compression and radiation, it has been rarely described in thyroid eye disease (TED).
Methods: Case report
Results: A 61-year-old male with a history of seropositive generalized myasthenia gravis with no ocular involvement, developed binocular vertical diplopia exclusively in upgaze. Exam showed mild limitation of supraduction of the right eye, eyelid retraction and exophthalmos ipsilaterally. Orbit CT revealed tendon-sparing enlargement of the right inferior more than the superior rectus muscle and of the left medial rectus muscle, and blood panel revealed low levels of thyroid-stimulating hormone (0.004 uUI/ml), and raised levels of free thyroxine (1.8 mg/ml), free triiodothyronine (8.0 pg/ml), TSH receptor antibodies (5.0 U/L), and thyroid stimulating immunoglobulin (2.2 U/L), consistent with TED. Treatment with methylprednisolone pulses, thiamazole and selenium was initiated. 1 year later, the patient reported multiple daily attacks of intermittent binocular vertical diplopia also occurring in straight and downgaze. On exam, during an attack, there was tonic downward deviation of the right eye and complete limitation of right supraduction lasting ~1 minute. Between attacks, there was no vertical misalignment in straight gaze and only partial limitation of right supraduction. A diagnosis of ONM was made. Treatment trials with carbamazepine and lacosamide have been unsatisfactory so far.
Conclusion: Despite its rarity, ONM should be considered in TED. Lack of response to voltage-gated sodium channel blockers in our case, suggests the presence of pathomechanism(s) other than ephaptic transmission.
Disclosure: The authors have no relevant financial or non-financial interests to disclose.

EPO-457

The origin of slow saccadic eye movements in Steinert's disease

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Background and aims: Myotonic dystrophy type 1 (DM1) or Steinert's disease is a multisystemic disorder with great phenotypical variability. Oculomotor disturbances in DM1 may be the result of peripheral (neuromuscular) or central dysfunction, e.g. due to the well known lesions in brain MRIs of many Steinert patients. We investigated whether the slowing of saccades has a myopathic/myotonic or a central neural origin.
Methods: Horizontal saccades and the fast vestibulo-ocular reflex (VOR) were examined in 9 DM1 patients and 15 controls by means of video-oculography and video head-impulse testing
Results: Peak velocity-to-amplitude ratios were lower in DM1 patients as compared to controls (19.6 deg/s vs 23.1 deg/s, $P<0.001$, respectively). Moreover, the VOR gain was decreased in patients, as well (0.78 vs 0.98, $P<0.01$). Importantly, there was a strong linear correlation between saccadic velocity and fast VOR movements ($R2=0.941$, $P<0.001$).
Conclusion: Patients with DM1 exhibit slow saccadic eye movements, accompanied by a reduced VOR gain. These results indicate that the patients' oculomotor dysfunction involving various fast eye movement types, is not due to central (supranuclear) causes, but occurs in the context of extraocular muscle dysfunction.
Disclosure: Nothing to disclose.

Movement disorders 3

EPO-458

Spinocerebellar ataxia autosomal recessive type 10 misdiagnosed as a Multiple System Atrophy Type C: a case report.

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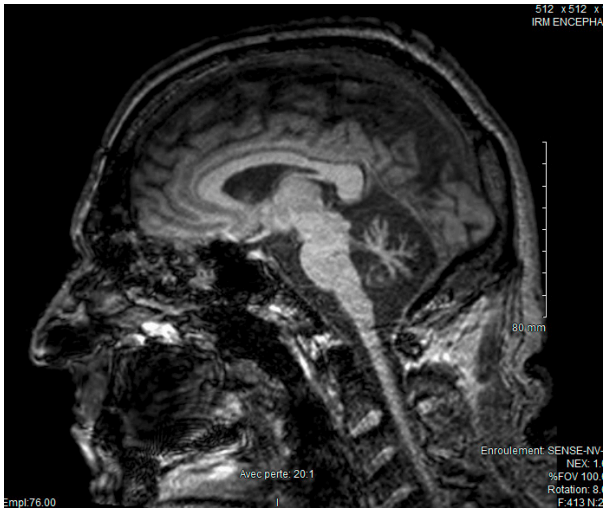
Background and aims: Spinocerebellar ataxia autosomal-recessive type 10 (SCAR 10) is a very rare cause of slowly pro-gressive cerebellar ataxia caused by mutations of ANO10 gene.
Methods: Here we present the case of a 51-years-old man who manifested a gait and balance problem over the past year. The patient had no previous medical disorders and his family history was unremarkable. The neurological examination revealed an ataxic gait, a dysarthric speech, bilateral dysmetria, mild bradykinesia, lateral and vertical nystagmus and abnormally vivid tendon reflexes in the four limbs. Furthermore, the patient reported erectile dysfunction and urinary urgency that improved after beginning an alpha-blocker. The tilt test demonstrated no signs of dysautonomia. The patient performed an MRI that showed significant atrophy of cerebellum and pons, while there was no involvement of dopaminergic pathways at DATSCAN. A polysomnography showed the presence of a nocturnal stridor.
Results: This clinical picture led to the conclusion for a possible MSA type C. However, over the next 12 years, the clinical picture was essentially stable apart from the onset of severe spasticity. The patient also developed a moderate dysphagia. Considering the absence of frank dysautonomia signs and the slow progression of symptoms an NGS analysis was performed and finally, a composite heterozygous genetic mutation of the gene ANO10 (p. Ala74pro e p.Phe171ser) was found.



Cerebellar atrophy

Conclusion: This is a very unusual case of an adult-onset cerebellar ataxia misdiagnosed as a MSA type C. This case is an example of how important it is to always question a
Disclosure: I have no financial disclosure or conflicts of interest with the material presented in this manuscript.

EPO-459

Abstract withdrawn

EPO-460

Is working memory training success in Parkinson's disease determined by cortical thickness and white matter lesions?

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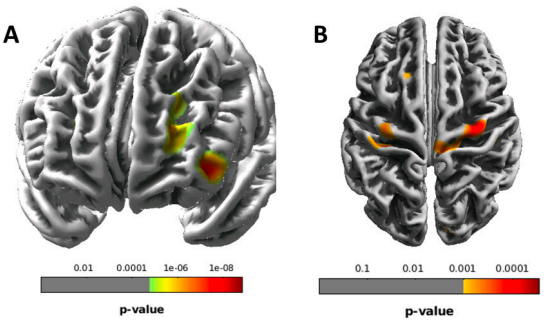
[1]Department of Nuclear Medicine, University Hospital Cologne, Cologne, Germany, [2]Department of Medical Psychology | Neuropsychology & Gender Studies, Center for Neuropsychological Diagnostic and Intervention (CeNDI), University Hospital Cologne, Cologne, Germany, [3]Department of Neurology, University Hospital Cologne, Cologne, Germany, [4]Department of Neurology, Knappschaftskrankenhaus Bottrop, Bottrop, Germany

Background and aims: Patients with Parkinson's Disease (PD) are highly vulnerable for cognitive decline. Therefore, early cognitive training interventions may be crucial for long-term preservation of cognition. While prediction of intervention responsiveness is important for tailored treatment, the influence of structural brain properties, specifically cortical thickness (CT) and white matter lesions (WML), on training success has not been studied. Thus, we aimed to evaluate the influence of CT and WML on working memory training (WMT) success in cognitively unimpaired patients with PD.
Methods: Behavioral and structural imaging (T1, FLAIR) data of 46 patients with PD, 21 of which engaged in home-based adaptive digital WMT, were analyzed. The relationships of demographic, disease-related and cognitive measures with CT and WML (number and volume of lesions) were estimated. For the intervention group, the effect of CT and WML on training success was investigated.
Results: Generally, increasing age had a negative effect on the brain indicated by more WML and less CT. Sex had an effect on CT in the right frontal cortex only (CT in females > males). Interestingly, when corrected for age and sex, disease duration was positively correlated with CT in right middle frontal gyrus. For cognition, better executive function performance at baseline was associated with greater CT in pre-central gyrus. CT and WML were neither correlated to any other demographic, disease-related or cognitive measure at baseline, nor to the responsiveness to WMT.



A: Positive correlation between disease duration and cortical thickness. B: Positive correlation between executive function performance at baseline and cortical thickness.

Conclusion: While structural brain properties might influence cognitive performance at baseline, they do not seem to determine WMT success in this patient cohort.
Disclosure: Nothing to disclose.

EPO-461

Prevalence of Headache on a Cohort of Patients With Parkinson's Disease

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Background and aims: Our aim was to assess the lifetime and last year prevalence and the phenomenology of the headache in a cohort of PD patients in comparison with control subjects (Ctrl).
Methods: We recruited 80 patients (36 F; 44 M) and 76 Ctrl (37 F; 39 M) comparable for age, sex and education. All participants underwent Beck Depression Inventory scale and a questionnaire assessing the presence of a history of headache and days with headache during the last year, describing characteristics of pain as well. Only patients were clinically evaluated by the motor section of Unified PD Rating Scale (UPDRS-III) and Hoehn and Yahr (HY) scale.
Results: No significant difference was observed in the overall prevalence of lifetime migraine among PD patients (30%; 5 M/9 F; p=0.387) compared to Ctrl (39%; 6 M/12 F; p=0.178), as well as the prevalence of tension-type headache (TTH) between the two groups (70% vs 61%; p=0.619). Migraine prevalence was significantly higher among women in both groups (11% M vs 25% F; p=0.067; 15% M vs 32% F; Ctrl: p=0.016). We found higher occurrence of headache family history (40% vs 13%; p=0.004), more common headache remission with age (p<0.001), particularly after the onset of motor symptoms (23%; p=0.037), among PD subjects rather than Ctrl.
Conclusion: PD does not seem to act as a risk factor in the development of headache, but the dopaminergic pathway degeneration might affect the severity and duration of the attacks and favor the improvement and remission of the headache in these patients.
Disclosure: Nothing to disclose.

EPO-462

Gender differences regarding non-motor symptoms in Parkinson's disease patients

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Background and aims: Parkinson's disease is a chronic progressive neurodegenerative disorder whose main hallmarks are motor symptoms such as bradykinesia, rigor, tremor, and postural instability. Several years before motor, various non-motor symptoms may be observed, such as depression, pain, fatigue, loss of smell, low blood pressure. The aim of this cross-sectional study was to investigate gender differences in non-motor symptoms in patients with Parkinson's disease.
Methods: This study included patients with idiopathic Parkinson's disease treated at the Osijek College Hospital. A demographic questionnaire, non-motor symptoms questionnaire (NMSQ) and autonomic dysfunction questionnaire (SCOPA-AUT) were used to assess clinical presentation.
Results: We studied 96 idiopathic PD patients (35 women and 61 men). Patients did not differ in age or disease duration. We found no difference in age at disease onset (60.1 years in women and 61.1 years in men) between the sexes. Among non-motor symptoms, we observed urinary urgency (P = 0.05) and feelings of anxiety and panic (P = 0.008) more frequently in women and decreased or increased sexual desire in men (P = 0.05). There was no statistically significant sex difference in other non-motor symptoms. In autonomic functions, the only difference was in thermoregulatory functions (P = 0.03), which were more impaired in women. No significant gender difference was found in the other five domains or in the total score.
Conclusion: Age of onset did not differ between genders. Symptoms such as urinary urgency, thermoregulatory dysfunction, anxiety and panic are more common in women, while decreased or increased sexual desire is more common in men.
Disclosure: The authors have nothing to disclose.

EPO-463

Apomorphine Sublingual Film for OFF episodes in PD: Impact on Orthostatic Hypotension during Dose-Optimization

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Background and aims: Apomorphine sublingual film (SL-APO) has been shown to be an effective and generally well-tolerated on-demand treatment for OFF episodes in patients with Parkinson's disease (PwPD) [1, 2]. Several dopamine agonists have been associated with orthostatic hypotension (OH). Objective: To assess the impact of SL-APO on the occurrence of OH during dose-optimization, based on blood pressure (BP) readings and adverse event (AE) reporting in two pivotal trials (CTH-300 and CTH-302).

Methods: SL-APO was optimized in PwPD and OFF episodes to obtain an effective and tolerable dose. Patients' BP was measured before and 1h after SL-APO intake when they visited clinics during the dose-optimization phase. We post-hoc analyzed OH-related AEs, BP readings, and their co-occurrence.

Results: At 652 dose-optimization visits from 240 patients, mean BP readings before and after SL-APO intake were comparable. In these visits, the frequency of OH appearing after SL-APO intake was similar to the frequency of OH occurring at pre-dosing only. Correspondingly, visits with reported OH-related AEs (5.4% of total visits) were accompanied by OH, based on BP readings, at a comparable frequency before and after SL-APO intake only (see Table).

Results Table		
	Pre-dose	Post-dose
Supine BP (μ±SEM, mmHg)	138.7±0.7 mmHg systolic BP, 81.5 ±0.4 mmHg diastolic BP	139.7±0.8 mmHg systolic BP, 82.0 ±0.4 mmHg diastolic BP
Standing BP (μ±SEM, mmHg)	135.0±0.7 mmHg systolic BP, 81.9 ±0.4 mmHg diastolic BP	136.4±0.8 mmHg systolic BP, 82.7 ±0.5 mmHg diastolic BP
Difference between standing and supine BP (μ±SEM, mmHg)	-3.6±0.5 mmHg systolic BP, 0.5±0.3 mmHg diastolic BP	-3.3±0.5 mmHg systolic BP, 0.7±0.3 mmHg diastolic BP
visits with OH based on BP readings (n, %)	52/652, 8.0%*	51/652, 7.8%**
visits with OH-related AE and OH based on BP readings (n, %)	4/652, 0.6%*	5/652, 0.8%**

*considered when OH occurred only at pre-dose and not at post-dose
**considered when OH occurred only at post-dose and not at pre-dose

Table

Conclusion: Overall, SL-APO did not affect general BP readings nor the frequency of OH as assessed by those readings during dose-optimization at in-clinic visits (co-occurring with or without reported OH-related AEs). 1. Olanow et al., Lancet Neurol. 2020; 19(2):135-144. 2. Stocchi et al., Mov Disord 2022; 37(Suppl 1, abstract 781).

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EPO-464

A role of transcranial sonography in dystonia and tremor: a possible insight into underlying pathophysiology?

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Background and aims: The association between tremor and dystonia has been recognized for over 100 years, but many uncertainties remain concerning possible shared underlying pathophysiology of these disorders. The discrimination between these conditions in clinical setting is still challenging and reliable biomarkers are needed. Transcranial sonography (TCS) is an easily available, non-invasive and inexpensive tool providing information about the morphology of the brain and it's been proven useful in the differential diagnosis of different movement disorders. The aim of this study was to investigate changes in TCS in patients with focal dystonia (FD) with or without tremor and to assess its role as a potential tool in differentiating these conditions.

Methods: Our study included 92 FD patients who were regularly monitored and treated at the Clinic of Neurology, University Clinical Center of Serbia. They were assessed for the presence of TCS changes.

Results: .The study included 92 FD patients, among them 31 had either head tremor or head and arm tremor combined. There were no clinically significant changes in echogenicity of the substantia nigra (SN) between the groups, neither in diameter of the third ventricle. However, TCS revealed significantly higher prevalence of hyperechogenic nucleus lentiformis (LN) ($p < 0.05$) in patients with FD and tremor (Table 1).

N=92	Focal dystonia without tremor (N=61)	Focal dystonia with tremor (N=31)	p (<0.05)
SN echogenicity (cm2)*	0,15±0,05	0,16±0,07	0,72
Third ventricle diameter (mm)*	6,03±2,13	6,10±2,09	0,89
LN hyperechogenicity (Y or N)£	11:50 (18:82%)	12:19 (39:61%)	**0,03**
SN hyperechogenicity (Y or N)£	19:38 (33:67%)	11:18 (36:64%)	0,67
Brainstem raphe (grade 0 or 1)£	25:33 (43:57%)	9:20 (31:69%)	0,35

*Mean values ± SD, £ number of patients with percentage in brackets, $p < 0.05$.

Table 1. TCS findings in patients with focal dystonia with and without tremor

Conclusion: The LN hyperechogenicity was more prevalent in patients with FD presenting with tremor. This result could suggest a possible role of LN in pathogenesis of tremor, but also highlight possible pathophysiological mechanism shared with dystonia. However, further investigation on a larger sample is needed.

Disclosure: Nothing to disclose.

EPO-465

Sleep quality and autonomic dysfunction in a-synucleinopathies

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Background and aims: Clinical observations suggest that the presence of dysautonomia can worsen RBD symptoms and vice versa in Parkinson's Disease. We aimed to determine whether PD patients with RBD have more severe dysautonomia and whether sleep quality is correlated with autonomic dysfunction in PD. Cardiovascular autonomic control was assessed through heart rate variability (HRV) analysis, a non-invasive method quantifying the activity of the two branches of the ANS.
Methods: We enrolled 15 PD patients (8 RBD+, 7 RBD-), at the Neurology Unit of Policlinico Hospital, Milan. ECG and respiratory traces were recorded for 10 minutes in supine position; subsequently, a segment of 250 ± 50 beats was selected for the HRV spectral and symbolic analysis. Sleep quality was evaluated using a wireless monitoring patch for 1 night (RootiRx; 3 channels: ECG, thoracic effort and actigraphy). Questionnaires for subjective evaluation of sleep quality and autonomic symptoms were administrated.
Results: PDSS score negatively correlated with LF/HF, an index of sympathetic modulation, suggesting that sleep impairment is related to a sympathetic predominance. Low sleep efficiency and higher Wake time After Sleep Onset (WASO) scores were associated with higher sympathetic modulation (0V%) and reduced parasympathetic modulation (2UV%). Moreover, RBD+ patients had higher COMPASS-31 scores and worse sleep quality, assessed by PDSS.
Conclusion: Our preliminary data showed that altered sleep quality is significantly associated with cardiovascular sympathetic predominance in PD patients and that RBD+ patients have severer global autonomic dysfunction. Overall, this suggests that the link between altered sleep and autonomic dysfunction in PD should be more deeply investigated.
Disclosure: The authors have nothing to disclose.

EPO-466

Heterogeneity in congenital disorders of glycosylation (CDG): a case series

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Background and aims: Congenital disorders of glycosylation (CDG) are multisystemic diseases due to defects in synthesis and attachment of glycoproteins/glycolipid glycans, with onset in infancy and high prevalence of neurological symptoms.
Methods: Retrospective case series.
Results: Case 1: A 28 years-old man with PMM2-CDG (AR), who presented delayed psychomotor development and over time also cerebellar syndrome, strabismus, microcephaly and other bone deformities. He had special education, but could not pursue a job. On MRI (27-years) there was cerebellar atrophy and T2/FLAIR hyperintensities in caudate and posterolateral thalami. Case 2: A 22 years-old man with MAN1B1-CDG (autosomal recessive), currently on special needs school, who had delayed developmental milestones, cerebellar syndrome by the age of 8 years, scoliosis, bone hypermobility and later generalized dystonia. MRI (8-years) disclosed mild posterior periventricular hypersignal in T2/FLAIR. Case 3: A 24 years-old man with SLC35A2-CDG (X-linked) with normal psychomotor development and stature.
Conclusion: Our cases highlight the range of severity of CDG. The four patients have a predominant neurological and bone phenotype, with patient 4 also having significant psychiatric symptoms.
Disclosure: No disclosures.

EPO-467

Transferrin as a possible CSF biomarker in neurodegenerative proteinopathies

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Background and aims: Transferrin is one of the key proteins involved in iron homeostasis within the CNS. Impaired iron homeostasis can induce toxic protein oligomers and abnormal intracellular aggregates; the aggregation of a-synuclein and tau protein has been shown in vitro to be triggered by iron. The aim of this study was to determine whether cerebrospinal fluid (CSF) levels of transferrin differ between patients with PD, MSA, PSP, CBD and healthy controls or in general between α-synucleinopathies and tauopathies.

Methods: CSF transferrin levels were compared between groups of patients suffering from PD (n=77), MSA (n=24), PSP (n=24), CBD (n=7) and HC (n=90) and subsequently between the groups of α-synucleinopathies (n=101) and tauopathies (n=31). Mann-Whitney U test and Spearman correlation analysis were used for statistical analysis; tests were performed at a significance level of 0.05.
Results: A significantly lower CSF transferrin level (p=0.012) was present in the PD group when compared to HC. Significantly higher CSF level of transferrin was found in the group of tauopathies when compared to α-synucleinopathies (p=0.024).
Conclusion: Transferrin cannot enter the brain from the blood directly, and the iron transport in the brain is mediated by transferrin synthesized by oligodendrocytes and choroid plexus epithelial cells. CSF transferrin levels, which varies depending mutually on the amount of iron in the brain, may reflect differences between underlying pathophysiology of neurodegenerative proteinopathies; transferrin therefore might be one of the CSF biomarkers useful for their differential diagnosis. Supported by: the European Regional Development Fund - Project ENOCH (No. Z.02.1.01/0.0/0.0/16_019/0000868) and IGA-LF-2022-014
Disclosure: There is nothing to disclose.

EPO-468

RFC1 intronic repeat expansion in Serbian patients with sporadic and seemingly autosomal recessive cerebellar ataxias

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Background and aims: Autosomal recessive intronic repeat expansion in the gene for replication factor C subunit 1 (RFC1) has been described as a common cause of late-onset sporadic cerebellar ataxia associated with sensory neuropathy and vestibulopathy. The aim of this study was to investigate the presence of pathogenic expansions in the RFC1 gene in patients with sporadic and seemingly autosomal recessive ataxia from the Serbian population.
Methods: The study included 96 patients with sporadic or seemingly recessive ataxia in whom symptomatic and most frequent hereditary ataxias (SCA1, 2, 3, 6, 7, 17 and Friedreich's ataxia) were excluded. RFC1 mutation analysis was performed by duplex PCR and Sanger sequencing. Biallelic expansions are not amplifiable by standard PCR and don't harbor the wildtype AAAAG repeat motif.
Results: We identified biallelic pathogenic repeat expansion of the AAGGG motif in the RFC1 in five out of 96 patients with late-onset ataxia (5.2%). The age at onset of individuals with expansion was 46-58 years and they all had gait ataxia and absent reflexes on lower extremities, while three patients had dysarthria. Most patients had oculomotor abnormalities such as broken smooth pursuit, downbeat and gaze-evoked nystagmus. One patient had dystonic head tremor. All patients reported chronic cough. Nerve conduction studies showed signs of sensorimotor neuropathy in all five patients and four of them had cerebellar atrophy on MRI, while two patients suffered from vestibulopathy.
Conclusion: Biallelic mutations in the RFC1 are a relatively frequent cause of late-onset sporadic ataxia with neuropathy. Additionally, they may present with oculomotor abnormalities, vestibulopathy, and dystonia.
Disclosure: We have nothing to disclose.

EPO-469

Depicting a single-center cohort of Friedreich ataxia

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Background and aims: Friedreich ataxia (FA) is a common recessive ataxia, with a wide spectrum of neurological and extra-neurological involvement. We aimed at characterizing the phenotype and genotype of a series of patients.
Methods: Unicentric prospective study, since 2017. Patients identified from an institutional ataxia database. Data collection and analysis performed on RedCap.
Results: Seventeen patients (12 families) were identified (58.8% male). Mean age-of-onset was 14.7±12.2 yrs, including one late-onset (LOFA) and one very late-onset (VLOFA) case. Seven probands (41.2%) had family history of FA, 2 families (11.8%) were known to be consanguineous. Presenting signs/symptoms were gait instability (64.7%), neuropathy (29.4%) and epilepsy (5.9%). Besides cerebellar syndrome in all, 76.4% had pyramidal signs and 52.9% segmental dystonia. Eight patients (47.1%) developed hypertrophic cardiomyopathy and 5 (29.4%) diabetes mellitus. The commonest MRI finding was cervical spinal atrophy (29.4%). Mean age at diagnosis was 22.2±14.6 years. Six patients (35.3%) were homoallelic, with a mean GAA repetition of ~800 [min:607; max:923]. When heteroallelic, repeat number was ~351 [90; 850] for the smaller and ~832 [707; 973] for the larger allele. Mean (GAA)n correlated with earlier age of onset (rS = -0.820, p<0.001). After a follow-up of 15.1±9.4 years, mean SARA was 21.4±12.4. Two patients died.
Conclusion: We highlight the presence of atypical forms, with late-onset or epilepsy, which may lead to diagnostic delay. The relatively high frequency of FA carriers in our general population (1/158) may explain the reduced proportion of known consanguineous cases in our cohort.
Disclosure: The authors have nothing to disclose.

EPO-470

Parkinson's Disease Burden and Device-Aided Therapy Utilization: Interim Results From the PROSPECT Observational Study

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Background and aims: As Parkinson's disease (PD) progresses, motor complications make it increasingly difficult for many patients to manage symptoms with oral anti-parkinsonian medications. We present interim outcomes of an ongoing international observational study evaluating clinical and economic outcomes, and treatment patterns of patients with PD whose symptoms are inadequately controlled with their current therapy.

Methods: PROSPECT (a PRospective Observational Study to evaluate the disease Progression and burdEn of disease of PD patients inadequately Controlled by conventional Therapy) is an ongoing 24-month study. PROSPECT enrolled adults (aged >=30 years) with idiopathic PD who had inadequately controlled motor symptoms (>=2.5 hours/day 'Off' time) despite optimisation of oral medications and were not receiving device-aided therapy (DAT). Interim 12-month outcomes are reported.

Results: This interim analysis includes 90 patients; the mean (SD) age was 68.7 (8.8) years, time since PD diagnosis was 8.7 (5.0) years, time since first motor fluctuation was 6.5 (5.0) years, and daily 'Off' time duration was 5.0 (2.7) hours (Table). By month 12 DAT was offered to 40.3% of patients (n/N=27/67), of whom 29.6% (n/N=8/27) initiated DAT (Figure). Patients who refused DAT reported needing more time to decide and feeling insecure with the procedure. At month 12, the average (SD) change in daily 'Off' time from baseline was −0.3 (1.8) hours (n=50) for patients remaining on oral anti-parkinsonian medication.

Characteristic	All Patients N = 90
Age, years, mean (SD)	68.7 (8.8)
Sex, n (%)	
Males	47 (52.2)
Duration of PD, years, mean (SD)	8.7 (5.0)
Time since first motor fluctuation, years, mean (SD)	6.5 (5.0)
Daily 'Off' time[a], hours, mean (SD)	5.0 (2.7)
History of levodopa-induced dyskinesia[b], n (%)	41 (45.6)
Duration of levodopa-induced dyskinesia, years, mean (SD)	4.3 (3.8)
Use of at least one PD medication, n (%)	77 (85.6)
Amantadine derivatives	22 (24.4)
Istradefylline	9 (10.0)
Dopa and dopa derivatives	70 (77.8)
Dopamine agonists	61 (67.8)
Dopaminergic agents	1 (1.1)
Monoamine oxidase B inhibitors	45 (50.0)
Other dopaminergic agents	26 (28.9)
Tertiary amines	1 (1.1)

PD, Parkinson's disease.
[a]'Off' time is reported as the average normalised 'Off' time, based on a 16-hour waking day, using the Hauser PD diaries completed by patients during the 3 days prior to each study visit.
[b]Obtained from medical reports.

Table. Baseline Demographics and Disease Characteristics

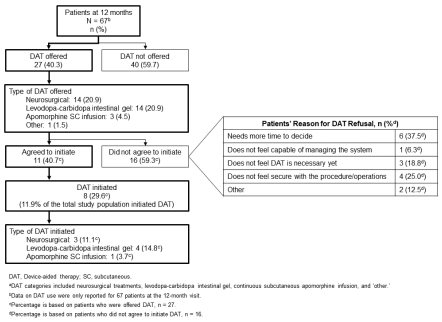

Figure. Patients' initiation of DAT, reported at 12 months.

Conclusion: Despite having a high initial burden of PD symptoms and no improvement in 'Off' time at month 12, most physicians and patients chose to remain on oral medications.

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EPO-471

Orthostatic Hypotension in Parkinson's Disease: Is there a role for Locus Coeruleus Magnetic Resonance Imaging?

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Background and aims: Orthostatic Hypotension (OH) is a common and debilitating non-motor symptom in Parkinson's disease (PD) but the mechanisms underlying its development remain largely elusive. Peripheral and central noradrenergic denervation are both likely to play a key role. Locus coeruleus (LC) is the main noradrenergic nucleus of the brain and its early degeneration in PD has been put in relation with a variety of non-motor symptoms, including OH, but with inconsistent results.
Methods: In a case-control study we compared the MRI-LC parameters (LC signal intensity -LC ratio- and the estimated number of voxels -nVox) in 11 PD patients with OH (PD-OH+) versus 11 without OH (PD-OH-), matched for sex, age and disease duration. We also tested for correlations between subject's LC-MRI features and orthostatic drop in systolic blood pressure (SBP).
Results: PD-OH- and PD-OH+ did not differ significantly based on demographics and clinical characteristics, except for blood pressure measurements and cardiovascular score in the SCOPA-AUT questionnaire. LC ratio and nVox were significantly lower in PD patients compared to the LC-MRI parameters of 52 age-matched healthy volunteers, while no differences were observed between PD-OH- and PD-OH+. Additionally, no correlation was found between the MRI-LC measures and the orthostatic drop in SBP or the clinical severity of autonomic symptoms.
Conclusion: Our results failed to indicate a link between the LC MRI features and the presence of OH in PD but confirmed a marked alteration of LC signal in PD patients.
Disclosure: We have nothing to disclose.

EPO-472

Functional disorders in Parkinson's disease patients with deep brain stimulation – a case series

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Background and aims: Functional neurologic disorders (FND) are disorders with a neurologic presentation but without a clear organic cause. They mostly present as symptoms mimicking actual disorders and can have an organic background, making their proper diagnosis especially challenging. A specifically interesting phenomenon is the emergence of FMDs in patients with Parkinson's disease (PD) with deep brain stimulation (DBS). We report 3 such cases.
Methods: We present three patients that were treated at the Clinic for Neurology in Rijeka and presented with FND-s after DBS. First is a 62-year old female patient with billateral STN-DBS that presented with severe right-sided tremor, the second is a 54-year old male with STN-DBS that presented with extreme „stiffness", hypophonia and a history of dopamine abuse and the third is a 50-year old bilateral STN-DBS patient that presented with bilateral leg weakness which would emerge only in walking, but not in other activities.
Results: After using broad diagnostic methods and excluding other potential causes for the symptoms, we utilized a multidisciplinary approach including physical therap and work therapy, psychological support as well as methods such as „sham" stimulation, distraction and suggestion, achieving a beneficial therapeutic effect in the end and the improvement of the symptoms over time.
Conclusion: FND-s pose a challenging diagnostic and therapeutic problem in modern neurology and even more so in patients with underlying conditions such as PD, especially in those with DBS. A multidisciplinary approach should be utilized when treating these complex patients and for the best therapeutic effect.
Disclosure: Authors have nothing to disclose.

Epilepsy 3

EPO-473

Biallelic Pathogenic Variants in RARS2 Cause Progressive Myoclonus Epilepsy and Variable Epilepsy Phenotype

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Background and aims: Biallelic pathogenic variants of RARS2 are associated with pontocerebellar hypoplasia type 6 (PCH6) typically manifesting with vermian hypoplasia and refractory seizures1. We aim to characterize the epilepsy phenotype of individuals with RARS2 mutations.
Methods: we included patients carrying pathogenic variants of RARS2, referred to our Institute. All patients underwent a comprehensive electro-clinical work-up.
Results: we selected 4 individuals (mean age 29,5±1,29 years) carrying compound heterozygous mutations of RARS2 [NM_020320 m1:c.1A>T(p.Met1 Leu), m2:c.1544A>G(p.Asp515Gly); m3:c.1586+3A>T, m4:c.1366C>T(p.Arg456Cys); m5:c.1305+1G>A, m6:c.1026G>A(p.Met342Ile)]. One variant is novel. The mean age at seizure onset was 12,08±16,19 months. One patient presented with myoclonic and GTCS evolving in status epilepticus, 2 with spasms, one with tonic and GTCS. A transient response to vitamin B6 was documented in one individual. With disease progression, 2 patients developed multiple seizure types, 2 showed myoclonic and GTCS, respectively. Two individuals with earlier age at onset showed microcephaly, spastic tetraparesis, profound intellectual disability (ID) and cortical blindness. Interictal EEG showed a severe slowing of background activity with multifocal epileptiform abnormalities. Brain MRI highlighted the typical pontocerebellar atrophy. The other 2 patients manifested a milder phenotype with moderate ID, cerebellar signs and action myoclonus, resembling Progressive myoclonus epilepsy (PME). Interictal EEG showed epileptiform discharges predominant posteriorly and a photoparoxysmal response. Brain MRI was normal.
Conclusion: Biallelic pathogenic variants of RARS2 cause mitochondrial encephalopathy with variable inter and intra-family severity: from classic PCH6 to a milder PME phenotype. Pontocerebellar atrophy is not a mandatory feature. Our data widen the epilepsy phenotype of RARS2, to include PME.
Disclosure: The authors have no disclosures.

EPO-474

Psychogenic Non-epileptic Seizures – Semiology, Time and the Role of a Multidisciplinary Follow-up

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Background and aims: Psychogenic non-epileptic seizures (PNES) are relatively common, however, factors that predict prognosis are still largely unknown.
Methods: We selected a group of patients with documented-PNES on video-electroencephalogram monitoring between 2012-2021 with follow-up data. Data on demographics, previous medical history, PNES semiology, time to diagnosis, medications, and type of follow-up were collected. PNES evolution was dichotomized as improvement (resolution/decreased frequency) and absence of improvement (maintenance/worsening frequency). Statistical analysis was performed to find prognostic factors.
Results: A total of 31 patients were included, 26 females, mean age 43,0±14, years. Mean time to diagnosis was 12,6±11,3 years. Mean follow-up time post-diagnosis was 3.1±2.9 years. Patients were followed in the outpatient clinic of neurology (n=27), psychiatry (n=21) and/or psychology (n=8). Seventeen patients improved (2 complete remissions); nine had no improvement. Patients with multiple PNES semiologies were less likely to improve (p=0.012). Sixteen patients reduced anti-seizure medications (ASM): this was more common in those with multiple PNES semiologies (p=0,023), in the presence of ictal-cry (p=0,033) and in patients with follow-up in psychology (p=0,040). Time to diagnosis was inversely related to degree of ASM reduction (p=0,011). There were no statistically significant differences in prognosis relating to: sex, age, education level, employment status, comorbidities (epilepsy/psychiatric diseases) or medications.
Conclusion: In our cohort, although PNES remission was rare, more than half of patients improved. Multidisciplinary follow-up, namely psychological intervention, seem to have an impact on the reduction of unnecessary medications. Although multiple PNES semiologies seem to predict a worse prognosis ASM reduction was still possible in these patients.
Disclosure: Nothing to disclose.

EPO-475

Late-onset epilepsy in cerebral amyloid angiopathy patients: a case-control study

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Background and aims: Sporadic cerebral amyloid angiopathy (CAA) is characterized by amyloid deposition in the walls of leptomeningeal and small cortical arteries of the central nervous system [1]. Epileptic seizures at CAA onset have been rarely reported and their prevalence is unknown. Given the high frequency of CAA in elderly population and the epileptogenic role of cortical hemorrhagic lesions, it may be hypothesized that CAA can explain a proportion of late-onset epilepsies of unknown etiology. This study aims to assess the prevalence of CAA in patients with late-onset (>50years) epilepsy of unknown or vascular etiology and in age-matched nonepileptic controls.
Methods: We included subjects with late-onset epilepsy and controls affected by other neurological conditions. All subjects underwent MRI (1.5 Tesla) including blood-sensitive sequences. In the epilepsy group, MRI had to be performed within 60 days from epilepsy onset. To evaluate differences between groups, a Chi-squared test was performed. We also calculated odds ratio (OR).
Results: We included 54 patients with late-onset epilepsy (29 males, mean age 70.3±8.7 years) and 128 age-matched controls (76 males, mean age 71.4±9.8 years). A diagnosis of probable CAA according to Boston criteria 2.0 [2] was done in 14.8% (8/54) of patients with late-onset epilepsy and in 3.1% (4/128) of the control group. This difference was statistically significant (p=0.01). OR for seizures in CAA vs. non-CAA was 5.4 (95% CI:1.55-18-8)
Conclusion: In our case-control study, the prevalence of CAA resulted significatively higher in patients with late-onset epilepsy, suggesting a significant association between probable CAA diagnosis and late-onset epilepsy.
Disclosure: Nothing to disclose.

EPO-476

Prognostic patterns and long-term seizure outcome of non-surgically treated patients with focal cortical dysplasia

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Background and aims: Focal cortical dysplasia (FCD) represents a relative common cause of surgically remediable focal epilepsy. However, some patients may not undergo surgery for multiple reasons, and little is known regarding their long-term prognosis. In this study, we aimed to investigate prognostic patterns and long-term seizure outcome in cohort of non-surgically treated FCD patients.
Methods: Data from patients with focal epilepsy followed from 1975 to 2022 were retrospectively reviewed. We included patients with an imaging diagnosis of FCD who did not undergo surgical treatment due to their choice or clinical reasons, followed-up for more than 5 years from epilepsy diagnosis.
Results: Thirty-eight patients were included. The median age was 49.5 years (Interquartile range [IQR] 36-62] and the median follow-up was 11.5 years (IQR 8-18) (table 1). Surgery was not performed because of bilateral seizures (n= 4, 10.5%), involvement of eloquent brain areas (n=10, 38% of patients), patient's choice (n=7, 18.4%) or lack of drug-resistance (n=7, 18.4%). The most common prognostic pattern was non-remitting course (n=20, 52.6% of patients), followed by relapsing-remitting and late-remission patterns (18.4% each), and by early remission (10.5%) (figure 1). Remission patterns were associated with a parietal localization of FCD, whereas no remission course with focal seizures with impaired awareness and epileptiform abnormalities on baseline EEG ($p < 0.05$).

Clinical characteristics of the population (n=38)		
Variable		**n**
Gender	Male, n (%)	20 (52.6)
	Female, n (%)	18 (47.4)
Age (median, [IQR]); years	49.5 [36-62]	
Age at epilepsy onset (median, [IQR]); years	10 [4-18]	
Follow-up (median, [IQR]); years	11.5 [8-18]	
FCD localization	Frontal, n (%)	16 (42.1)
	Parietal, n (%)	8 (21.1)
	Temporal, n (%)	14 (36.8)
Prognostic patterns	No remission, n (%)	20 (52.6)
	Relapsing-remitting, n (%)	7 (18.4)
	Early remission, n (%)	4 (10.5)
	Late remission, n (%)	7 (18.4)
EEG abnormalities	Normal, n (%)	6 (15.8)
	Focal slowing, n (%)	5 (13.2)
	Epileptiform abnormalities, n (%)	27 (71)
Seizure frequency at last follow-up	Daily, n (%)	6 (15.8)
	Weekly, n (%)	9 (23.7)
	Monthly, n (%)	7 (18.4)
	Annually, n (%)	5 (13.2)
	No seizures, n (%)	11 (28.9)

Table 1 - Clinical characteristics of the population

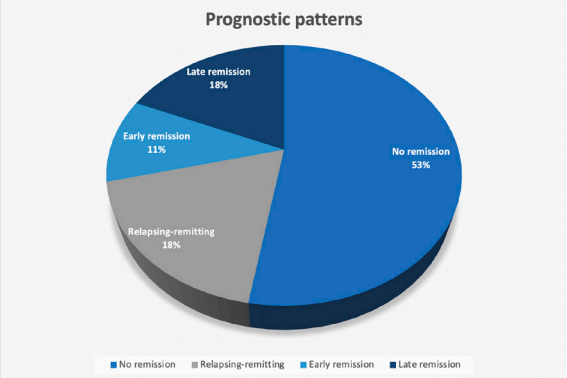

Figure 1 - Prognostic patterns

Conclusion: Our study highlights the prognostic patterns of non-surgically treated FCD patients and provides some electroclinical factors associated with long-term outcome.
Disclosure: Nothing to disclose.

EPO-477

Inflammatory cytokines, synaptic proteins and oxidative stress in children with epilepsy: A cross sectional study.

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Background and aims: Oxidative stress, inflammatory cytokines and synaptic proteins play a pivotal role in the pathogenesis of epilepsy. The study explored the underlying mechanism of excitotoxicity with respect to the roles of interleukin-1β (IL-1β), IL-6, α-synuclein, neuron-specific enolase (NSE), C-reactive protein (CRP) and free radicals.
Methods: Eighty-five children from 9 months to 12 years of age with epilepsy were compared to healthy controls (n=70) in this study. The concentrations of CSF NSE, 1L-1β, IL-6, α-synuclein and CRP were measured by specific ELISA methods. Saliva parameters for free radicals were analyzed.
Results: Mean salivary values of peroxidase and SOD activity increased by 19 % as compared to the controls. The lower plasma Nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) level in epileptic group was highly significant as compared to controls. The mean concentrations of NSE, IL-1β, Il-6 and CRP in the epileptic group showed a significant increase ($P < 0.05$) as compared with the control group. The mutual correlations of NGF, NSE, α-synuclein, 1L-1β, IL-6 and CRP were also analyzed. Results inferred that there were positive correlations between the markers and seizure severity and frequency.
Conclusion: Our results provide insights into high rate of oxidative metabolism coupled with increased inflammatory cytokines in pediatric epilepsy. The results support the possibility of using an appropriate selection of serum cytokine for early diagnosis and emphasize the need to standardize quantitative methods for serum analysis. Our findings also contribute to the ongoing efforts toward identification of early biological markers specific to subphenotypes of epilepsy.
Disclosure: Nothing to disclose and nothing to declare no conflict among the authors.

EPO-478

Admission neutrophil-to-lymphocyte ratio predicts need for ICU admission in Status Epilepticus

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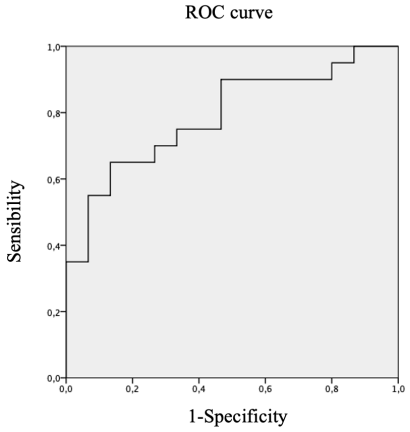
Background and aims: Status epilepticus (SE) is a time-dependent neurological emergency characterized by a high mortality and morbidity rate, and high healthcare costs associated. The introduction of reliable prognostic markers into clinical practice could be useful in rapidly identifying critically-ill patients. The current study evaluates the correlation between admission neutrophil-to-lymphocyte ratio (NLR) and need for ICU admission.
Methods: In this retrospective observational cohort study we enrolled consecutive patients with a diagnosis of SE from 1st January 2022 and 31st December 2022. Anagraphic data, STESS, NLR and SE etiology and semeiology were collected. Multivariate analyses were conducted to test the association of NLR with the need for Intensive Care Unit (ICU) admission and 30-day mortality. Receiver operating characteristic (ROC) analysis was performed to identify the best cutoff for NLR to identify patients who will need ICU admission.
Results: A total of 35 patients were enrolled in our study. Demographic data are reported in table 1. NLR was correlated with the need for ICU admission at stepwise multivariate (OR= 1.787 CI (1.141-2.799); p=0.011). Thirty days mortality was correlated with STESS (OR= 6.391 CI (1.965-2.079); p=0.002), but not with NLR. ROC analysis identified an NLR of 7.0 as the best cutoff value to discriminate the need for ICU admission (area under the curve [AUC]=0.790; p=0.004; Youden's index=0.430; sensitivity, 70.0%, specificity, 73.3%).



Receiver operating characteristic (ROC) analysis

Sex n (%)	
M	11 (31.4%)
F	24 (68.6%)
Age (y)	69 (64 – 83)
STESS	4.2 (3 – 5)
Clinical presentation n (%)	
CSE	7 (20.0%)
NCSE	28 (80.0%)
ICU admission n (%)	20 (57.1%)

Demographic characteristics of the included sample (n = 35). Medians (IQRs) and proportions as appropriate. CSE = Convulsive Status Epilepticus, NCSE = Non-Convulsive Status Epilepticus, IQRs = Interquartile Range (25th -75th percentile).

Conclusion: In patients with SE admission NLR could be a predictor of the need for ICU admission. Serum biomarkers could be considered to implement clinical prognostic scores in SE.
Disclosure: Nothing to disclose.

EPO-479

Long-term outcome of Status Epilepticus: The relationship between aetiology and the risk of subsequent epilepsy

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Background and aims: The aim of our study was to evaluate the incidence of late seizure (LS) in a cohort of first-ever Status Epilepticus (SE) survivors.
Methods: Retrospective monocentric study of adults patients with a SE who were consecutively admitted to the Modena Academic Hospital (Italy), from September 2013 to March 2022. Post-anoxic episodes and patients with a previous diagnosis of epilepsy were excluded. Kaplan–Meier survival analyses were used to calculate the probability of seizure freedom following the index event, whereas a Cox proportional hazard regression model was used to identify outcome predictors.
Results: Patients were included, 280 (66%) of whom survived at 30 days from SE onset. Overall, 55 out of 280 patients (19.6%) developed LS or experience SE recurrence (mean follow-up: 29.8 months). For the majority of cases (36/55; 65%), the first relapse occurred within the first year of follow-up, whereas the cumulative probability of seizure freedom was 84% and 68% at 12 months and 5 years, respectively. The risk of LS was significantly higher after SE due to structural aetiologies (HR 1.84 95% CI 0.98 – 3.43), or in case of early prominent motor episodes with evolution into non-convulsive SE (HR 2.86 95% CI 1.31 – 6.27).
Conclusion: after a first-ever SE, the cumulative probability of seizure freedom remained high up to 5 years from the index event. However, in case of SE due to structural aetiologies, and in case of motor SE evolving to NCSE, patients may be at higher risk of relapsing, especially within 12 from SE.
Disclosure: Nothing to disclose.

EPO-480

Prolongation of cortical sleep spindles during hippocampal interictal epileptiform discharges in epilepsy patients

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Background and aims: Memory deficits are frequent among patients with epilepsies affecting the temporal lobe. Hippocampal interictal epileptic discharges (hIED), the presumed epileptic exaggeration of sharp wave-ripples (SWR) are known to contribute to memory dysfunctions, but the potential underlying mechanism is unknown. The precise temporal coordination between hippocampal SWRs and corticothalamic spindles during sleep is critical for memory consolidation. In the present study we aimed to assess the influence of hIEDs on neocortical spindles.
Methods: Methods We analyzed the spindle characteristics (duration, amplitude, frequency) of 21 epilepsy patients implanted with foramen ovale (FO) electrodes during a whole night sleep. Scalp sleep spindles were categorized based on their temporal relationship to hIEDs detected on the FO electrodes. Three groups were created: (i) spindles coinciding with hIEDs, (ii) spindles "induced" by hIEDs, and (iii) spindles without hIEDs co-occurrence.
Results: We found that spindles co-occurring with hIEDs had altered characteristics in all measured properties, they lasted longer, had higher amplitude and their frequency

range shifted towards the higher frequencies. Also hIED-induced spindles had identical oscillatory properties with spindles without any temporal relationships with hIEDs.
Conclusion: We investigated the effect of hippocampal IEDs on neocortical spindle activity and found spindle alterations in cases of spindle-hIED co-occurrence, but not in cases of hIED-initiated spindles. We propose that this is a marker of a pathologic process, where IEDs may have direct effect on spindle generation. It could mark a potential mechanism where IEDs disrupt memory processes, and also provide a potential therapeutic target to treat memory disturbances in epilepsy.
Disclosure: None of the authors has any conflict of interest to disclose.

EPO-481

What do 90-99% responder rates mean in patients treated with cenobamate: results from an open label extension study

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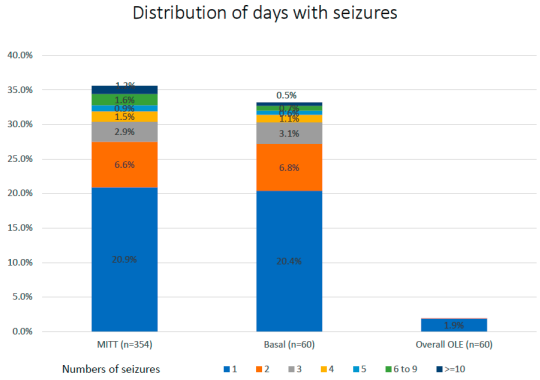
Background and aims: Cenobamate is an antiseizure medication (ASM) approved in Europe as adjunctive therapy for adults with inadequately controlled focal seizures. Maintained seizure freedom is the goal of epilepsy treatment, however, it is not always possible to achieve. Here we analyze the long-term 90-99% responder population during the whole C017 open label extension (OLE) study.
Methods: Adults with focal seizures despite treatment with 1-3 concomitant ASMs completed the double-blind treatment and entered the CO17 OLE study. A Post-hoc analysis was performed in patients who achieved responder rates ≥90% but did not achieve seizure freedom to quantify seizure-free days during the whole OLE.
Results: 17% (60/354) of participants achieved 90-99% responder rates during the length of their participation in the OLE study (median 291.3 weeks). 90- 99% responders had a median duration of epilepsy of 24 years compared to 23 years for the mITT (modified Intention to treat) population. Baseline seizure frequency was 8.75 for 90-99% responders vs 9.5 for mITT. The proportion of days with seizures during the baseline period was similar in both populations: 43.3% (27/60) of the 90-99% responders were seizure free for 99% of the days and more than 90% (55/60) were seizure free for at least 95% of the days. 90-99% responders had one seizure 1.9% of the days, two seizures 0.2% of the days, and >2 seizures less than 0.05% of the days.
Conclusion: While seizure freedom is the goal of epilepsy treatment, the ≥90% seizure reduction obtained with cenobamate, might be also an optimal long-term outcome. This outcome measure may be used in other ASM studies.
Disclosure: The original study (NCT01866111) was supported by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Angelini S.p.a. (Rome, Italy).



EPO-482

Focal adenosine A1 receptor activation through photopharmacology as a potential treatment for drug-resistant epilepsy

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Background and aims: The inhibitory adenosine A1 receptors (A1Rs) possess potent seizure-suppressive effects. However, A1R agonists cannot be administered systemically due to severe side-effects. Local A1R activation could be achieved with photopharmacology, which provides control over the activity of a drug using light. In this study, photocaged cyclopentyladenosine (pcCPA; an inactivated A1R agonist) is being tested in vivo as a potential epilepsy treatment.
Methods: The possibility to activate pcCPA in vivo was first studied by investigating effects on hippocampal evoked potentials (EPs). Healthy mice were implanted with an optrode in the hippocampus through which light was delivered after intracerebroventricular (ICV) injection of pcCPA. Effects were compared to those of ICV injection of the active compound CPA. To test the effect of local pcCPA activation on hippocampal seizures, epileptic mice received an injection of pcCPA through a cannula implanted above the lateral ventricle after which light was delivered via an optrode implanted in the hippocampus. The occurrence of

seizures was compared before and after the intervention.
Results: Local illumination in the hippocampus after ICV injection of pcCPA resulted in suppression of hippocampal EPs, similar to that obtained with administration of CPA, indicating successful activation of A1Rs. In a pilot study with epileptic mice, ICV administration of pcCPA combined with hippocampal illumination suppressed the occurrence of seizures.
Conclusion: This study provides proof of concept that local activation of A1Rs can be achieved in vivo using photopharmacology. The first results with pcCPA in epileptic mice show that this approach could be effective for suppressing seizures.
Disclosure: Nothing to disclose.

EPO-483

Interim analysis of adjunctive perampanel as 2nd or 3rd anti-seizure medication from the observational PERPRISE study

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Background and aims: Prospective data on perampanel use in Germany mainly consist of late adjunctive therapy for refractory epilepsy. In this interim analysis from a subset of patients in PERPRISE (PERampanel in patients with PRImary or SEcondarily generalised seizures; NCT04202159), we compared those receiving perampanel-only adjunctive therapy as the 2nd versus 3rd anti-seizure medication (ASM).
Methods: PERPRISE is a multicentre, prospective, observational, non-interventional study to evaluate perampanel as the only adjunctive to current ASM monotherapy or as a substitute for one ASM during dual therapy. Patients (>=18 years) with focal or idiopathic generalised epilepsy who had >=1 focal to bilateral tonic-clonic seizure (FBTCS) or generalised tonic-clonic seizure (GTCS) within 3 months prior to inclusion were eligible. The Interim Analysis Set (IAS) includes patients who received >=1 dose of perampanel and attended or discontinued prior to the 6-month visit. Endpoints include retention rate, response rate, seizure-freedom rate and safety.
Results: As of 25 November 2021, 38 patients in the IAS were receiving adjunctive perampanel as 2nd (n=13) or 3rd (n=25) ASM. Retention rates were 92.3% and 84.0%, respectively, compared with 78.0% in the overall IAS (Figure 1). Response rates were comparable between 2nd or 3rd ASM groups for FBTCS+GTCS (Figure 2). However, seizure-freedom rates varied with the number of previous ASMs (Figure 3). Treatment-emergent adverse events (TEAEs) were reported in 48.0% of patients in the IAS; 7.0% reported serious TEAEs.
Conclusion: These data demonstrate favourable retention and seizure-freedom rates with perampanel-only adjunctive therapy as the 2nd or 3rd ASM for FBTCS and/or GTCS.

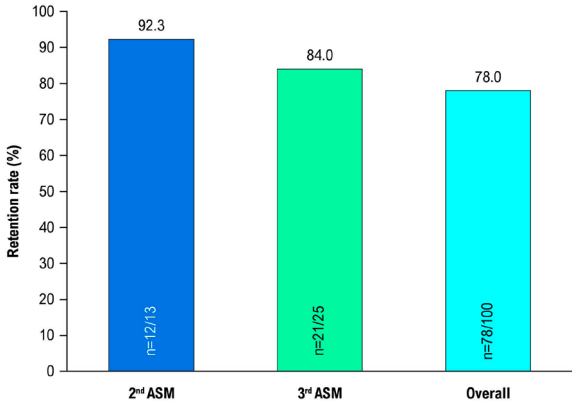

Figure 1. Retention rate of perampanel as 2nd or 3rd ASM administered as only adjunctive therapy at 6 months compared with the overall population (Interim Analysis Set)

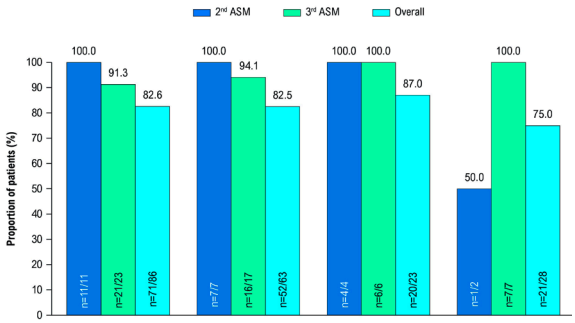

Figure 2. Response rate of perampanel as 2nd or 3rd ASM administered as only adjunctive therapy by seizure type at 6 months compared with the overall population (Interim Analysis Set)

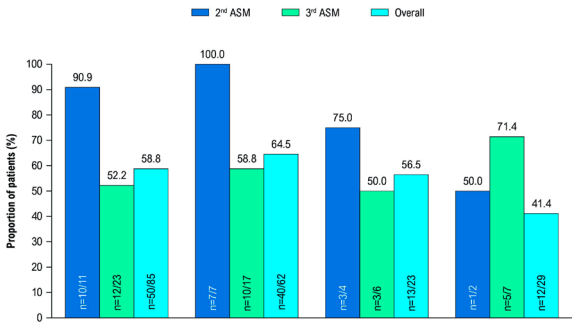

Figure 3. Seizure-freedom rate of perampanel as 2nd or 3rd ASM administered as only adjunctive therapy by seizure type at 6 months compared with the overall population (Interim Analysis Set)

Disclosure: This study was funded by Eisai GmbH. Bernhard J Steinhoff has received speaker honoraria from Angelini, Arvelle Therapeutics, Desitin, Eisai, GW Pharmaceuticals, Tabuk Pharmaceuticals, Teva and UCB Pharma; and has served as a paid consultant for Angelini, Arvelle Therapeutics, B. Braun Melsungen, Eisai, GW Pharmaceuticals and UCB Pharma. Tobias Goldmann is an employee of Eisai GmbH. Yaroslav Winter has received honoraria for educational presentations and consultations from Arvelle Therapeutics, Bayer AG, BIAL, Eisai, LivaNova, Novartis and UCB Pharma.

EPO-484

Psychiatric Comorbidities and Their Relationship With Quality of Life and Stigmatization in Patients With Epilepsy

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Background and aims: This prospective study aims to evaluate comorbid psychiatric diseases and stigmatization in patients with epilepsy, by investigating their relationship with clinical and sociodemographic data, to determine their effects on patients' quality of life and perceived stigma.
Methods: 300 patients were evaluated aged between 18-65 and diagnosed with epilepsy in the epilepsy outpatient clinic. Demographic, clinical, laboratory and, imaging features were assessed. Patients were classified using the International League Against Epilepsy's 2017 Classification of Epilepsy Syndromes and Seizures. Symptom Check List (SCL90-R), Quality of Life in Epilepsy Scale (QOLIE-10), and Perceived Stigma Scale were applied to all patients. Patients having SCL90-R general symptom index ≥ 1 were assessed using the Mini International Neuropsychiatric Interview by psychiatrists. The frequency of psychiatric comorbidities, relationship of comorbid psychiatric disorders with quality of life, and stigmatization in epilepsy patients were evaluated.
Results: Psychiatric comorbidities were found in 24% (n=64) of epilepsy patients. Mood (18.7%, n=50) and anxiety disorder were the most common (10.4%, n=28). The frequency of seizures (p=0,004), number of antiepileptics (p=0,015), previous epilepsy surgery and psychiatric disorder (p<0,001), high perceived Stigma (p<0,001), and QOLIE-10 (p<0,001) scores were all correlated to psychiatric comorbidities.
Conclusion: This study showed that a history of psychiatric disease, poor quality of life, and high perceived stigma were the most significant predictors of psychiatric comorbidities in epilepsy patients. This suggests that screening patients for comorbid psychiatric conditions in epilepsy outpatient clinics is critical to reduce psychosocial issues, economic burden of stigmatization, and improving quality of life.
Disclosure: The authors declare no conflicts of interest.

EPO-485

Re-operation after failed first epilepsy surgery: Our clinical experience

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Background and aims: Resective epilepsy surgery can lead to sustained seizure control in up to 70-80% of selected patients whereas seizure recurrence is about 20-30% after first epilepsy surgery. The aim of this retrospective study is to evaluate re-operated patients' clinical features, EEG/MRI findings and their seizure outcome.
Methods: We included consecutive patients who were re-operated between the years 1995-2018. The clinical characteristics, EEG findings, seziure outcome and the reason for second epilepsy surgery were analyzed.
Results: There were 620 patients who underwent resective epilepsy surgery. Twenty-seven(12 female, 15 male) patients(4.35%) re-operated after failed first surgery. The mean time between second and first surgery was 3±2.72, mean age of the re-operated patients were 18(3-35). Sixteen of the patients had focal cortical dysplasia, two patients had mesial temporal sclerosis three of them had neuroectodermal tumor and others were dual pathologies(FCD+MTS) and reactive gliosis. Tailered resection, anterior temporal lobectomy, corpus callosotomy and disconnection were the re-operation types. Most common pathologies were FCD type 2(n=6), type 3(n=5) and type 1(n=3). Engel classification after second epilepsy surgery were class 1 in 10 and class 2 in 8 patients end 70% of the patients in Engel1 group had FCD. Five patients couldn't be reached seizure information after re-operation.
Conclusion: Re-operation is possible after failed first surgery and some patients have chance for seizure freedom after it. Patients should be re-evaluated for the re-operation after first epileptic surgery who have consistant auras, continuation of the seizures, different auras and/or seizures.
Disclosure: Nothing to disclose.

EPO-486

Access to health care in patients with epilepsy in Latin America

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Background and aims: The lifelong prevalence of epilepsy in Latin America and the Caribbean (LAC) stands at an average of 17.8 per 1,000 inhabitants. The treatment gap is greater than 50%, thus more than half are not receiving any type of care. Our objective was to assess the access to epilepsy care in LAC.
Methods: We conducted a cross-sectional survey regarding access to care of people with epilepsy in LAC. Neurologists and epilepsy specialists were surveyed either by mail or in-person during the XII Latin American Epilepsy Congress in Medellin, Colombia from October 1st to 4th, 2022.
Results: 98 of 101 physicians answered our survey in person. Information was obtained from 17 countries in

LAC, 37,8% epilepsy specialists and 62.2% neurologists. 85% of physicians reported issues accessing education and work for people with epilepsy. 62.1% countries had prenatal care programs. 78% of physicians reported a high cost of care as the main access barrier. EEG was available in 94.5% countries and CT scan in 82.7%. 54% countries did not have legislation related to access to epilepsy surgery and 85.6% physicians reported there is no information available regarding this treatment.
Conclusion: There is a low prevalence of educational and work opportunities for patients with epilepsy in LAC. Government support is weak, as evidenced by a low prevalence of preventive measures for epilepsy. Most countries have access to neurologists and diagnostic equipment, yet with high cost of ASM. There is a need for improved access in the treatment, evaluation, and education of epilepsy in LAC.
Disclosure: Nothing to disclose.

EPO-487

Obstetric and neonatal outcome in women with epilepsy – a single center study in Poland.

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Background and aims: Pregnancy in women with epilepsy can be challenging due to the known teratogenicity of some antiseizure medication (ASM) and the risk associated with seizures during pregnancy.
Methods: We retrospectively reviewed the medical records of 190 pregnancies in 127 women with epilepsy treated in our outpatient clinic over the years 2010-2022.
Results: The average age at delivery was 30.1 years (±4.4). 78.3% of patients were on monotherapy and the majority were prescribed ASMs with low teratogenic potential (78.3%). Levetiracetam and lamotrigine were the most commonly used (70, 37.0% and 63, 33.3%). Valproic acid was used in 31 pregnancies (16.4%), topiramate in 11 (5.8%). Seizures during pregnancy occurred in 87 cases (46.5%) – more often in women on polytherapy (25, 29.1% versus 12, 12.0%; p= 0.009). Furthermore, seizures during the postpartum period (45, 56.3% versus 15, 15.8%; p<0.001) and caesarean section were more frequent (55, 73.3% versus 48, 55.8%; p=0.022) in this group. Among all pregnancies, there were 12 miscarriages (6.4%) and 6 cases (3.2) of termination of pregnancy. The majority delivered by caesarean section -103 cases (64.0%). Low birth weight (<2,500g) was detected in 13 newborns (11.3%), low Apgar score (≤7) in 9 (5.9%). 107 women (68.2%) decided to breastfeed - fewer in the polytherapy group (42.9% versus 74.2%, p=0.001)
Conclusion: Due to the use of new antiepileptic drugs with low teratogenic potential, most of the patients in our group gave birth to healthy children, and the percentage of congenital defects was low.
Disclosure: Nothing to disclose.

MS and related disorders 5

EPO-488

Association of multi-sensor derived motor features with established functional outcomes in people with MS

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Background and aims: Sensor-based measurements promise an accurate, objective, and reliable assessment of motor function in people with multiple sclerosis (PwMS). Within our study validating smartphone-based digital biomarkers (dreaMS, NCT05009160), we investigate the association of motor features derived by a multi-sensor inertial motion capture system with established functional outcomes.

Methods: Study participants were equipped with an 18-sensor inertial motion capture system (Xsens MVN) and performed the following tests in our outpatient clinic: Timed-up-and-go (TUG), 30-second walk, chair-rising, stair-climbing, and tandem walk. Signals captured by this system underwent automatic pre-processing, segmentation, and feature extraction (Figure 1). We examined correlations between these motor features and the Neurostatus-Expanded Disability Status Scale (EDSS), timed 25-foot walk (T25FW), and self-reported MS walking scale (MSWS-12).

Results: We included 52 PwMS (40 female [77%], mean age 45.9±11.1 years, median disease duration 11.2 years [range 0.2-37.1], median EDSS 2.0 [range 0-6.0], median T25FW 4.6s [range 3.3-13.2], and median MSWS-12 8.3% [range 0-100]). The strongest correlations were found for chair-rising (T25FW Pearson r=0.66 [95% CI 0.46-0.80], EDSS r=0.52 [0.28-0.70]), stair-climbing (T25FW r=0.57 [0.33-0.74], MSWS-12 r=0.50 [0.24-0.69]), and TUG (T25FW r=0.51 [0.24-0.71], MSWS r=0.43 [0.15-0.65]), see Figure 2.

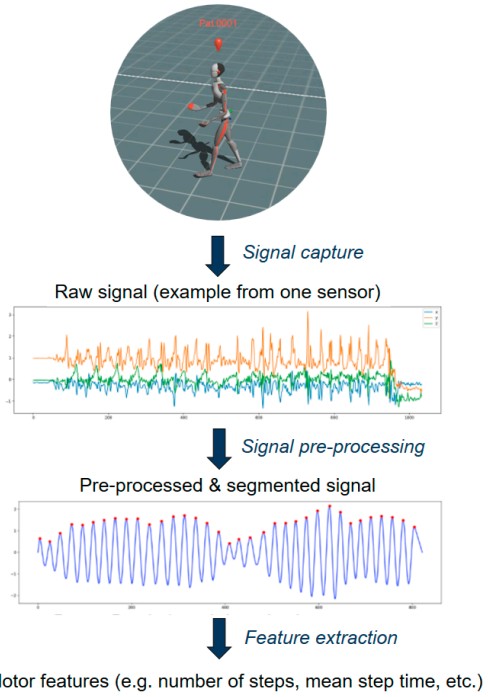

Figure 1. Processing of 18-sensor motion-capture system

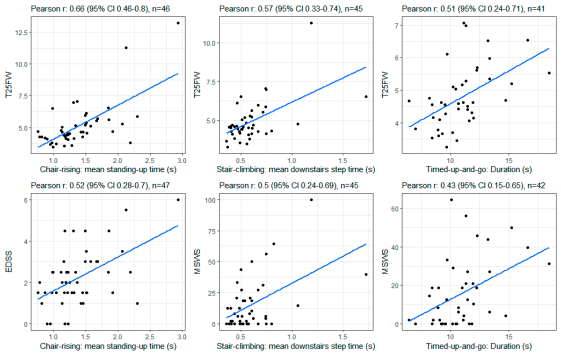

Figure 2. Best correlations of multi-sensor derived motor features with reference tests

Conclusion: Precise ground truth datasets for diverse motor tests can be generated with a multi-sensor motion capture system in the clinic. Extracted motor features show strong correlations with established functional outcomes in PwMS. Exploring this relation will inform further cross-validation with features derived from smartphone sensors that can be easier and more frequently applied in patients' natural environment.

Disclosure: T.W. nothing to disclose. A.E. is an employee of Healios AG. L.K.: fees for board membership, consultancy or speaking, or grants in the past 3 years from Actelion, Advancell, Allozyne, Bayer, Bayhill, Biogen Idec, BioMarin, CSL Behring, Eli Lilly EU, Genmab, GeNeuro SA, Gianni Rubatto Foundation, Glenmark, Merck Serono, MediciNova, Mitsubishi Pharma, Novartis, Novartis Research Foundation, Novo Nordisk, Peptimmune, Roche, Roche Research Foundation, Santhera, Sanofi-Aventis, Swiss MS Society, Swiss National Research Foundation,

Teva Pharmaceutical Industries Ltd, UCB, and Wyeth. O.R. is an employee of Healios AG. C.G.: (i) advisory board and consultancy fees from Actelion, Novartis, Genzyme and F. Hoffmann-La Roche; (ii) speaker fees from Biogen and Genzyme-Sanofi; (iii) research support by F. Hoffmann-La Roche Ltd.. J.L.: research grants from Novartis, Biogen and Innosuisse (Swiss Innovation Agency), honoraria for advisory boards and/or speaking fees from Novartis, Roche and Teva.

EPO-489

Abstract withdrawn

EPO-490

Serum Neurofilaments are a reliable biomarker to early detect PML in Multiple Sclerosis patients

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Background and aims: The earliest detection of progressive multifocal leukoencephalopathy (PML) is crucial in Natalizumab (NTZ)-treated Multiple Sclerosis patients. This study aims to assess serum Neurofilaments (sNFL) to early detect PML in longitudinal patients' follow-up

Methods: sNFL were retrospectively measured in the four PML cases occurred at CRESM, in samples collected from one year before PML onset, at PML onset, during PML and in post-PML follow-up. Levels were interpreted according to reference values. sNFL were also measured in 45 NTZ-treated patients in NEDA-3 status.

Results: Different PML onsets were observed: in 3 patients brain MRI revealed radiological-PML signs followed by different clinical manifestations; one patient showed a clinical onset confirmed by MRI. sNFL were analyzed during the different PML phases: 1)up to 4 months before PML onset: sNFL values were in the normal range in all patients (median 8.7 pg/ml, range 6.2-10.7). 2)within 3 months before PML onset: sNFL were elevated in all samples (median 17.5 pg/ml, range 15.1-81.0). 3)PML onset: sNFL were elevated (median 67.6 pg/ml, range 11.1-148.8). 4)PML/IRIS: the peak of sNFL (median 82.3 pg/ml, range 20.5-272.9) was observed. 5)Post-PML: sNFL levels demonstrated a decrease (median 13.20 pg/ml, range 9.3-30.6), but were still elevated in 2 patients according to reference values. Median sNFL values in NEDA-3 patients were 4.5 pg/ml (range 2.2-9.6).

Conclusion: Elevated sNFL were observed at radiological/clinical PML onset, but also prior to the onset. During PML recovery, sNFL weren't normalized in all samples, suggesting ongoing neuronal degeneration. sNFL represent a reliable biomarker to early detect and monitor PML.

Disclosure: Nothing to disclose.

EPO-491

New insight of gender effect on cognitive profile of a cohort of early Multiple Sclerosis patients

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Background and aims: Gender seems to influence disease phenotype and evolution in people with Multiple Sclerosis (PwMS). With our study we aimed to investigate the interplay between gender and fatigue on cognitive performances in early PwMS.

Methods: 200 PwMS (F: 64%, mean ± SD age 38.2±12.42 years, EDSS median, IQR= 2, 0-5.0) were enrolled at the diagnosis. All subjects underwent Selective Reminding Test (SRT), Spatial Recall Test (SPART), Symbol Digit Modalities Test (SDMT), Paced Auditory Serial Additional Test (PASAT-2, PASAT-3), Word List Generation (WLG) and Stroop Color-Word Interference Test (ST) for cognition; Fatigue Severity Scale (FSS) was used to report fatigue. Cognitive performances were compared between different groups using Chi-squared, Mann-Whitney-U test, and multivariate regression analysis, as appropriate.

Results: In our cohort the proportion of PwMS with cognitive impairment varied across different tests, from 3.1% in SPART-D to 8% in SRT. Fatigue was reported in 25% of PwMS. Female subjects had worse scores at SRT-LTS ($p=0.002$), SPART ($p=0.001$), SDMT ($p=0.009$), PASAT-3, ($p<0.0001$), PASAT-2 ($p<0.0001$) and STROOP ($p=0.039$). PwMS with fatigue had worse performances in STROOP ($p=0.002$) , PASAT-3 ($p=0.14$) and PASAT-2 ($p=0.004$). Multivariate analysis confirmed the predictive values of gender for impairment in SRTLTS, SPART-D and SDMT.

Conclusion: In MS previous studies, conducted some years postdiagnosis, showed male sex to be a significant predictor of worse cognitive impairment, except for visuospatial memory. This last, appears to be the more compromised cognitive domain in female subjects in our cohort at disease beginning.

Disclosure: Dr. Oggiano, Biasi, Guerra T, Guerra S, Vitobello, Iaffaldano A, Taurisano and Bianco have nothing to disclose. Dr Manni has served on scientific advisory boards for Merck Serono, Sanofi Genzyme and Roche. Prof Paolicelli, Prof Trojano and Prof Iaffaldano have served on scientific advisory boards for Biogen, Novartis, Roche, Merck and Genzyme, and they have received speaker honoraria from Biogen Idec, Merck, Roche, Teva, Sanofi-Genzyme and Novartis.

EPO-492

Leptomeningeal Enhancement in Stem Cell Transplantation Treated Multiple Sclerosis and in Other Neurological Diseases

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Background and aims: In multiple sclerosis (MS) Leptomeningeal Enhancement (LME) is a MRI marker of leptomeningeal inflammation. Aims of this study were to assess the frequency and number of LME in patients affected by MS and Other Neurological Diseases (OND), and to evaluate whether previous treatment with Autologous Hematopoietic Stem Cell Transplantation (AHSCT) determined differences in this marker.

Methods: Monocentric study in patients affected by MS or OND who in the period 2020-2022 performed one 3T brain MRI with a standardized protocol, including a post-contrast FLAIR. For a subset of AHSCT patients follow-up MRI scans, including one before treatment, were analyzed.

Results: Fifty-eight MS (40 Relapsing Remitting [RR-MS], 18 Progressive [Pr-MS]) and 12 OND patients were included. Among MS patients, 24/58 (41%) underwent AHSCT (MS AHSCT group) and the remaining 34 received approved treatments (MS CTRL; Table 1). At least one LME was identified in 20/58 (34%) MS and in 7/12 (58%) OND patients (p=0.112). No differences in the frequency of LME positive patients between the MS AHSCT (10/24, 42%) and MS CTRL group were observed (10/34, 29%) (p=0.405). However, in the MS AHSCT group we identified a direct correlation between LME number and age at AHSCT, but not at MRI (R=0.44). Furthermore, in the longitudinal pilot study (n=4), one LME disappeared following AHSCT in one case.

	MS AHSCT n=24		MS CTRL n=34		
	median	(range)	median	(range)	p value
Age at MRI, years	46	(29-57)	44.5	(22-74)	0.874
Disease duration, years	17	(6-31)	14.5	(0-52)	0.420
Progressive phase duration, years	6	(1-24)	6	(1-8)	0.620
Treatment duration, years	13	(5-26)	10	(0-25)	0.017
Duration of treatment with second-line DMTs, years	8.5	(3-14)	6	(0-11)	0.048
EDSS at MRI	3.5	(1-7)	4	(0-7)	0.536
Number of DMTs received prior to MRI	4	(2-7)	2	(0 – 5)	<0.001
Age at AHSCT, years	42.5	(27-53)	-	-	-
	n	(%)	n	(%)	p value
Gender, female	20	(83%)	20	(58%)	0.082
MS phenotype: RR-MS	16	(67%)	24	(70%)	0.312
Patients receiving treatment at MRI	0	(0%)	19	(56%)	<0.001

Table 1: Clinical-demographic characteristics of MS patients in the MS AHSCT (Multiple Sclerosis Autologous Hemopoietic Stem Cell Transplantation) and MS CTRL (Multiple Sclerosis Control) groups.

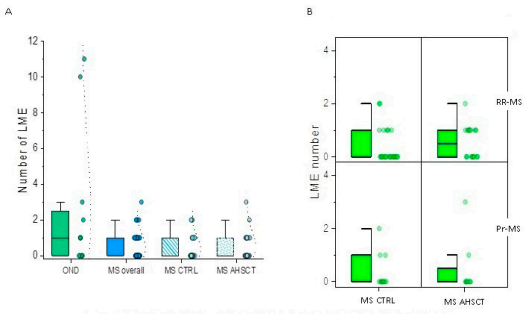

Figure 1. Median (interquartile range) number of LME in the MS and OND groups. (A) The MS cohort is further stratified according to the previous exposure to AHSCT (A) and MS form (B).

Conclusion: Based on our results AHSCT may halt the formation of new LMEs, reinforcing the indication of early use of this treatment and of high efficacy disease modifying therapies targeting inflammation.

Disclosure: Nothing to disclose.

EPO-493

Sensorineural hearing loss (SNHL) as the initial manifestation of Multiple Sclerosis with acoustic Uhthoff phenomenon

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Background and aims: Albeit uncommon, SNHL may be a manifestation of Multiple Sclerosis (MS), even less often at disease onset, and can be sudden, progressive, unilateral, bilateral or a/symmetric. Disruption of hearing neural pathways (plaques involving from brainstem to the auditory cortex) is the proposed mechanism, but inner ear involvement is also suggested. Uhthoff phenomenon is a transient worsening of neurological function, usually visual, related to increases in core body temperature.
Methods: A 20-year-old woman consulted for sudden hearing loss, tinnitus and aural fullness in the right ear for 2 weeks. The neurological examination showed horizontal nystagmus at the right gaze and upper limb pyramidalism. Audiometry test showed right SNHL of 60%. 1.5 T MRI showed T2 periventricular and subcortical hyperintensities suggesting MS.
Results: Immunologic analysis was normal. High-dose intravenous corticosteroids were indicated for 5 days, with substantial improvement (100% recovery in audiometry). CSF oligoclonal bands were positive. Six months later, a MRI showed new hyperintensities establishing MS diagnosis. During the follow-up, she reported numerous brief episodes of hearing worsening and aural fullness with hot temperatures or during exercise.
Conclusion: Neurologists should be aware of the auditory MS manifestations that over time can occur in 25%, predominantly with lesions in the medullary tegmentum. Sudden SNHL can be the sentinel presentation as clinical isolated syndrome, with a good chance of complete recovery with steroids or plasmapheresis. Temperature-sensitive conduction blockade of partially demyelinated axons is the most widely accepted mechanism of Uthoff. To our knowledge, this is the first report of acoustic Uhthoff phenomenon in MS.
Disclosure: Authors declare no conflicts of interest.

EPO-494

Accuracy of multiple sclerosis diagnostic criteria in detecting perivenular de-myelination visualized in vivo by MRI

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Background and aims: In multiple sclerosis (MS) diagnosis, caution is needed in cases carrying red flags (MS-plus). To assess the performance of the diagnostic criteria in the setting of MS-plus, perivenular topography of the lesions, a cardinal and highly specific pathological feature of MS noninvasively detectable by brain MRI, was used as a "reference standard".
Methods: Cases of typical relapsing-remitting (RR) MS (n= 28), RR MS-plus (n=59), and non-MS cases carrying MS-like brain white matter lesions (WML; n=32) received one brain MRI including conventional and FLAIR* images. PVL number/WML number (PVL-f) and conventional lesion characteristics were evaluated. For evaluating the performance of the MS diagnostic criteria, a PVL-f threshold selected by ROC analysis of the typical RRMS and non-MS cases was then applied to the MS-plus cases.
Results: Typical MS cases had a median PVL-f of 91% (range 67–100%), non-MS of 23% (range 0-89%, $p<0.00001$), and MS-plus of 55% (range 8–100%, $p=0.001$). The 52% PVL-f threshold selected by ROC analysis was exceeded by 28 (100%) of the typical RRMS cases and 1 non-MS (3%; $p<0.00001$) indicating 98% accuracy of the diagnostic criteria when compared to PVL-f. However, only 32 (53%) of the MS-plus cases had PVL-f >52% ($p=0.001$), corresponding in these cases to 68% nominal accuracy of the diagnostic criteria. In patients with low PVL-f, atypical brain lesions and cerebrovascular comorbidities were common.
Conclusion: In the setting of MS-plus, incorporating PVL-f analysis into the MS diagnostic criteria could remarkably improve diagnostic accuracy.
Disclosure: Prof Massacesi received: - educational unrestricted support from Biogen; Sanofi-Genzyme; Novartis Roche and Merck-Serono; - honoraria for scientific lectures, scientific consultation, or participation in advisory boards from Biogen; Novartis; Sanofi-Genzyme; Roche; Mylan; Merck- Serono. - research grants (recipient: University Dept.) from Sanofi-Genzyme; Biogen; Roche; Merck-Serono; Novartis

EPO-495

K index improves MS diagnosis and supports the differential diagnosis between MS and MS-like syndromes

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Background and aims: Despite validated diagnostic criteria, MS diagnosis is sometimes difficult because of MS-like clinical and/or radiological syndromes. K-index (K-index = CSF/serum K-free light chains divided by CSF/serum albumin) is a CSF biomarker, that can easily and quickly be assayed through an automatic technique that, unlike oligoclonal bands (OB) assay, releases quantitative results. To date its role in diagnostic process is controversial.
Methods: We analyzed pts with MS according to fulfillment of the 2011 McDonald diagnostic criteria and other inflammatory/vascular CNS diseases (nMS) who underwent to CSF analysis in our MS Centre. CSF biomarkers OB and K-index were analyzed. Pts were then classified according to OB presence (OB+), K-index >6,49 (k-index+) and, when magnitude susceptibility weighted images (SWI) were available, Central Vein Sign >50% (CSV+).
Results: 106 pts were included, 62 pts (58,5%) MS and 44 pts (41,5%) nMS. Frequencies of CSF biomarkers are reported in table 1-2. A subgroup of 40 pts with 3T MRI (n= 25 MS and n= 15 nMS) was also analyzed. 14/25 MS pts and 1/15 nMS pts were OB+K-index+CVS+ and 1/25 MS and 8/15 nMS pts were OB-K-index-CSV-. The inclusion of K-index in addition to OB improved the specificity (0,8 vs 0,7). The specificity of the diagnosis was higher when CVS was included (0,93) despite a lower sensitivity (0,56 vs 0,77) compared to only OB evaluation.
Conclusion: In clinical practice the combination of CSF biomarkers (OB and K-index) with MRI marker (CVS) could be a good approach to minimize misdiagnosis.
Disclosure: The authors declare that they have no conflict of interest.

Table 1. **MS** (62 pts)

K index	BO	Totale	%
+	+/-	53	85,5%
+/-	+	48	77,4%
+	+	46	74,2%
+	-	7	11,3%
-	+	2	3,2%
-	-	7	11,3%

+/- = independent from biomarker result

Table 2. **nMS** (44 pts)

K index	BO	Totale	%
+	+/-	14	31,8%
+/-	+	13	29,5%
+	+	9	20,5%
+	-	5	11,4%
-	+	4	9,1%
-	-	26	59,1%

+/- = independent from biomarker result

EPO-496

Wearing Off Phenomenon in MS Patients in Treatment With Monoclonal Antibodies: Clinical and Biological Implications

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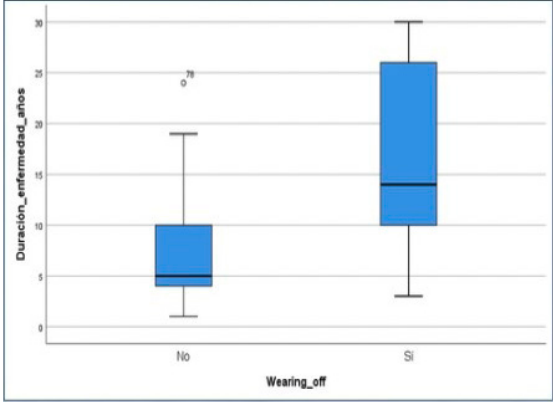
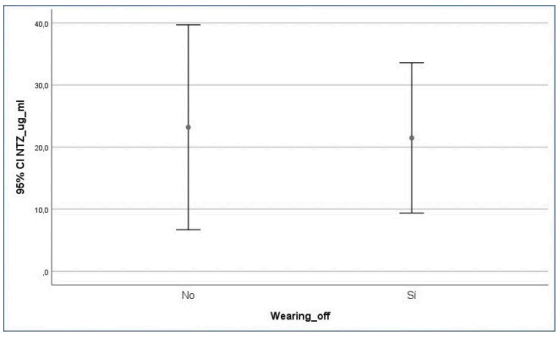
Background and aims: Multiple Sclerosis(MS)patients treated with monoclonal antibodies occasionally report some symptoms before the next dose of treatment called"wearing off phenomenon"that relate to drug "exhaustion".This phenomenon is called "wearing-off phenomenon"and its clinical relevance is controversial.Our objective is to analyze the prevalence of the wearing-off phenomenon in our MS patients who use natalizumab and ocrelizumab, describe the clinical phenomenon and investigate the. associated factors as well as possible etiologies.
Methods: Cross-sectional study in MS patients treated with natalizumab and ocrelizumab.A survey on the wearing off phenomenon is provided to the patients. We correlated this phenomenon with different clinical factors: evolution time, age, EDSS, relapses, concentration of the drug in blood of Natalizumab and CD19+ count in Ocrelizumab patients. We use statistical package SPSS v.25.
Results: The frequency of wearing off is higher with Natalizumab (48%) than with Ocrelizumab(25%)with significant differences(chi square, p=0.043).The most common symptom if wearing off is fatigue. No significant association between relapses, age, baseline EDSS or progression between patients with and without wearing off was observed in the two drugs. In Ocrelizumab there is no association with wearing off, CD19+,or NfLs, and with Natalizumab there is no relationship with serum levels of Natalizumab. Only association in Ocrelizumab and EDSS month 36 relapsing MS, and time of evolution of the disease in progressive forms(U Mann Whitney p<0.05).
Conclusion: Although the perception of wearing off is not uncommon in MS patients treated with monoclonal antibodies, its association with disease evolution and impact on clinical and analytical biomarkers has not been demonstrated in our sample
Disclosure: Nothing to disclose.





EPO-497

Ocrelizumab use in the real-world experience: data from a hot spot area for Multiple Sclerosis

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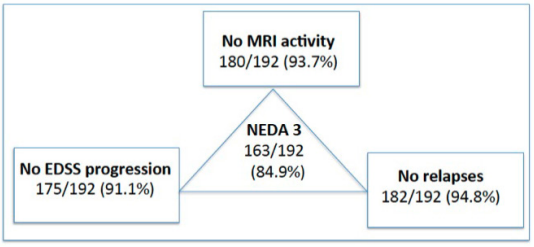
Background and aims: Despite the growing use of Ocrelizumab, data of the real-world experience are limited. Aim of this study was to examine the OCR use in primary progressive (PP) and relapsing remitting (RR) patients categorized as naïve and switchers, also evaluating predictors of treatment response and adverse infusion events (AIEs).
Methods: MS patients exposed to OCR between 2016 and 2022 were considered. NEDA-3 status at 24 months was evaluated for RR patients; determinants of NEDA 3 and AIEs were explored by regression analyses.
Results: The sample included 421 patients, of which 33 (7.9%) were PP and 388 (92.1%) RR. Among these, 67(17.3%) were naïve, while the switchers from I° and II° line DMTs were 199 (51.3%) and 122 (31.4%), respectively. OCR use as exit strategy from Natalizumab has been reported in 25 JCV+ patients. Among these, 6 patients presented with MS reactivation in the first 12 months, despite the short latency to OCR initiation (3.4 ± 2.0 months). NEDA 3 status after 24 months was calculated for 192 RR patients and achieved by 163(84.9%), with lower age (p=0.05) and ARR in the year prior OCR (p=0.005) emerged as determinants. AIEs occurred in 128 (30.4%) patients; a relationship with previous allergic diathesis (p=0.001), reported for 37 (8.8%) patients, was observed,

while the short protocol administration, used for 279 (66.8%) patients, was not related.

	Total MS patients (421)		RRMS		
	PPMS (33)	RRMS (388)	Naive (67; 17.3 %)	Switchers from I°line DMTs (199; 51.3%)	Switchers from II°line DMTs (122; 31.4%)
Male Gender	17 (51.5%)**	132 (34%)	30 (44.7%)	62 (31.1%)	40 (32.8%)*
Age at OCR initiation (years)	53.0 ± 9.0**	42.4 ± 10.1	40.1 ± 10.8	43.7 ± 10.4	41.7 ± 9.1
MS duration at OCR initiation (years)	16.2 ± 11.7*	13.1± 8.6	3.9 ± 6.2	13.6 ± 8.4	16.0 ± 6.6
EDSS score at OCR initiation	6.1± 0.9**	3.3 ± 2.2	2.4 ± 1.7*	3.5 ± 2.2	3.3 ± 2.2
OCR exposition (months)	22.4 ± 11.1	25 ± 15.3	23.5 ± 11.8	25.6 ± 17.6	24.7 ± 12.9

Demographic and clinical features of progressive and relapsing remitting patients exposed to ocrelizumab, categorized as naive or switchers from I° and II° line DMTs.



Different components of NEDA 3 status at 24 months of OCR exposure (192 MS patients)

NEDA 3	B	Sig.	Exp(B)	95% C.I.for EXP(B)	
				Lower	Upper
Age at OCR initiation (ys)	-0.048	**0.058**	,953	,906	1,002
ARR in the year prior OCR	-0.653	**0.005**	,520	,332	,817
MS duration	0.024	0.417	1,024	,966	1,086
EDSS at baseline	0.055	0.624	1,057	,847	1,318
Naive	0.438	0.476	1,549	,464	5,167

Predictors of therapeutic response of MS patients exposed to 24 months of OCR (192 subjects)

Conclusion: OCR is confirmed as a high efficacy option for naïve and switchers patients. Further real-world data are needed to understand its efficacy and safety in different patients' groups.

Disclosure: Mellino P has received travel grants from Sanofi. Lorefice L, Frau J, Coghe G and Cocco E, have received honoraria for consultancy or speaking from Biogen, Novartis, Sanofi Genzyme, Serono, Teva, and Almirall. Pilotto S. has received travel grants from Biogen, Teva and Bristol Myers Squibb. Barracciu M has nothing to disclose.

EPO-498

Transorbital Ultrasound for Morphological and Haemodynamical Assessment of Optic Nerve in Multiple Sclerosis

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Background and aims: Changes of the optic nerve (ON) reflect the overall pathology in multiple sclerosis (MS). Transorbital ultrasonography (TOUS) is a promising tool for detecting ON changes after exposure to optic neuritis. We aimed to explore ON haemodynamic in addition to morphological changes in a sample of MS patients.

Methods: Sixty-seven MS patients (Thompson diagnostic criteria) were included in this preliminary study: 53 women and 14 men aged 41.6 (11.3) and 40.1 (11.0) (p=ns) years. EDSS score was 0-2.5 in 47 (70.1%) and >2.5 in 20 (14.9%) subjects. ANCOVA was used to investigate the association between US morphological (ON diameter (OND) at 3 and 5 mm from papilla, ON sheath diameter (ONSD) at 3 mm from papilla and myelination index (MI) ratio), a history of optic neuritis, controlling for sex and EDSS.

Results: Out of 134 eyes no history of optic neuritis was recorded in 89 (66.4%), while at least 1 episode was recorded for 45 (33.6%). A higher proportion of affected eyes among women (86.4%) than men (13.6%) was observed (p=ns). OND – at 5 mm from papilla especially - and ONSD at 3 mm were significantly reduced in ONs with optic neuritis. MI ratios were higher in affected vs unaffected eyes. Mean ON diameters were lower in patients with higher EDSS score, irrespective of history optic neuritis. Mean flow velocity was reduced in affected eyes for all principal arteries explored.

Conclusion: TOUS and Doppler US examination can detect ON changes in MS, showing potential for prognostic marker.

Disclosure: The authors have nothing to disclose.

Table 1

US parameters	Marginal means (95% CIs)		p^a
	Eye with optic neurities	Unaffected fellow eyes	
OND3 (mm)	2.87 (2.78, 2.96)	2.99 (2.93, 3.05)	***0.031***
ONSD3 (mm)	4.47 (4.33, 4.61)	4.56 (4.46, 4.65)	*0.266*
ONSD5 (mm)	4.77 (4.60, 4.93)	4.88 (4.76, 4.99)	***0.030***
MI ratio (mm)	0.940 (0.928, 0.952)	0.937 (0.928, 0.945)	***0.009***
OA MFV (cm/sec)	18.97 (17.33, 20.61)	19.50 (18.35, 20.66)	***0.008***
CRA MFV (cm/sec)	7.47 (6.97, 7.97)	7.75 (7.40, 8.10)	*0.473*
PCA MFV (cm/sec)	17.44 (15.80, 19.09)	18.66 (17.50, 19.82)	*0.522*

[a]ANCOVA: dependent variables history of ON is the fixed factor; covariates: sex, EDSS (0-2.5 vs >2.5)
US=Ultrasound; ON=optic nerve; OND3=ON diameter at 3mm from papilla; ONSD3= ON sheath diameter at 3mm from papilla; ONSD5= ON sheath diameter at 5mm from papilla; MI=myelination index; OA=Ophthalmic Artery; CRA=central retinal artery; PCA=posterior ciliary artery; MFV=mean flow velocity.

EPO-499

Family Functioning and Multiple Sclerosis: preliminary data of a multicentric Italian project

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Background and aims: Multiple Sclerosis (MS) may influence family functioning, with effects on both marital relationships and parental bonding. Our aim is to evaluate family functioning and related factors in patients with MS and their families.

Methods: A dedicated platform has been used for filling in the questionnaires for MS patients and their families. As controls, we selected families with no subjects referring chronic diseases. Socio-demographic and clinical information were preliminary collected. Administered questionnaires included: (1) the short form of the Family Assessment Measure Third Edition (FAM3); (2) the Hospital Anxiety and Depression Scale (HADS); (3) the Multidimensional Scale of Perceived Social Support (MSPSS); Dyadic Adjustment Scale (DAS) and the Inventory of Parent and Peer Attachment (IPPA).

Results: 129 MS patients, 93 family members (21 aged between 13 and 20 years), and 210 control subjects (100 aged between 13 and 20 years) completed the online questionnaires. Sociodemographic characteristics are displayed in table 1. MS family members showed to be more anxious than control subjects (p= 0.0016) and MS partners had a higher degree of dyadic agreement (on finances, leisure time, home organization) than control subjects (p= 0.0167). Young people with age between 13 and 20 years, who have at least one member with MS in their family, had higher quality attachments with significant others (both parents and peers), as assessed with the IPPA (Table 2).

Conclusion: MS may affect the psychological state and family functioning by making MS family members more anxious, but also make more compliant partners and mature adolescents.

Disclosure: The authors have no conflicts of interest or disclosures in connection with this article.

		MS patients	MS family members N=59 With ages between 13 and 20 years old N=21	MS family partners N=34	HC With ages between 13 and 20 years old N=100	HC With age over 21 years old N=110
Sex	Female, n (%) Male, n (%)	91 (70,54%) 38 (29,46%)	39 (66,10%) 20 (33,90%)	15 (44,12%) 19(55,88%)	/	/
Age	Mean (SD)	41.16 (11.66)	33.23(19.18)	44.76 (10.09)	18.1 (1.51)	40.22(12.03)
Years of schooling	Mean (SD)	16.64 (1.97)	15.72 (2.32)	16.82 (1.67)	/	/
PDDS	Median (IQR)	1 (0-3)	/	/	/	/
Percentage of MS patients and MS family members **who had children**	n (%)	86 (67,72%)	/	26 (76,47%)	/	/
Percentage of MS patients and MS family members **who** are religious	n (%)	103 (79,84%)	41 (69,49%)	24 (70,48%)	/	/

MS, multiple sclerosis;
HC, helathy controls;
PDDS, Patient-determined Disease Steps.

Table 1. Sociodemographic characteristics of MS patients and their family members and partners.

		MS patients N=129	MS family members Tot N=59 With ages between 13 and 20 years old N=21	MS partners N=34	HC Aged from 12 to 20years N=100	HC Aged over 21 years old N=110	P
HADS							MS Vs HC
Anxiety	Mean	7.79(4.80)	6.62 (4.72)	7.52(4.86)		8.47(3.10)	0.0923
Depression	(SD)	6.41(4.15)	4.79 (3.77)	5.20(3.47)		4.97(2.98)	**0.0129***
							MS family members Vs HC
							0.0016*
							0.3554
MSPSS							MS Vs HC
Significant Other Subscale	Mean (SD)	24.01(4.46)	24.15(4.20)	22.76 (5.79)		23.31(4.90)	0.2265
Family Subscale		23.34(5.44)	23.81(4.10)	23.11 (5.63)		23.35(4.49)	0.2719
Friends Subscale		20.55(6.04)	21.01(5.70)	18.94 (6.10)		20.48 (4.81)	0.6602
Total Scale		67.92(12.81)	68.98(10.60)	64.82(13.69)		67.14(12.30)	0.5567
							MS family members Vs HC
							0.3632
							0.8512
							0.3539
							0.5589
FAM3							MS Vs HC
	Mean (SD)	12.43 (6.26)	12.067(5.56)	12.08 (6.08)		14.07(7.42)	0.1595
							MS family members Vs HC
							0.1604
DAS							MS partners Vs HC partners
Dyadic consensus							
Dyadic satisfaction	Mean	50.49 (9.90)	45.5 (10.60)	53.46 (8.29)		37.4 (4.65)	**0.0167***
Dyadic cohesion	(SD)						
Affective Expression		27.72 (3.35)	27(1.41)	27.64 (2.31)		31.38 (4.48)	0.2891
Total score							
		14.95 (3.87)	15 (2.82)	15.28 (3.53)		14.65(3.77)	0.5715
		8.91 (2.56)	7.5 (0.70)	8.92 (2.41)		8.7 (2.6)	0.9689
		102.09 (15.74)	95 (15.55)	105.32 (11.95)		102.88 (16.67)	0.1210
IPPA-Mother§							
Trust	Mean		39.28 (4.74)		37.4 (4.65)		**<0.005***
Communication	(SD)		31.71 (7.29)		32.45(5.07)		0.8611
Alienation			19.90 (4.04)		12.8 (4.42)		**<0.005***
Total score			90.90(13.62)		82.65 (7.19)		**<0.005***
IPPA-Father§							
Trust			41.35 (5.80)		35.81 (5.78)		**<0.005***
Communication			29.75 (6.91)		29 (6.23)		0.5303
Alienation			21.95 (3.41)		13.61 (5.12)		**<0.005***
Total score			93.05 (13.41)		78.42 (8.38)		**<0.005***
IPPA-Peers§							
Trust			42.19 (5.44)		39.27 (5.32)		**0.0213***
Communication			29.85 (6.01		31.32 (5.64)		0.3005
Alienation			27 (4.65)		15.98 (4.63)		**<0.005***
Total score			99.04 (13.39)		86.57 (8.93)		**<0.005***

*p<0.005; § filled only by people between 13- to 20-year-old.
MS, multiple sclerosis; HC, healthy controls; HADS, the Hospital Anxiety and Depression Scale; MSPSS, the Multidimensional Scale of Perceived Social Support; FAM3, the short form of the Family Assessment Measure Third Edition; DAS, Dyadic Adjustment Scale; IPPA, the Inventory of Parent and Peer Attachment.

Table 2. The results of questionnaires in MS patients, MS family members and Healthy controls with no subjects with chronic diseases in their families.

EPO-500

Depressive symptoms and monoaminergic network changes in multiple sclerosis: a longitudinal study

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Background and aims: Growing evidence suggests that depression in multiple sclerosis (MS) patients might be a symptom with a neurobiological basis rather than a mere consequence of the disability accumulation. This study aimed to investigate whether the development of depressive symptoms in MS is associated with monoaminergic functional network changes.

Methods: Forty-nine MS patients and 27 healthy controls (HC) underwent clinical and 3.0T resting state (RS) functional MRI assessment at baseline and after 1.6 year median follow-up (interquartile range=1.0-2.1 years). Depressive symptoms were evaluated at both time points using the Montgomery-Asberg Depression Scale (MADRS); MS patients were included if their baseline MADRS was <9 (i.e., no depression). Monoaminergic-related RS functional connectivity (FC) was derived by independent component analysis, constrained to PET atlases for dopamine, noradrenaline and serotonin transporters.

Results: Fourteen (29%) MS patients developed depressive (D) symptoms at follow-up, while 35 (71%) remained not depressed (ND). At baseline, MS patients showed decreased RS FC vs HC in all three PET-guided monoaminergic networks in frontal, cingulate and cerebellar cortices, and increased RS FC in parieto-occipital regions. ND-MS patients showed limited RS FC changes over time. Conversely, D-MS patients showed a widespread RS FC decrease over time in the PET-guided dopamine network, mainly in orbitofrontal, middle occipital, anterior cingulate and precuneal cortices (all significant at time-by-group interaction analysis), and in occipital regions. They also presented decreased RS FC over time in parahippocampal and occipital regions of the PET-guided noradrenaline network.

Conclusion: Specific patterns of monoaminergic networks changes were associated with development of depressive symptoms in MS patients.

Disclosure: The authors have nothing to disclose.

EPO-501

Influence of cardiorespiratory fitness and neuroinflammation on hippocampal volume in multiple sclerosis

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Background and aims: The hippocampus is characterized by neuroplasticity and neurogenesis also in adulthood. Neuroinflammation and cardiorespiratory fitness (CRF) may influence hippocampal integrity by modulating the processes promoting neurogenesis and neuroprotection that contribute to the preservation of functions. Here, we investigated whether higher CRF may limit the detrimental effects of neuroinflammation on hippocampal volume in the main multiple sclerosis (MS) clinical phenotypes.

Methods: Brain structural MRI scans and maximum oxygen consumption (VO2max), a proxy of CRF, were acquired from 81 MS patients (27 relapsing-remitting [RR] and 54 progressive [P]), and 45 age- and sex-matched healthy controls (HC). T2-hyperintense white matter lesion volume (T2-LV) and choroid plexuses volume (CPV) were quantified as neuroinflammatory measures. Association of demographic, clinical, neuroinflammatory and CRF measures with normalized brain, gray matter, hippocampal and thalamic volumes in RRMS and PMS patients were assessed using Shapley and best subset selection regression.

Results: For most volumetric outcomes, largest portions of variance were explained by T2-LV (variable importance [VI]=9.4-39.4) and CPV (VI=4.5-26.2). VO2max explained the largest portion of variance of normalized hippocampal volume in RRMS patients (VI=16.9) and was retained as a relevant predictor (Std. β=0.374, p=0.023) together with T2-LV (Std. β=-0.330, p=0.016), while explaining a small amount of variance of this outcome in PMS subjects (VI=0.1) and of all the other volumetric outcomes in both groups (VI from 0.3 to 2.2).

Conclusion: By exerting beneficial neurotrophic effects, a higher CRF may have a specific neuroprotective role for the hippocampus mainly in the early phases of MS.

Disclosure: The authors have nothing to disclose.

EPO-502

Eculizumab in AQP4+ neuromyelitis optica spectrum disorder: 3 years of data from Japanese post-marketing surveillance

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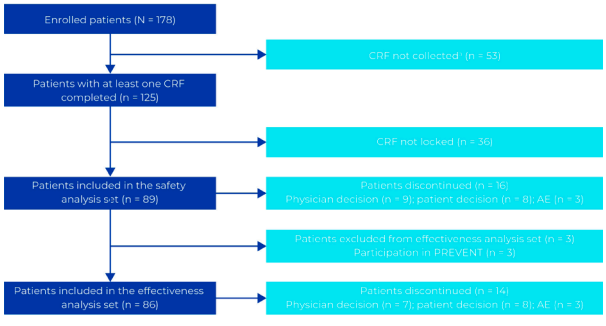
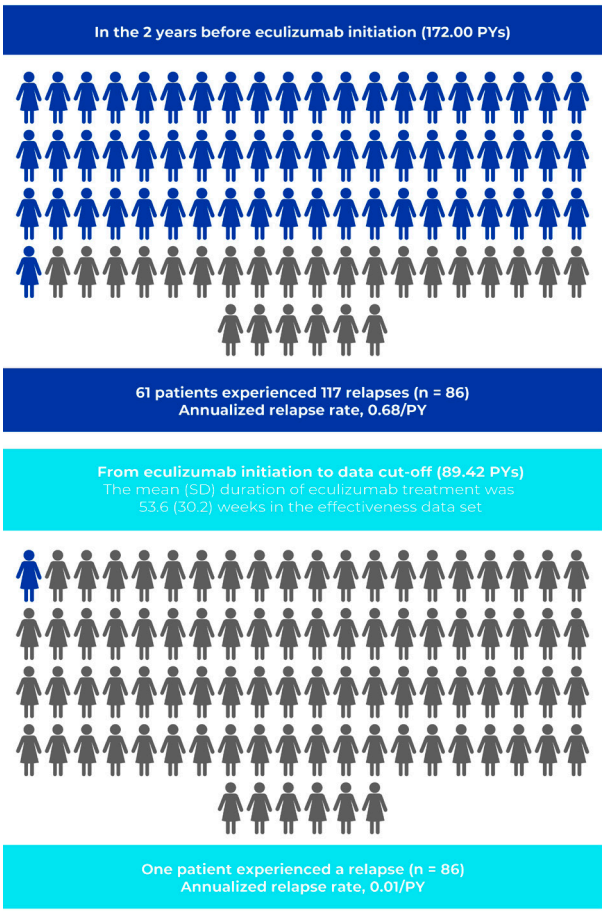
Background and aims: Eculizumab (ecu) is approved in Japan for prevention of aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD) relapse and is undergoing mandatory post-marketing surveillance (PMS) of real-world use.
Methods: This PMS interim analysis assessed long-term safety and effectiveness of ecu in Japanese patients (pts) from approval (November 2019) to data cut-off (October 2022).
Results: The safety set comprised 89/178 pts; 16 discontinued (9 physician decisions, 8 patient decisions, 3 adverse events [AEs]). Overall, 62 AEs (25 deemed treatment-related) were observed in 31 pts; of these 62 AEs, 40 were serious AEs (14 deemed treatment-related), observed in 22 pts. No meningococcal infections occurred. The effectiveness set comprised 86 pts. In the 2 years (172.00 patient years [PY]) before ecu, relapse rate was 0.68/PY; 28 pts (32.6%) had 1 relapse, 33 pts (38.4%) had ≥2 relapses. During ecu treatment (89.42 PY), relapse rate was 0.01/PY (1 relapse). In the 6 months before ecu, 46 pts (53.5%) were receiving immunosuppressant therapy (IST), whereas during 6–12 months after ecu, 25 pts (44.6%) were receiving IST. The proportion of pts taking prednisolone >10 mg/day decreased from 44.2% at 24–20 weeks before ecu treatment to 18.2% and 11.2% at 52–56 and 100–104 weeks after ecu, respectively.



[a]Patients for whom a CRF was not collected were not included in the analysis.
Patients may be counted to more than one reason for discontinuation.
AE, adverse event; CRF, case report form.

Patient disposition



Incidence of relapses before and after eculizumab initiation

Table 1. Summary of patients with treatment-related AEs

Event, n (%)	Safety analysis set (n = 89)
Any treatment-related AE	15 (16.9)
Any treatment-related SAE	8 (9.0)
Gonococcal infection	2 (2.2)
Bacteraemia	1 (1.1)
Cellulitis	1 (1.1)
Meningitis bacterial	1 (1.1)
Meningitis herpes	1 (1.1)
Pneumonia	1 (1.1)
Bacterial sepsis	1 (1.1)
Device related infection	1 (1.1)
Pulmonary hypertension	1 (1.1)
Systemic lupus erythematosus	1 (1.1)
Cystitis haemorrhagic	1 (1.1)
Renal impairment	1 (1.1)
Pyrexia	1 (1.1)

AE, adverse event; SAE, serious adverse event.

Summary of patients with treatment-related AEs

Conclusion: In a real-world setting, ecu was highly effective in preventing relapses and well tolerated in Japanese pts with AQP4+ NMOSD, consistent with findings from the PREVENT study. The observed reduction in IST use, also aligned with other real-world experiences, underlines the benefits of C5 inhibition in these pts.
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CSL Behring, Daiichi Sankyo, Eisai, Kyorin, Mitsubishi Tanabe Pharma, Novartis, Otsuka, Roche, Takeda, Teijin Pharma, research scholarships from AbbVie, Boehringer Ingelheim, Chugai Pharmaceutical, Daiichi Sankyo, EA Pharma, Eisai, Japan Blood Products Organization, Mitsubishi Tanabe Pharma, Otsuka, Shionogi, Sumitomo Pharma, Teijin Pharma and Tsumura, and grants from Biogen, the MEXT of Japan and the MHLW. IN: personal fees from Alexion Pharma GK, Chugai Pharmaceutical, Biogen Japan, Mitsubishi Tanabe Pharma, Novartis and Takeda, and grants from LSI Medience, the MEXT and the MHLW of Japan. HY: personal fees from Alexion Pharma GK, Biogen Japan, Chugai Pharmaceutical, Mitsubishi Tanabe Pharma and Novartis, and grants from the MHLW of Japan. YM: personal fees from Alexion Pharma GK, Biogen Japan and Chugai Pharmaceutical. KO and KH: employees of, and hold stock in, Alexion Pharma GK, AstraZeneca Rare Disease. KF: personal fees and other support from AbbVie, Asahi Kasei Medical, Biogen, Chugai Pharmaceutical, Eisai, Merck Biopharma, Mitsubishi Tanabe Pharma, Novartis, Ono, Roche, Sumitomo Dainippon, Takeda, Teijin Pharma, UCB and Viela Bio and grants from the MEXT of Japan and the MHLW of Japan.

MS and related disorders 6

EPO-503

Spasticity Plus Syndrome model in Multiple Sclerosis: an operative approach in a real life cohort

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Background and aims: Spasticity Plus Syndrome (SPS) has been recently conceptualised to enclose several symptoms that might coexist with spasticity in Multiple Sclerosis (MS). In this study we aimed to test the SPS model through a web-based tool exploring the symptomatic profile of a cohort of patients with MS relying on patients reported outcomes (PROs).
Methods: A web-based questionnaire was sent to MS patients followed at the MS Center of Tor Vergata University to assess the symptomatic burden of spasticity, spasms, pain, fatigue, sleep disorders, depression, bladder and bowel dysfunctions and sexual disturbances. The impact of each symptom on daily life was rated from 0 to 5 and symptoms ≥ 3 were considered for the analysis.
Results: Analysing 400 questionnaires we found that frequency of fatigue was 64%, depression 46%, spasticity 33%, pain 25%, spasms 19%, bladder 37% and bowel 21% dysfunctions, sexual disturbances 30%, sleep disorders 31%. Defining SPS as the association of spasticity or spasms plus at least one symptom among pain, urinary dysfunction and fatigue, SPS was detected in 26% of patients with EDSS ≤ 2.5 and in 24% with EDSS 3-4 and 50% with EDSS >4.
Conclusion: Our PROs-web-based questionnaire confirms the validity of SPS model in a real-life setting and provides an operative frame to assess SPS model. Moreover, our analysis shows that SPS can be found also in patients with low disability. Adoption of this self-reported SPS questionnaire in clinical practice might allow an earlier detection of SPS and prompt an innovative model of care.
Disclosure: All authors report no disclosures relevant for the purpose of this manuscript.

EPO-504

Prophylaxis of HBV reactivation in multiple sclerosis patients treated with ocrelizumab

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Background and aims: There are some recommendations starting antiviral prophylaxis to prevent hepatitis B virus (HBV) reactivation in the case of immunosuppressive treatment for hematologic and oncologic diseases.
Methods: 62 MS individuals qualified for OCR therapy were enrolled in the prospective study. Serum HBV surface antigen (HBsAg), anti-HBV core antigen (anty-HBcAg total) and HBV-DNA were evaluated before OCR therapy and after administration of prophylactic agents for HBV reactivation: nucleosid(t)e analogs (PA-HBV).
Results: Positive anty-HBcAg total and negative HBsAg were found in 4 patients with primary progressive multiple sclerosis (PPMS) and in 4 individuals with relapsing-remitting (RRMS). Oral treatment with PA-HBV: entecavir (0.5 mg/day) and tenofovir (245 mg/day) were included in 7 patients and in 1 individual, respectively. The time from starting PA-HBV therapy to initiation of ocrelizumab treatment was 31.4±17.5 [days]. The number of OCR infusion was 3.0±1.0. Mean value of anty-HBcAg total was 5.5±4.4 [ratio] at baseline and 4.59±3.4 during OCR therapy after PA-HBV administration. Serum hepatic parameters (aspartate;-alanine aminotransferase bilirubin) were 20.1±3.2; 26.1±15.9 [U/L] and 7.6±2.7 [umol/l], repectively. HBsAg and HBV-DNA were not detected.
Conclusion: OCR therapy is related to the risk for HBV reactivation. However, additional treatment with PA-HBV prevent HBV viral replication in MS patients. No hepatic impairments and side effects were observed after PA-HBV administration. While tenofovir was found as potent inhibitor of Epstein-Barr virus reactivation, it seems an appropriate therapeutic approach in MS patients.
Disclosure: Authors declare no conflicts of interest.

EPO-505

Evaluation of paramagnetic rim lesions as a marker of disability

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Background and aims: In multiple sclerosis (MS) brain lesions with a paramagnetic rim (PRL) detected by brain MRi are considered a biomarker of chronic inflammatory active lesions and their presence seems to correlate with disability accumulation.
Methods: MS patients under treatment and with disease activity (n=119) were included (RR, n= 99; SP, n= 20). Each of them received one 3T MRi scan with 3D-EPI susceptibility weighted image (SWI) for the detection of PRLs. MRi data were analyzed with the clinical characteristics by descriptive and multivariate analysis. T2 lesion load was obtained in 99 patients using MIPAV, while brain volumes were evaluated by FreeSurfer software.
Results: Overall, the patients with PRL were 73/119 (61,3%), average PRL number/patient = 3,3 (1-18).

Bivariate and multivariate analysis between PRL presence and baseline clinical and demographic parameters showed association with EDSS. Multiple linear regression analysis showed close correlation between EDSS and PRL number (r= 0,34; p= 0,00001) in the RR patients, but not in the SP patients. Moreover, presence of just one PRL seem associated to the total brain volume changes independently from the total T2 lesion.

Conclusion: Presence of PRLs correlates with disability. One single PRL seems sufficient to increase high EDSS development risk and brain atrophy independently from T2 lesion load. No correlation was observed at the higher EDSS values in SP patients, despite a higher PRL number/patient, probably because of a ceiling effect.

Disclosure: Nothing to disclose.

EPO-506

Medically unexplained symptoms are common in women in tertiary neurological healthcare center: a survey study

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Background and aims: Persons with suspicious onset of multiple sclerosis (MS), 18-67% do not fulfil diagnostic criteria of MS. Although some of them are diagnosed with other neurological diagnoses, most of them remain undiagnosed and are often not followed-up in healthcare. In our previous study, persons with undetermined diagnosis (PwUD) showed signs of impaired cognition and reduced quality of life. In this study, we invited PwUD to answer a survey to further characterize this cohort.

Methods: The studied cohort of suspected MS included 271 patients in a tertiary neurological healthcare center who were prospectively followed for 40 months (range 31-52). PwUD (n=72) answered a questionnaire based on Epidemiological Investigation of MS (EIMS), a population-based case-control study using incident cases of MS and a control population aged 16-70 years. For each case, two controls were randomly selected from the Swedish national population registry, matched by age, gender and residential area.

Results: The response rate was 83% and 61% reported persisting MS-like symptoms. The proportion of PwUD in the studied cohort was 20.3%. Compared to PwMS and/or controls, PwUD consisted of more women with non-Swedish origin, had more children and higher education. There were more non-smokers among PwUD and they consumed less alcohol. PwUD reported higher occurrence of autoimmune disease (Table).

Study	Sahlgrenska	EIMS			
Case-control status	PwUD	PwMS	P value[1]	Controls	P value[2]
Total	72	256		531	
Age of onset (mean, SD) Age of onset (median, range)	34.3 (9.4) 33.0 (16-56)	33.5 (10.0) 32.0 (12-62)	0.7		0.4
Age at study inclusion (mean, SD) Age at study inclusion (median, range)	38.5 (9.7) 37.5 (20-60)	37.5 (10.9) 36.0 (17-70)	0.2	38.3 (11.2) 37.0 (17-69)	0.1
Women (n, %)	57 (79)	175 (68.4)	0.06	364 (68.6)	0.05*
Swedish[3] (n, %)	44 (61)	192 (75)	0.006*	382 (72)	0.02*
Currently living with an adult (n, %) Lived with an adult 5 years ago (n, %)	52 (72) 49 (68)	192 (76) 184 (73)	0.4 0.3	385 (77) 379 (76)	0.3 0.06
Children (n, %) Number of children (mean, SD)	53 (74) 1.4 (1.0)	130 (52) 1.0 (1.1)	0.002*	314 (63) 1.2 (1.2)	0.09
Autoimmune disease[4] (n, %)	21 (29)	41 (16)	0.002*	78 (15)	<0.001*
Heredity for AI disease[5] (n, %)	46 (64)	190 (74)	0.05	379 (71)	0.06
University (n, %) Number of terms (mean, SD) Exam (n, %)	45 (62) 4.2 (5.3) 41 (57)	114 (45) 3.3 (4.3) 66 (26)	0.002*	242 (46) 3.3 (4.2) 144 (27)	0.003*
Ever smoking[6] (n, %) Current smoking[9] (n, %) Past smoking[10] (n, %) Number of pack years (mean, SD)	29 (39) 13 (19) 16 (23) 2.3 (5.9)	138 (54) 76 (30) 62 (24) 3.5 (6.6)	0.08 0.03* 0.6 0.1	230 (43) 116 (22) 114 (21) 2.7 (6.1)	0.9 0.4 0.98 0.5
Snuff use (n, %)	13 (18)	43 (17)	0.6	93 (18)	0.7
Exercise[11] at inclusion (mean, SD) Exercise 5 years ago (mean, SD)	2.5 (1.1) 2.6 (1.1)	2.5 (1.0) 2.7 (1.0)	0.6 0.5	2.6 (0.9) 2.7 (1.0)	0.9 0.7
Low intake of fatty fish[12] (n, %)	7 (10)	44 (18)	0.2	93 (18)	0.1
Alcohol drinkers (n, %) Gram alcohol/week (mean, SD)	47 (65) 29.8 (37.2)	178 (70) 45.3 (66.9)	0.3 0.04*	360 (68) 53.0 (98.7)	0.4 0.04*
Tiredness[13] (mean, SD)	16.5 (5.1)	15.7 (4.1)	0.4	14.4 (3.9)	<0.001*
Trust[14] outside home (mean, SD)	1.4 (0.6)	2.3 (1.0)	<0.001*	2.2 (1.0)	<0.001*
Trust at home (mean, SD)	1.5 (0.9)	1.7 (0.9)	0.2	1.6 (0.8)	0.2
Economy[15] (mean, SD)	1.4 (0.7)	1.5 (0.9)	0.5	1.5 (0.8)	0.5

1=p value for difference between PwUD and PwMS; 2=p value for difference between PwUD and controls;

Differences in variables between categories of case-control status were assessed using one-way analysis of variance (ANOVA) for continuous variables and the Kruskal-Wallis test (Mann-Whitney U test) for categorical variables.

3=born in Sweden with parents who have not immigrated from outside Sweden; 4= autoimmune disease except MS; 5=heredity for any of the mentioned autoimmune diseases; 6=ever smoking before index; index=year of disease onset among cases and corresponding controls, or first disease symptoms among non-cases; 9=smoking at index; 10=past smoking at index; 1 pack year=20 cig smoked daily during 1 year; 11=exercise was given a value between 1 (lowest exposure) and 4 (highest exposure); 12=fish intake never or seldom (less than monthly); 13=each of the seven questions on tiredness was given a number ranging between 1 (disagree) and 4 (agree), an index ranging between 7 and 28 was created by adding the numbers together, questions 1, 3, 5 and 7 were reversed; 14= feelings of trust (TrustOTR) were given a value between 1 (agree) and 4 (disagree); 15=question on money was given a value between 1 and 4, a higher value indicates financial problems.

Table: Characteristics of PwUD, PwMS and controls.

Conclusion: Approximately 20% of persons investigated for suspected MS had undetermined neurological diagnosis. PwUD seemed to have higher performance but reported lower quality of life. Although the diagnostic workup did not reveal a specific diagnosis, almost one third of PwUD reported other autoimmune diagnosis than MS.

Disclosure: LN has received honoraria for lecture from Biogen, Merck, Novartis, Teva, and has served on advisory boards for Merck, Sanofi, Janssen. JL has received travel support and/or lecture honoraria and has served on scientific advisory boards for Biogen, Novartis, and Sanofi Genzyme; and has received unconditional research grants from Biogen and Novartis. TO has academic grants from the Knut and Alice Wallenberg foundation, the Swedish Research Council and the Swedish Research Council; has received lecture and/or advisory board honoraria, as well as non-restricted MS research grants, from Biogen, Novartis, Sanofi and Merck on projects not related to the one reported here.

EPO-507

Persistence with Botulinum Toxin Treatment for Spasticity Symptoms in Multiple Sclerosis

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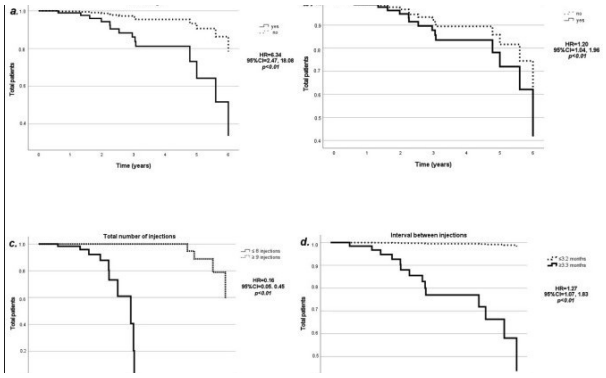
Background and aims: Botulinum toxin (BT) is an effective treatment for spasticity symptoms in multiple sclerosis (MS). We aim to evaluate the rate of discontinuation of BT treatment and the correlation with MS, spasticity, and injection variables.
Methods: This retrospective study on 3-year prospectively collected data included 122 MS patients. We collected MS clinical variables (disease durations, Expanded Disability Status Scales [EDSSs], disease-modifying treatments [DMT], and Symbol Digit Modalities Tests), modified Ashworth scales [MASs], concomitant treatments, and injection variables (formulation, dose, number of injections, and intervals between injections).
Results: A total of 14 patients discontinued BT. In the Cox regression model including the MS clinical variables, the probability of BT discontinuations increased in patients with DMT changes (HR = 6.34; 95%CI = 2.47, 18.08; $p < 0.01$) and with impaired SDMTs (HR = 1.20; 95%CI = 1.04, 1.96; $p < 0.01$). In the model including the spasticity variables, there were no associations between BT discontinuation and MAS or other spasticity treatments. In the model including the injection variables, the probability of discontinuation decreased by 80% for each cumulative injection (HR = 0.16; 95%CI = 0.05, 0.45; $p < 0.01$), but increased by 1% for each additional day over the 3-month interval between injections (HR = 1.27; 95%CI = 1.07, 1.83; $p < 0.01$).



Kaplan–Meier curves showing the rate of BT discontinuation in relation to the DMT changes (a); impaired SDMT (b); total number of injections (c); interval between injections (d); HR, 95%CI, and p-values are shown from from the Cox regression models.

		BT Continuation (n = 108)	BT Discontinuation (n = 14)	p-Value
Age, years		50.1 ± 9.4	44.0 ± 10.6	0.02 *
Sex, females		46 (42.6%)	6 (42.8%)	0.98
Follow-up duration, years		2.7 ± 1.5	3.0 ± 1.5	0.47
Disease duration, years		14.4 ± 8.3	13.1 ± 9.1	0.58
EDSS		5.8 ± 1.2	5.4 ± 1.3	0.26
DMT	None	9 (8.3%)	0 (0%)	0.30
	Low/Medium efficacy	35 (32.4%)	3 (21.4%)	
	High efficacy	64 (59.3%)	11 (78.6%)	
DMT change		29 (26.8%)	2 (14.3%)	0.54
SDMT, adjusted score		38.0 ± 11.3	35.4 ± 17.5	0.37
SDMT, impaired		40 (37.0%)	6 (42.8%)	
MAS, highest score		1.8 ± 0.5	1.9 ± 0.5	0.77
Concomitant spasticity treatments		48 (44.4%)	6 (42.8%)	0.91
BT formulation	Botox	39 (36.2%)	7 (50.0%)	0.56
	Dysport	45 (41.6%)	4 (28.6%)	
	Xeomin	24 (22.2%)	3 (21.4%)	
BT dose, uDU		263.4 ± 157.0	225.0 ± 131.19	0.38
BT changes		28 (25.9%)	4 (28.6%)	0.83
Total number of BT injections		10.3 ± 5.5	8.1 ± 5.6	0.17
Interval between BT injections, months		3.1 ± 0.4	4.9 ± 1.3	<0.01 *

Demographic, MS, spasticity, and injection variables. The p-values show the differences between the MS patients continuing or discontinuing the BT injections, using a t-test, a chi-square test, or a Fisher's exact test, as appropriate.

Conclusion: BT discontinuation was associated with concomitant MS-related issues, which should be accounted for when planning injections. The interval between injections should be kept as short as possible to reduce discontinuation in the long term.
Disclosure: The authors declare no conflict of interest.

EPO-508

Safety and Efficacy of Tolebrutinib from the Long-term Extension Study in Relapsing Multiple Sclerosis: 2.5-Year Results

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Background and aims: In the phase 2b trial (NCT03889639), brain-penetrant Bruton's tyrosine kinase inhibitor tolebrutinib was well-tolerated and elicited dose-dependent reductions in new gadolinium-enhancing T1 and new/enlarging T2-lesions in participants with relapsing multiple sclerosis. This study reported safety and efficacy at Week (W) 120 in long-term safety (LTS) extension (NCT03996291) of the phase 2b trial.
Methods: In double-blind LTS Part-A, participants continued receiving tolebrutinib 5, 15, 30, or 60mg/day until phase 3 dose selection (60mg/day). In open-label Part-B, participants received tolebrutinib 60mg/day. Safety was assessed via adverse events (AEs). Efficacy outcomes included annualised relapse rate (ARR) and change in Expanded Disability Status Scale (EDSS) score from baseline.

Results: As of July 7th, 2022, 107 (85.6%) participants had ongoing treatment. Reasons for treatment discontinuation were perceived lack of efficacy (n=5), progressive disease (n=4), participant's decision (n=3), AEs (n=3), immigration (n=2), and planned pregnancy (n=1). At W120, no new safety signals were observed. Most common treatment-emergent AEs (TEAEs) were COVID-19 (24.8% [31/125]), headache (13.6% [17/125]), nasopharyngitis (12.8% [16/125]), upper respiratory tract infection (11.2% [14/125]), cystitis bacterial, arthralgia and back pain (7.2% each [9/125]), and pharyngitis (6.4% [8/125]). There was no observed tolebrutinib dose effect for TEAEs or serious AEs (Part-A) and no safety signals emerged upon switching to tolebrutinib 60mg/day. In participants receiving tolebrutinib 60mg/day for >=8 weeks (n=124), ARR was 0.20 (95%CI: 0.14-0.28) and 73.4% remained relapse-free. Mean EDSS remained stable to W120.
Conclusion: Through LTS extension W120, tolebrutinib 60mg/day continued demonstrating favourable safety profile with low ARR and stable disability. FUNDING: Sanofi.
Disclosure: Jiwon Oh: Consulting or speaking fees (Biogen Idec, BMS, EMD Serono, Novartis, Roche, and Sanofi) and research support (Biogen Idec, EMD Serono, and Roche). Sana Syed, Tong Li, Naji Salloum, Timothy J. Turner: Employees of Sanofi (may hold shares and/or stock options in the company). Robert J. Fox: Consulting fees (AB Science, Biogen, Celgene, EMD Serono, Genentech, Greenwich Biosciences, Immunic, Janssen, Novartis, Sanofi, and TG Therapeutics) and research support (Biogen, Novartis, and Sanofi).

EPO-509

Hemibody paroxysmal dystonia as the first manifestation of multiple sclerosis

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Background and aims: Movement disorders (MD) are relatively frequent in multiple sclerosis (MS). Paroxysmal dystonia (PD) is among the most prevalent MD in MS, but rarely a first manifestation.
Methods: Clinical case report of a patient admitted to the emergency room with PD.
Results: A 32-year-old male, former smoker, with benign papillary urothelial neoplasm, was admitted with episodes of painless involuntary right wrist and metacarpophalangeal flexion with fingers extension; and right knee extension, plantar flexion, and toe flexion, with cramp-like pain in hallux. He reported 5-8 episodes/day, lasting around 30 seconds, some occurring during sleep, with complete remission of symptoms between episodes and no other focal neurological signs. He also referred right hemibody tingling sensation, starting 3 months before, with progressive worsening. Head CT and CT-angiography, and blood analysis including metabolic, autoimmune, and infectious panels were unremarkable. Onconeuronal and antineuronal antibodies were negative. He had a clinical event during EEG, without paroxysmal activity. He was started on 0,5mg clonazepam. 15 days later he was asymptomatic, without symptoms recurrence since then. Brain MRI revealed T2 hyperintense/T1 hypointense left precentral circumvolution, left midbrain and multiple small juxta-cortical, deep, and juxtaventricular white matter lesions; without gadolinium enhancement nor diffusion restriction; suggestive of a demyelinating/inflammatory aetiology. Spinal MRI was normal. CSF analysis was normal except for oligoclonal bands presence. The patient was diagnosed with MS (McDonald 2017 criteria) and is being treated with interferon beta-1b.
Conclusion: The left precentral circumvolution or the left midbrain demyelinating lesions may have caused erratic activation of corticospinal axons explaining the right hemibody PD.
Disclosure: Nothing to disclose.

EPO-510

Multiple sclerosis treatment and holistic patient care: Consensus of the Spanish Society of Neurology

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Background and aims: The management of patients with multiple sclerosis (MS) is complicated and entails several challenges, both in diagnosis and treatment. The growing number of disease-modifying therapies (DMTs) available, the scarcity of accurate biomarkers to predict their effectiveness and safety, and individual patient preferences make therapeutic decision-making very complex. The objective of the study was to offer a set of recommendations on the complete management of the MS patient in clinical practice.
Methods: The recommendations were developed following the Delphi method and taking into consideration the latest scientific evidence and the limitations of existing resources.
Results: The recommendations address nine dimensions, including early diagnosis, early start of DMT, escalation versus early start of high-efficacy DMT, face-to-face and remote follow-up, suboptimal response detection, patient perspective, biomarkers, pregnancy, and vaccination. Early treatment is recommended when possible. The classic terminology of treatment lines is obsolete, since the so-called "second line" DMTs are high-efficacy drugs that can be used as the first treatment option, depending on the patient characteristics and disease. It is also recommended to assess the patient experience using validated tools. Most potential biomarkers are not yet considered useful or feasible enough for routine use, further validation and standardization is required.
Conclusion: This consensus is intended to be a useful tool to improve and standardize MS patient management in clinical practice in Spain.
Disclosure: The authors declare fees for lectures, consultations, assistance to congresses, advisory meetings, personal compensation, teaching or research from: Actelion, Alexion, Almirall, Aventis, Bayer, Bial, Biogen Idec, BMS, Bristol Myers Squibb, Celgene, Daiichi Sankyo, Genzyme, GW Pharma, Janssen, Merck, Novartis, Roche, Sandoz, Sanofi, Teva, UCB Pharma and Viatris.

EPO-511

Association of upregulated serum miR-34a-5p with enhancing lesions and lower brain volumes in early Multiple Sclerosis

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Background and aims: Different circulating microRNAs (miRs) have recently emerged as candidate biomarkers in Multiple Sclerosis (MS). This cross-sectional study investigates the association between a panel of candidate miRs expression in serum samples of patients with recent MS diagnosis and disease course, lesion load and brain volumes.
Methods: 51 patients (33 females) aged 18-40 years recently (≤2 years) diagnosed with MS were consecutively enrolled in the study; a brain MRI scan performed between 6 months before and 1 month after inclusion was mandatory. Clinical and demographic variables were collected, and T2-lesion, global brain, white matter (WM) and gray matter (GM) volumes, and presence of gadolinium-enhancing (Gd+) lesions were assessed. Serum levels of miR-15b-5p, miR-27a-3p, miR-30b-5p, miR-34a-5p, miR-122-5p, miR-128-3p, miR-196b-5p, miR-326-3p, miR-432-5p, miR-155-5p, miR-223-3p, miR-140-5p were detected by Real-Time PCR and expressed as ratio of each miR level to a normalizer.
Results: Mean age at diagnosis was 33.3±6.18 years. Mean EDSS was 1.5±1. 45 patients had relapsing-remitting MS, 6 had primary progressive MS. Serum miR-34a-5p level was higher in patients with Gd+ lesions (mean 0.29±0,50 vs 0.07±0.25, p=0.005); miR-34a-5p was also inversely correlated with global brain volume (r= –0.46, p=0.001) and with WM volume (r= –0.44, p=0.002). In addition, miR-128-3p was inversely correlated with global brain volume (r= –0.31, p=0.034) and GM volume (r= –0.31, p=0.035).
Conclusion: Serum miR-34a-5p could be related to biological mechanisms underlying overt inflammation with blood-brain barrier disruption in MS; longitudinal studies are required to assess the possible link of miR-34a-5p and miR-128-3p with brain atrophy in MS patients.
Disclosure: Nothing to disclose.

EPO-512

Ocrelizumab dose-interval extension: a new approach to decrease adverse events while maintaining efficacy

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Background and aims: Ocrelizumab, one of the most effective treatments for MS, can induce side effects such as lymphopenia, low IgG count, infections and decreased response to vaccines. To decrease adverse events while maintaining efficacy, time-interval extension between infusions has been proposed.
Methods: 71 patients from the Hôpital Pitié-Salpetrière in Paris and the IRCCS Besta in Milan, were recruited. 44 patients were treated with an extended dose-interval (EDI) (one infusion at 9 months) after at least 2 years of treatment, while 27 patients followed standard protocol (SDI, 6 months +/- 10 days). Data about ARR (mean annualised relapse rate), EDSS (expanded disability status scale), MRI activity, PI (progression index), lymphocytes count, CD19+ and IgG were collected.
Results: No statistically significant differences were found between the two groups at treatment beginning concerning EDSS, MS type, number of previous treatments, age and sex ($p>0.05$; C.I. 95%). No statistically significant differences concerning ARR, MRI outcomes and PI ($p>0.05$, C.I. 95%) were found between the two groups. Infection incidence was higher in the SDI group, even though not statistically significant ($P=0.34$; $Z=-0.42$). A slightly higher percentage of patients in the SDI group developed hypogammaglobulinemia (EDI 31.8%; SDI 33.3%, $p>0.05$).
Conclusion: Extending time between infusions doesn´t affect treatment efficacy, while incidence of immunological AE shows a decreasing trend. However, given the importance of the topic longer studies with greater MS population should be conducted
Disclosure: Dr. Papeix, has received consulting or travel fees from Alexion , Biogen, Novartis, Roche, Sanofi-Genzyme, Teva and Merck Serono, none related to the present work. Dr Brambilla received honoraria for speaking from Novartis and Sanofi-Genzyme, and for traveling from Sanofi-Genzyme, Merck-Serono, Coloplast, and Roche. She acted as an Advisory Board member for Novartis, Sanofi-Genzyme, Biogen, Merck-Serono, and principal investigator in trials for Roche and Merck-Serono. Dr Mantegazza acted as an Advisory Board member of Biomarin. He received funding for traveling and honoraria for speaking from Sanofi-Aventis, Grifols, Teva, Bayer, Biomarin, Alexion, Argenx. He is involved as principal investigator in clinical trials for Alexion, Merck Serono, Hoffman-La Roche, Teva, Biogen, Biomarin, Almirall, Novartis, Genzyme, Catalyst. Dr Crisafulli received travel grants from Merk and Novertis. Dr Confalonieri has received honoraria from Novartis and Biogen, has received funding for travel from Merck Serono, Biogen Idec, Teva, Mylan and Roche. Dr Perugini has no disclosures No funding was received for the present study

EPO-513

Metabolomic profile changes during pregnancy and puerperium in Multiple Sclerosis

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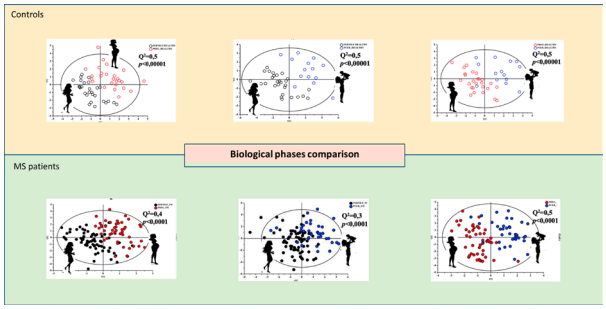
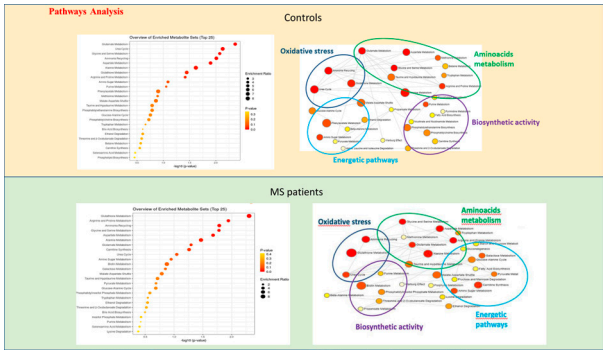
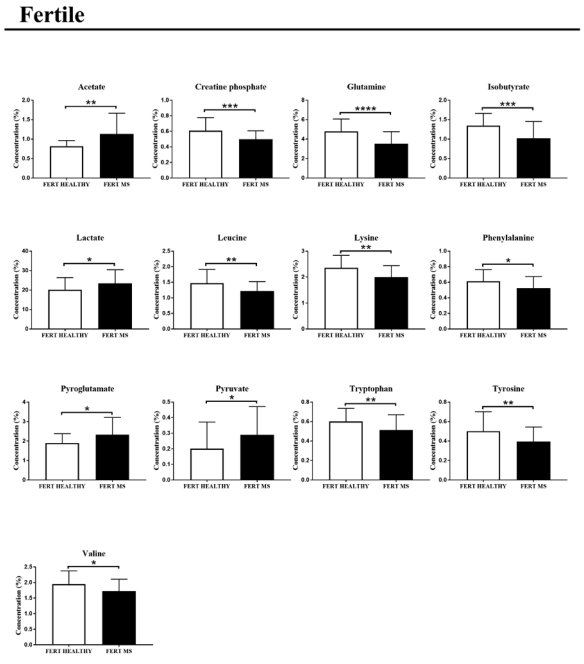
Background and aims: Pregnancy represents a protective condition for women with Multiple Sclerosis (MS) but is often accompanied by post-partum disease reactivation. The present study aims at evaluating possible metabolomic changes of MS women compared to healthy women (HCs) during the fertile phase, pregnancy, and puerperium.
Methods: Serum samples from women with MS and HC during fertile life, pregnancy and puerperium were collected and analyzed by high-resolution nuclear magnetic resonance spectroscopy. Univariate and multivariate statistics as well as pathways' analysis were performed.
Results: Samples of 155 MS women free from disease modifying treatments (68 during fertile life, 49 during pregnancy, 38 during puerperium; mean age 33.8±4.7) and 68 HCs (28 during fertile life, 26 during pregnancy, 14 during puerperium; mean age 31.8±4.5) were analyzed. Significant metabolic differences resulted by the comparison of the three different biologic phases were found in both MS ($R\ ^2X=0,5$; $R^2Y=0,5$; $Q^2=0,3$; $p<0,00001$) and HC samples ($R^2X=0,5$; $R^2Y=0,7$; $Q^2=0,4$; $p<0,00001$), with altered pathways principally related to biosynthesis activity, oxidative stress, energetic pathways and aminoacidic metabolism. After comparison between HC and MS samples at each phase, a significant metabolomic difference in fertile life ($R^2X=0,4$; $R^2Y=0,4$; $Q^2=0,3$; $p<0,00001$) was found. An increase in tryptophan levels has been reported in postpartum MS women.



Description of the metabolic Patterns after comparing different biologic phases in MS patients and HCs



Pathway analysis in MS patients and HCs



Metabolomic differences in MS patients and HCs in the fertile phase

Conclusion: The comparison between MS and HCs revealed that the main metabolomic differences are driven by the disease state during fertile phase. Despite the presence of the disease state, the metabolomic changes related to the presence of the foetus seem to prevail on the metabolomic signature connected to MS.

Disclosure: Pilotto S. has received travel grants from Biogen, Teva and Bristol Myers Squibb. Lorefice L, Fronza M, Fenu G, and Cocco E, have received honoraria for consultancy or speaking from Biogen, Novartis, Sanofi Genzyme, Serono, Teva, and Almirall. Other co-authors have nothing to disclose. We acknowledge Fondazione di Sardegna for financial support.

EPO-514

Predictive role of spinal cord MRI in multiple sclerosis: a monocentric real-world experience

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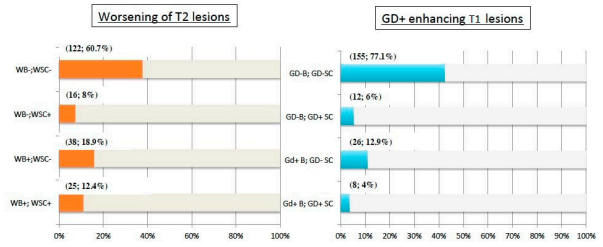
Background and aims: The 2021 Magnetic Resonance Imaging in Multiple Sclerosis (MAGNIMS) group consensus has confirmed the importance of spinal cord MRI acquisition for MS diagnosis, while spinal cord MRI monitoring is not recommended due to technical, time and cost limitations. Here we investigate the frequency of spinal cord and brain lesion load changes and their association with clinical activity, also exploring how changes in spinal cord MRI acquisition influence disease modifying treatment (DMT) choice and switch.

Methods: 1.5T brain and spinal cord MRI scanners were acquired from each patient at two timepoints spaced by at least 6 months. Radiological activity was defined as new, enlarged or gadolinium-enhancing (Gd+) lesions and clinical and demographic data were collected. Descriptive and multivariate analyses were performed.

Results: 201 relapsing-remitting MS (RRMS) patients were enrolled (145 women and 56 men, mean age: 42.5±12.1 years, mean EDSS-score:2.7±1.9). 44 (21.9%) patients presented both clinical and MRI activity, while 84 (41.8%) patients had asymptomatic MRI activity, with worsening limited to spinal cord in 16 (8%) cases. An association between spinal cord MRI activity and the occurrence of clinical relapses within 3 months after MRI was observed (p=0.024) independently of brain MRI activity. Spinal cord MRI activity resulted a determinant for DMT switch in patients with stable brain lesion load (p=0.021) and without clinical activity (p=0.003), respectively.



Worsening of brain and spinal cord MRI, and Gd+ enhancing lesions (WB+: worsened lesions in brain MRI; WSC+: worsened lesions in spinal cord MRI; GD+B: Gd+ enhancing lesions in brain MRI; GD+SC: Gd+ enhancing lesions in spinal cord MRI).

DMTs	MS Patients (201)	DMTs exposure (months) at MRI	Clinical MS activity at MRI	MRI activity (new T2 lesions/Gd+)	Concomitant clinical and MRI activity
First Line	110 (54.7%)	39.7 ± 31.6	Yes 39/201(19.4%) Intragroup 39/110 (35.4%)	Yes 44/201 (21.9%) Intragroup 44/110 (40%)	Yes 22/201(10.9%) Intragroup 22/110 (20%)
Interferon beta	30 (14.9%)				
Glatiramer Acetate	23 (11.4%)				
Teriflunomide	9 (4.5%)				
Dimethyl-fumarate	48 (23.9%)				
Second Line	57 (28.4%)	28.5 ± 27.3	Yes 20/201(10%) Intragroup 20/57 (35.1%)	Yes 21/201 (10.4%) Intragroup 21/57 (36.8%)	Yes 11/201 (5.5%) Intragroup 11/57 (19.3%)
Fingolimod	11 (5.5%)				
Alemtuzumab	8 (4%)				
Cladribine	6 (3%)				
Ocrelizumab	30 (14.9%)				
Natalizumab	2 (1%)				
No DMTs	34 (16.9%)		Yes 20/201(10%) Intragroup 20/34 (58.8%)	Yes 19/201 (9.5%) Intragroup 19/34 (55.9%)	Yes 11/201 (5.5%) Intragroup 11/34 (32.3%)

Descriptive statistics of disease modifying treatment (DMT) exposure and clinical and MRI activity at MRI acquisition.

	Clinical activity within 3 months after MRI in patients without brain MRI activity (N=138)		DMTs shift in patients without brain MRI activity (N=138)		DMTs shift in patients without clinical activity (N=155)	
	Beta	*P value*	Beta	*P value*	Beta	*P value*
Age at study time	0.002	0.902	-0.034	0.315	-0.052	0.029
Disease duration	-0.014	0.636				
EDSS at study time					0.254	0.056
DMDs exposure (months)	0.003	0.465	0.012	0.213	0.011	0.035
Gd+ spinal cord lesions	1.113	0.024				
New spinal cord lesions			2.292	0.021	1.482	0.003
Enlarged spinal cord lesions			2.792	0.046		

Multivariate analysis models between clinical activity and DMT switch (independent variables) and spinal cord radiological activity while controlling for demographic and clinical variables in specific population subgroups (p value<0.05).

Conclusion: Our results support the utility of spinal cord MRI monitoring in MS. The definition of standardized protocols for the application of MRI in evaluating spinal cord changes is needed given its prognostic and therapeutic implications.

Disclosure: Pilotto S. has received travel grants from Biogen, Teva and Bristol Myers Squibb. Lorefice L, Fenu G, and Cocco E, have received honoraria for consultancy or speaking from Biogen, Novartis, Sanofi Genzyme, Serono, Teva, and Almirall. Other co-authors have nothing to disclose.

EPO-515

Risk factors of Dimethyl fumarate-associated lymphopenia

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Background and aims: Dimethyl fumarate (DMF) is a disease-modifying treatment (DMT), approved for treatment of relapsing-remitting multiple sclerosis (RRMS). Treatment with DMF results in a reduction in clinical (annual relapse rate) and MRI activity, but is associated with a reduction in absolute lymphocyte counts. Some patients even develop severe (Grade II/III) lymphopenia under 500 lymphocytes/mikroliter during treatment. Moreover, patients with lymphopenia exhibit a higher risk of progressive multifocal leukoencephalopathy (PML). At the same time, recent studies also suggest that lymphopenia might be associated with further reduction of relapse rate and MRI activity within DMF treated patients.

Methods: In this study, we retrospectively studied the clinical and laboratory data of RRMS patients treated with DMF in our outpatient clinic. The aim was to identify risk factors of Grade II/III lymphopenia during DMF treatment.

Results: 42 out of 144 patients developed Grade II/III lymphopenia. Patients with lymphopenia were significantly older, had a higher overall JC virus titer (indicative of increased PML risk) and the absolute lymphocyte count at baseline was lower. Furthermore, lymphopenic patients received a higher number of immunomodulatory therapies before DMF initiation.

Conclusion: DMF is one of the most used DMT for RRMS. A frequent reason for discontinuation of treatment with DMF is severe lymphopenia. We identified age and absolute lymphocyte count at DMF initiation, as well as a positive JC virus status as possible risk factors to develop lymphopenia under DMF treatment.

Disclosure: Nothing to disclose.

EPO-516

Real World Experience With Early Treatment With Cladribine in Mild-Moderate Relapsing Multiple Sclerosis

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Background and aims: Cladribine is indicated for patients with highly active relapsing multiple sclerosis (RMS), but real world-evidence remains scarce.
Methods: Prospective collection of clinical, radiological and safety variables in RMS patients treated with Cladribine from October 2018 to December 2022 in a specialized MS centre.
Results: We included 68 patients treated with a first cycle of cladribine, of whom 43 received a second cycle. Median (IQR) age at treatment initiation was 37.2 (30.5–43.3) years. Time from MS diagnosis to first dose was 1.55 (0.26–9.80) years. Cladribine was mainly administered in naïve (55.9%) or first-switch (17.7%) patients, even if older than 50 years (14.7%). At baseline, MS was considered mainly as mild-moderate (median [range] of 1 [0-3] relapse in the previous year and only 8.8% of patients with >50 T2 lesions). Annualized relapse rate (ARR) was decreased by 86.4% and 95.2% after one and two years, respectively. NEDA-3 was achieved in 35.1% and 66.7% in years first and second, respectively. NEDA-3 at first year was 43.2% whenever first two months (until full onset of action) were excluded. Two patients received additional cycles but treatment was subsequently discontinued due to lack of efficacy. All adverse events reported were considered mild, with an incidence rate of infections of 76.7 per 100 patient-years. Lymphopenia was frequent and mild-moderate, with no cases of grade 4 lymphopenia.
Conclusion: In our cohort, cladribine showed an excellent benefit-risk ratio, with a high efficacy and safety in patients with early MS, including older patients and/or with mild-moderate activity.
Disclosure: FRJ received research grants and travel support for speaking engagements from Janssen, Novartis and Sanofi-Genzyme.

EPO-517

Virtual Patient Simulation Improves Performance in Distinguishing MS Severity and Making Holistic Therapy Choices

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Background and aims: It can be challenging for neurologists to select appropriate multiple sclerosis (MS) diagnostic investigations, distinguish severity, and make appropriate treatment choices including newer therapies. We used patient simulation, engaging neurologists in a practical learning experience to assess performance in making these choices.
Methods: This CME-certified virtual patient simulation consisted of 2 patient cases presented in a platform allowing neurologists to conduct assessments and complete open-field entries, choosing from an extensive database of diagnostic and treatment options reflecting the scope and depth of actual practice. After each decision, learners received clinical guidance (CG) based on current evidence and faculty recommendations. Clinical decisions were compared pre- and post-CG using a 2-tailed paired t-test to determine P values (P<.05 is significant). Rationales for clinical decisions were collected in real time. Data were collected July-December 2022.
Results: 145 neurologists completed case 1 and 72 completed case 2. Statistically significant improvements in diagnosis including MS severity, and appropriate treatment choice were observed (Figures). In case 1, 15% chose a novel S1P-Receptor modulator (RM) due to ease of use, disease activity and efficacy; 85% did not mainly due to unfamiliarity with use. In case 2, 31% chose a novel S1P-RM due to efficacy and disease activity; 69% did not mainly due to unfamiliarity with use or unavailability on formulary; in addition, 13% chose ofatumumab primarily due to efficacy and disease activity.

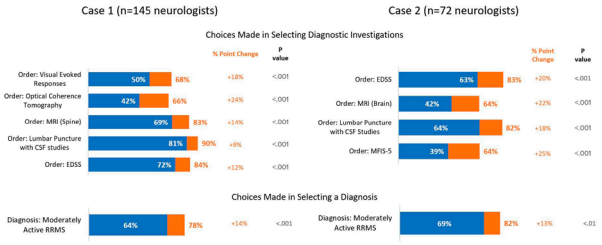

Figure 1.

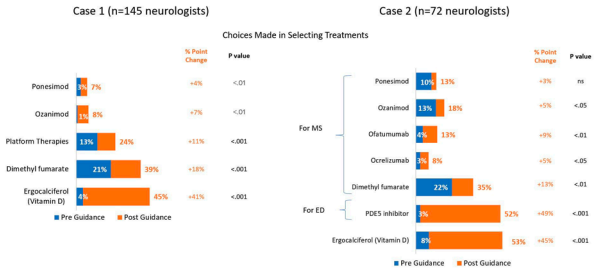

Figure 2.

Conclusion: These results demonstrate the success of immersive, online simulation education in improving performance in selecting appropriate investigations, diagnosis, and treatments according to patient characteristics.
Disclosure: Nothing to disclose.

ePosters

Tuesday, July 04 2023
Cerebrovascular diseases 4

EPO-518
Abstract withdrawn

EPO-519
Skeletal muscle changes and statokinetic instability in the patients with chronic cerebral circulation insufficiency

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Background and aims: The assessment of the relationship between skeletal muscle status and statokinetic instability (SI) in the patients with chronic cerebral circulation insufficiency (CCCI).

Methods: Patients with CCCI (n=64) were categorised as having SI (n=33) and without SI (n=31) by the data of computerized static stabilometry using the parameters: the ellipse area (EA) and the quality of balance function (QBF). The appendicular lean mass index (ALMI) was measured using dual-energy X-ray absorptiometry. Maximum grip strength was measured using a digital handgrip dynamometer. Muscular performance status was evaluated using the Short Physical Performance Battery (SPPB).

Results: It was found that more pronounced skeletal muscle changes in the patients with SI in CCCI was evidenced by significant loss of lean muscle mass (ALMI), reduced handgrip strength as well as the functional decline (decrease of SPPB score) compared to the subjects without SI in CCCI and healthy controls. There was no significant difference in muscle status in the patients without SI in CCCI and the healthy controls (Table 1). The significant positive correlation ($p<0.05$) between QBF and ALMI ($R=0.42$), grip strength ($R=0.39$) and SPPB score ($R=0.45$) were found.

Variable	Patients with SI in CCCI (n=33)	Patients without SI in CCCI (n=31)	Healthy controls (n=30)
	1	2	3
male/female	15(45,5)/18(54,5)	12(38,7)/19(61,3)	13(43,3)/17(56,7)
age (years)	63,0±7,5	61,1±8,1	60,3±8,4
ALMI man (kg/m^2)	7,27 [7,05; 7,56] p_{1-3}=0,008 p_{1-2}=0,006	8,09 [7,84; 9,29] p_{2-3}>0,05	8,05 [7,79; 8,91]
ALMI woman (kg/m^2)	5,83 [5,24; 6,17] p_{1-3}=0,004 p_{1-2}=0,023	6,78 [6,15; 8,46] p_{2-3}>0,05	7,28 [6,84; 7,67]
Maximum grip strength man (kg)	31,0 [29,5; 31,5] p_{1-3}=0,013 p_{1-2}=0,011	38,5 [33,0; 43,0] p_{2-3}>0,05	39,0 [35,5; 40,0]
Maximum grip strength woman (kg)	24,0 [22,0; 30,0] p_{1-2}=0,012 p_{1-3}=0,003	31,5 [28,5; 34,5] p_{2-3}>0,05	32,7 [30,0; 36,0]
SPPB-test (score)	9,0 [9,0; 10,0] p_{1-2}=0,003 p_{1-3}=0,001	12,0 [11,0; 12,0] p_{2-3}>0,05	12,0 [12,0; 12,0]
Confirmed sarcopenia by EWGSOP2 criteria	12 (36,4) p_{1-2}=0,045	3 (9,7)	-
Severe sarcopenia by EWGSOP2 criteria	3 (9,1)	-	-
Notes: Values are means (± SD), median [interquartile range] or numbers (percentages). *p*-values was based on the Mann-Whitney U test and the chi-square			

Table 1 – Characteristics of the patients included

Conclusion: Skeletal muscle changes typical for sarcopenia was associated with the SI in CCCI detected by static stabiloplatform. These findings add new information about the significant role pathology of the muscular system in the occurrence of SI in CCCI and suggest new therapeutic targets.

Disclosure: Nothing to disclose.

EPO-520

The real-life reliability of modified rankin scale used in stroke unit and rehabilitation ward

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Background and aims: Modified Rankin Scale (mRS) is the gold standard for measuring stroke-related disability in clinical trials and everyday practice. Inter-observer variability may be considered as a source of bias in retrospective observational studies. It may also depend on the clinical background of the assessing physician. Our aim was to assess real-life consistency between stroke unit physicians (SUP) and rehabilitation medicine physicians (RMP) using mRS in patients transferred directly to rehabilitation ward (RW).
Methods: We enrolled 50 consecutive acute stroke patients transferred within the same hospital from tertiary SU to RW. Patients were scored in mRS by SUP and RMP at the day of transfer. Reference mRS score (REF) was obtained by a single blinded stroke physician using Rankin Focused Assessment form to guide the interview.
Results: mRS score was reported for all patients admitted to RW and n=34 patients discharged from SU. The overall agreement was 76.5% between SUP and RMP (kappa 0.58), 73.5% between SUP and REF (kappa 0.89), and 70.6% between RMP and REF (kappa 0.50). Similar agreement was observed for RMP and REF in the whole sample of n=50 patients (66.7%, kappa 0.48). Patients with REF mRS score of 2 (n=6) were often scored 3 both by SUP (4/6) and RMP (5/6). In patients with REF mRS of 3 and 4 there was no clear tendency towards overrating disability levels.
Conclusion: The reliability of mRS assessment done for the purpose of everyday practice is modest and does not seem to depend on the clinical background of assessing physician.
Disclosure: Nothing to disclose.

EPO-521

Stroke and troponin, a comparison between treated and not treated patients in wake up stroke (WUS)

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Background and aims: The Stroke-heart syndrome (SHS) has been identified as a frequent complication of acute stroke characterized by a cardiac injury following the cerebrovascular event. It is thought that could be caused by a cytokines storm involving the sympathetic system. Wake up stroke (WUS) may be linked to similar pathophysiology. The aim of this study was to compare the maximum troponin level reached between WUS and no-WUS patients (treated and no treated with reperfusion therapy) looking at the OCSP classification.
Methods: We analyzed anamnestic and clinical data of 408 patients admitted in the Stroke Unit of Trieste between January 2021 and October 2022 with an acute ischemic stroke. For each patients we followed the troponin levels until the maximum level reached. Moreover we collect also the site of lesion if it was in anterior circulation (ACI), posterior circulation (POCI) or lacunar (LACI) infarction.
Results: In general, troponin level over 18 ng/l (99th percentile of our laboratory test) in the treated cohort was 48% in n-WUS and 46% in WUS, instead the same parameter in non treated patients was 37% in n-WUS and 29% in WUS (any significant differences with $p<0.05$). The comparison between the no-WUS and WUS patients in each OCSP subgroup lesion type, none of them have a significant difference in troponin rise ($p<0.05$).
Conclusion: More study are needed to understand the complex relationship between WUS and cardiac injury after an ischemic stroke. We didn't find any difference in WUS and no-WUS patient in treated and no treated patients in each OCSP subgroup.
Disclosure: Nothing to disclose.

EPO-522

TIA management in Trieste: Day Hospital admission is effective as a Stroke Unit assessment?

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Background and aims: Transient ischemic attack (TIA) management is still challenging. It is know that TIA needs a rapid access in clinics or Stroke Unit (SU) or in ED (emergency departement). We decided to evaluate if our DH (day hospital) evaluation has the same effectiveness in reducing recurrence rate of ischemic events confronting to the SU work up.
Methods: This is a 4-years restrospective study (between January 1 2018 and December 31 2021) including all the confirmed TIAs in the Trieste province from ED, DH, SU. For each patients we look at the recurrence rate of an ischemic event <90 days and >90 days and the overall mortality rate.
Results: We collect data of 490 patients referred to our ED/outpatients/SU. 53 Patients were discharged with a diagnosis of TIA from SU, 227 from the ED and 210 from DH. Comparing the effectiveness in preventing new ischemic events within 90 days and beyond 90 days between SU and DH patients, no significant difference was found in all the endpoints considered ($p<0.05$).

Patients' characteristics	SU (53 pt)	DH (210 pt)	p value
Age (years)	76 (66-81)	73 (62-81)	p>0.05
Sex, n (%) Male (M) Female (F)	 23 (44%) 30 (56%)	 111 (53%) 99 (47%)	p>0.05
Recurrence rate < 90 days	2 (3,5%)	3 (1,6%)	p>0.05
Recurrence rate > 90 days	6 (11%)	13 (6%)	p>0.05
Overall mortality rate	5 (9%)	12 (6%)	p>0.05

Table 1: comparison between the outcomes after a SU and DH evaluation

Patients' characteristics	ED (227 pt)
Age (years)	82 (74-88)
Sex, n (%) Male (M) Female (F)	 100 (44%) 127 (56%)
Recurrence rate < 90 days	14 (6%)
Recurrence rate > 90 days	18 (8%)
Overall mortality rate	44 (19%)

Table 2: outcomes after only a ED evaluation

Conclusion: There is a no defined TIA management in practice guidelines. We found a similar recurrence rate <90days and beyond 90 days between a DH evaluation and a SU assessment.
Disclosure: Nothing to disclose.

EPO-523

The use of TMS-hdEEG as an advanced neurophysiologic tool in patients with acute and chronic stroke

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Background and aims: Structural lesions lead to functional alterations of brain activity beyond the site of neuronal loss. This can be studied either by observing spontaneous activity or by assessing brain reactivity to direct perturbations.
Methods: Considering recent evidence, here we exploited this second option and performed a neurophysiological assessment based on Transcranial Magnetic Stimulation coupled with high density EEG recordings (TMS-hdEEG) in a group of twelve stoke patients affected by focal ischemic lesions both during their stay in the stroke unit as well as during rehabilitation.**Results:** Perilesional cortical stimulations were characterized by low frequency responses associated with an extracranial marker of the transient suppression of neuronal activity both in the acute and chronic phase. Longitudinal assessment revealed a reduction of such alterations following physical therapy. Notably, the renormalization of the EEG responses to TMS was found proportional to patients' clinical improvement.**Conclusion:** We confirmed previous evidence of altered local perilesional reactivity following focal brain injury. Importantly, the association between the reduction of such alterations following rehabilitation with the patients' clinical improvement suggests a causal link between the two. More in general, our findings demonstrate the feasibility of advanced neurophysiological assessments by TMS-hdEEG in stroke unit facilities, thus paving the way for an early, neurophysiologically-informed planning of appropriate interventions based on neuromodulation strategies and physical rehabilitation protocols.
Disclosure: I declare that all the participants to this study don't have conflict of interest.

EPO-524

Comparison of the predictive value of hematological factors and ABCD2 in predicting transient ischemic attack recurrence

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Background and aims: Cerebral vascular accidents (CVA) or strokes are major causes of morbidity and mortality worldwide. Although, previous research has been paid to detecting patients with transient ischemic attack (TIA) who are at higher risk of developing CVA since up to 20% of ischemic strokes have been preceded by TIA.
Methods: 465 patients were referred to Razi Hospital in Birjand with TIA between 2019 and 2021, and their ABCD2 scores and hematology factors were recorded.
Results: The mean age in transient ischemic stroke was 67.14±8.94 and non-transient ischemic stroke was 64.925±14.33 years. The mean age did not differ between the two groups (t=1.14, p=0.25). It was determined in the past medical history, hypertension (p<0.001) and hyperlipidemia (p=0.01) in the two groups of transient ischemia and non-ischemia are significantly different. The median MCH levels in the transient ischemic group (30.0 [28.9–31.5]) were significantly higher than in the transient non-ischemic group (29.3 [28.2–30.6]). Other blood factors were not significantly different between the two groups. The median level of systolic and diastolic blood pressure in the transient ischemic stroke group was significantly higher than in the non-transient ischemic stroke group (p<0.05). The ABCD2 index in the transient ischemic stroke group (6.0 [5.0–6.0]) was significantly higher than the non-transient ischemic stroke group (4.0 [3.0–5.0], p<0.001).
Conclusion: ABCD2 score, along with blood factors in patients who presented with TIA after 3 months of follow-up, can be a suitable indicator for the possibility of TIA recurrence in this group of patients, although it is recommended to do more research on this index.
Disclosure: There is nothing to disclose in regards to transparency, relationships/activities/interests related to the manuscript.

EPO-525

Using DRAGON score for prediction of outcome in patients receiving intravenous thrombolysis for acute ischemic stroke

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Background and aims: In everyday clinical practice, neurologist usually rely on their own experience in predicting functional outcome and mortality in patients with acute ischemic stroke (AIS). Predictive scales represent objective outcome measures. DRAGON score is a 10-point system, consisting of 6 variables which are available immediately on admission. We aimed to test DRAGON score in prediction of favorable functional outcome in patients treated with IVT for AIS.
Methods: This retrospective cohort study included patients treated with intravenous thrombolysis for acute ischemic stroke in 10-year period. Variables constituting DRAGON score were collected from medical histories. Favorable outcome was defined as functional independence (mRS 0-2).
Results: Total of 397 patients received IVT for AIS. Functional independence was achieved in 54.9% of cases. Out of 6 variables entering DRAGON score, 4 showed predictive value in our sample. The DRAGON score showed highly statistically significant positive correlation of mean to high intensity with mRS after 3 months (p=0.000, Spearman's ρ=0.580). Values of DRAGON score below 5 predict favorable functional outcome with sensitivity of 82% and specificity of 72%.
Conclusion: Tested score showed significant positive correlation with functional outcome, as well as good predictive value. Using simple, reliable and cost-free tools like DRAGON score can help us predict outcome in patients treated with IVT for AIS.
Disclosure: Nothing to disclose.

EPO-526

Moving from CT to MRI paradigm in acute ischemic stroke: effects on time metrics and revascularization rates and safety

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Background and aims: Neuroimaging is necessary before intravenous thrombolysis (IVT) and endovascular treatment (EVT) for acute ischemic stroke (AIS). Both CT and MRI are possible first-line approaches in the acute setting. In May 2018, we switched from CT to MRI as first line imaging for suspected AIS. Here, we aimed at retrospectively assessing the effects of this paradigm change on revascularisation metrics and safety.
Methods: From the Acute STroke Registry and Analysis (ASTRAL) we selected identical number of patients during the MRI-first-period (05/2018–08/2022) and the preceding CT-first-period. We compared outcome measures in the two periods by univariate and multivariate analysis.
Results: We assessed 1,131 consecutive thrombolyzed and 662 thrombectomized patients. After switching the imaging-paradigm, 80% of patients underwent MRI. Median door-to-needle-time was 31min (IQR=24–48) in the CT-period vs. 43min (IQR=33–58) in the MRI-period (+12 min, puniv<0.01), while door-to-groin-time was unchanged (-3 min, puniv=1). In the CT vs. MRI periods, rates of missed thrombolysis opportunities were respectively 3.1% vs. 0.8% (puniv<0.01); rates of symptomatic intracranial haemorrhage (SICH) after IVT were numerically, but non-significantly, lower (5.6% vs 3.2%, padj=0.07) and SICH after EVT(±IVT) were similar (6.5% vs 4.2%, padj=0.21). Disability at 3 months was unaffected for both IVT and EVT-treated patients (common adjusted odds ratio for favourable Rankin shift 1.23,95%CI=0.96–1.58; p=0.1 and 0.93,95%CI=0.67–1.29, p=0.674 respectively).
Conclusion: In our comprehensive stroke centre, transition from CT to MRI as first-line imaging before revascularizing AIS reduced the rates of missed thrombolysis opportunities. We observed longer door-to-needle and stable door-to-groin times during the MRI-period. Safety (SICH) and 90-day disability were not affected.
Disclosure: Costanza Maria Rapillo received a Research Fellowship Grant from EAN to conduct her research project at Lausanne University Hospital - CHUV.

EPO-527

Investigating Temporal Muscle Thickness (TMT) as a predictor of functional outcome after acute ischemic stroke treatment

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Background and aims: Measurement of temporal muscle thickness (TMT) has been introduced as an easily obtainable surrogate marker to identify patients at risk of sarcopenia, known to be a major cause of disability and frailty, especially among the elderly. Reliability of TMT as a tool to identify sarcopenic patients has been confirmed in a mixed stroke population (ischemic and hemorrhagic) but there isn't available data regarding its relationship with ischemic stroke outcome after acute phase treatment.
Methods: TMT of patients who underwent revascularization was measured on brain CT images acquired upon arrival in the ER. Modified Rankin Scale (mRS) scores at 3 months represented the main endpoint of functional outcome. Patients were further divided into two groups: at-risk vs not-at-risk of sarcopenia. Univariate and multivariate analyses were performed to assess the significance of mean TMT as predictor of functional outcome.
Results: Patients with unfavorable outcomes at 90 days (mRS >3) had lower values of mean TMT (4.9 vs 5.6 mm, p=0.02), as well as the subgroup of patients who passed away (n=17, 13.5%; 4.1 vs 5.6 mm, <0.001). In the multivariate analysis, neither mean TMT nor belonging to the at-risk of sarcopenia group were confirmed as independently associated with worse outcomes.
Conclusion: A trend in higher frequencies of very severe outcomes for patients at-risk of sarcopenia undergoing revascularization treatments for acute ischemic stroke was identified. Actual evidence fully supports treatment of this frail population according to established guidelines. Further investigations are needed to verify if sarcopenia may be an independent prognostic factor.
Disclosure: Nothing to disclose.

EPO-528

Clinico-radiological profile at admission and hemorrhagic risk in cardioembolic stroke under anticoagulant therapy

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Background and aims: Hemorrhagic transformation (HT) is a potential complication of cardioembolic stroke, even more in patients under anticoagulant treatment (AC). Our aim was to assess HT risk in acute cardioembolic stroke patients continuing AC based on their clinico-radiological profile at admission.

Methods: Retrospective observational study of acute cardioembolic stroke patients admitted to a Stroke Center between 2014 and 2021 who were maintained on AC therapy after admission at the physician's discretion. We describe clinical and radiological characteristics on admission non-contrast and CT-angio (blinded assessment) including ASPECTS, presence of leukoaraiosis and intracranial occlusion, mechanical thrombectomy (MT) performance and unsuccessful recanalization (TICI 0-2A) after MT. We used cross-tables to compare these variables with the incidence of HT during hospitalization.

Results: We identified 189 patients (age mean 78.4±8.8 years), initial NIHSS median (IQR) 5 (3–11) points. ASPECTS median (IQR) 10 (8–10) points. Leukoaraiosis was present in 121 (64%) patients, and medium-large vessel occlusion in 66 (34.9%). MT was performed in 28 (14.8%) patients, 8 of them (28.6%) with unsuccessful recanalization. HT during admission occurred in 24 (15.6%) patients, but only 2 (1.1%) presented with neurological worsening. There were not significant differences regarding ASPECTS, leukoaraiosis, intracranial occlusion, MT, or unsuccessful recanalization between patients with and without incident HT.

Conclusion: In our study, only 1.1% of patients with recent cardioembolic stroke who maintained AC presented symptomatic HT. None of the radiological variables analyzed increased HT risk. Further prospective studies are needed to confirm the safety of AC continuation in these patients.

Disclosure: Nothing to disclose.

EPO-529

Reporting from the real world: Health benefits of successful recanalization in acute stroke

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Background and aims: Stroke caused by large vessel occlusion is associated with severe disability, dependency and death. Although thrombectomy is the standard treatment, benefit stems from reperfusion/recanalization. We aim to model the effects of successful recanalization in quality of life and mortality in a lifetime horizon.

Methods: Patients from a Portuguese tertiary center were included from 2016–2021 if they underwent thrombectomy and were followed or deceased in the center. Expanded Thrombolysis in Cerebral Infarction (eTICI) 2b/2c/3 were considered successful recanalization. Modified Rankin Scale (mRS) was collected, and EuroQol-5dimensions-5levels at 3 and 12 months was used in a subset of patients from 2021–2022. We developed a Markov Model (software TreeAge Pro©) with cycles considering background mortality from life tables and specific mRS mortality. Quality-adjusted life years (QALYs) with 95% prediction intervals (95%PI) were calculated using patient simulation.

Results: We included 311 subjects, median age 75 (20 to 96) years, median National Institute of Health Stroke Scale 18 at admission. One-year mortality was 34.7% for successful and 52.2% for unsuccessful recanalization. The model predicted a mean of 4.30 (95%PI 4.10–4.51) QALYs for successful recanalization and 2.69 (95%PI 2.52–2.86) QALYs for unsuccessful, per patient. For patients ≤65 years the results were 9.83 (95%PI 9.54–10.12) and 6.01 (95%PI 5.77–6.25) QALYs, respectively, and for >65 years were 1.85 (95%PI 1.75–1.94) and 1.22 (95%PI 1.14-–1.30) QALYs.

Conclusion: Unsuccessful thrombectomy dramatically decreases lifetime QALYs, with relevant gains from better recanalization. Our results are in line with a published meta-analysis where a 65-year-old person with eTICI 3 has 6.73 QALYs.

Disclosure: PhD grant from CUF Healthcare.

EPO-530

Stroke-related delirium in patients undergoing revascularization treatments: a retrospective, observational study.

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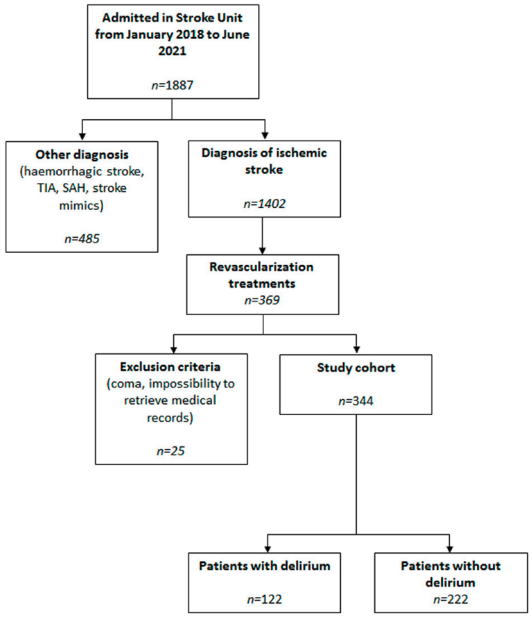
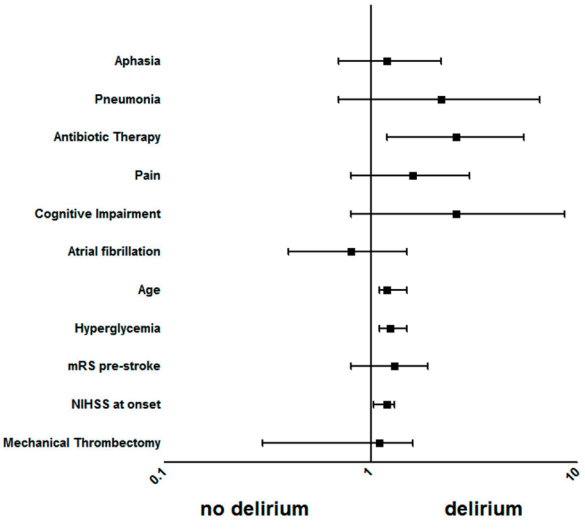
Background and aims: Delirium is a complex neuropsychiatric disorder, which often complicates acute illnesses, including acute stroke. The aims of the present study were to evaluate the prevalence and risk factors of delirium in stroke patients undergoing revascularization treatments, and to assess its impact on stroke outcome.

Methods: We retrospectively reviewed the clinical charts of patients admitted to the Stroke Unit of Policlinico Gemelli from 2018 to 2021. Inclusion criteria were: ischemic stroke; treatment with thrombolysis and/or mechanical thrombectomy. Exclusion criteria were: impossibility to retrieve medical records; coma. Delirium was diagnosed based on the DSM-V criteria by reviewing nurse and medical records.

Results: The study cohort consisted of 344 patients. Mean age was 73.63±12.93. Mechanical thrombectomy was performed in 161(46.8%) patients, thrombolysis in 270(78.5%), both in 87(35.6%). Delirium prevalence was 122/344 (35.5%). In the univariate analysis, delirium was associated with aphasia (p<0.033), atrial fibrillation (p<0.022), hyperglycemia at stroke onset (p<0.001), use of central nervous system acting drugs (p=0.029), cognitive impairment (p<0.025), pain (p=0.033), pneumonia (p<0.001), antibiotic therapy (p<0.001). Patients with delirium had higher NIHSS at stroke onset (p<0.001), and after treatment (p<0.001). In the multivariate analysis, risk factors for delirium were age (OR=1.03; 95% C.I.=1.01–1.06; p=0.039), NIHSS at onset (OR=1.09; 95% C.I.=1.03–1.15; p=0.003), antibiotic therapy (OR=2.56; 95% C.I.=1.18–5.52; p=0.017), hyperglycemia (OR=1.02; 95% C.I.=1.01–1.02; p=0.001). Patients with delirium were less often discharged home (p<0.001), had prolonged hospitalization (p<0.001) and increased 90-days disability (p<0.001).



Study flow chart



Multivariate logistic regression analysis.

Conclusion: Delirium is a frequent complication in acute stroke patients undergoing revascularization treatments and negatively affects the outcome of stroke.

Disclosure: Nothing to disclose.

EPO-531

Evaluating the antiplatelets use before intravenous infusion of rtPA for AIS

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Background and aims: Antiplatelet therapy is one of the most frequent therapies used in prevention of cardiovascular events. The aim of this study is to evaluate the effects of prehospital antiplatelet therapy (AP) before thrombolysis and to assess the rate of intracranial hemorrhage (ICH) and functional outcome in patients with acute ischemic stroke (AIS).
Methods: Retrospective study from a hospital based registry and medical records of the patients admitted to the Department of Neurology, County Clinic Hospital Brasov, over a course of a 36-month period starting in March 2019. We identified patients who had taken at least one dose of any APs within the previous 24 hours before thrombolysis. They were divided into groups based on AP drug, single versus dual AP treatment (DAPT).
Results: A total of 526 patients received rtPA for AIS. The use of any AP was not associated with an increased rate of ICH (20.8% vs 20.94%) with ICH more frequent in the DAPT group. Patients on any AP had a better functional outcome that those without pre stroke AP-treatment (60% vs 51.87%, p=0.265). In addition, significant difference was noted in the rate of good outcome in patients with ICH and pre stroke AP when compared with patients that presented ICH without AP treatment (46.15% vs 32.14%, p=0.04).
Conclusion: Our study didn't show a statistically significant correlation between the risk of ICH and antiplatelet use before intravenous thrombolysis. Patients with AIS and AP had a good a better functional outcome following thrombolysis.
Disclosure: Nothing to disclose.

EPO-532

The Oslo Study of Visual Impairment after Stroke - StrokeVIS

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Background and aims: Studies have shown that up to 60% of patients have some form of new visual impairment after stroke (Rowe et al., 2019). In the annual report of the Norwegian Stroke Register from 2021, only 16% of stroke patients were registered with visual impairment. Notably, this figure is significantly lower than expected from the literature and indicates a significant under-reporting and/or under-diagnosis. The Oslo study of visual impairment (StrokeVIS) intends to measure the prevalence of visual impairment after stroke, validate a Norwegian version of the VISA screening tool (Rowe et al., 2020) and evaluate vision outcomes of acute stroke patients.
Methods: Consenting patients, who fulfill the exclusion and inclusion criteria, will undergo a baseline neuro-ophthalmological examination by an experienced orthoptist, and this expert examination will function as the prevalence as well as a comparable "gold standard". Within 24hrs, the Vision Impairment Screening Assessment (VISA) tool is administered by a nurse. Participating nurses undergo short instruction but are otherwise untrained in vision diagnostics. Patients will attend a 90-day follow-up with reassessments by the same orthoptist, including automated perimetry, and clinical neurological assessments by a neurologist (NIHSS, MOCA and Modified Ranking Scale score).
Results: So far, 62 patients have been included. Recruitment is still ongoing at Oslo University hospital, with a completion date of October 2023 and at least 100 patients to be included.
Conclusion: Preliminary findings indicate feasibility for the use of VISA as a screening tool, for visual impairment after stroke, in Norway.
Disclosure: Nothing to disclose.

Neurogenetics 2

EPO-533

Pyridostigmine for treatment of neuromuscular deficits in PURA syndrome; a gloablly expanding obervation

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Background and aims: PURA syndrome is a rare central nervous system disorder caused by heterozygous variants in the PURA gene. However, several phenotypic features suggested a peripheral/NMJ source of weakness and clinical improvement in treatment with pyridostigmine was reported in one published case. We questioned if this treatment response is generalizable, in patients from multiple countries and with different PURA variants, across the 3 PURA functional domains.
Methods: Observational study with patients from the US and Europe. Approval from local thical committees were obtained, as applicable. Pyridostigmine was administered in a dosis 3 to 7 mg/kg, in divided doses 4 to 6 times, under the supervision of the local, treating neurologist. Before and after treatment observations were compared.
Results: 5 patients from 3 countries were studied. Further patients are included and the number will be update upon presentation. All patients showed an improvement after pyridostigmine, including neurodevelopmental improvements, as evidenced by achievement of new developmental milestones in some cases. Treatment response over time seemed to be sustained and was not restricted to variants in any single functional domain in the PURA protein. No major side effects, including bradycardia, were noted.
Conclusion: Pyridostigmine treatment response in PURA syndrome neuromuscular deficits is generalizable, and not limited to PURA variants in any one functional domain in this small observational study. Additional studies are needed to corroborate these findings with greater confidence.
Disclosure: Nothing to disclose.

EPO-534

A relatively common cause of hereditary motor neuropathy due to a founder mutation in VWA1

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Background and aims: Recently, rare biallelic variants in VWA1 encoding Von Willebrand factor A domain containing 1 were identified as a cause of a subtype of hereditary axonal motor neuropathy. The allele frequency of the most common pathogenic VWA1 variant p.(G25Rfs*74) is estimated to be around 1/1,000 in European populations. Since its first description in early 2021, 34 patients from 23 families, including 17 patients from the UK or western Europe, have been reported in the literature.
Methods: We present the clinical features and variants of 10 newly diagnosed patients from European-, and non-European ancestries along with reviewing all the previously reported patients.
Results: Age of onset varied from childhood to adulthood. Disease progression was slow, and ambulation largely preserved. Clinical presentation included foot deformities, proximal and distal muscle weakness predominantly of the lower limbs, and upper motor neuron signs without any sensory involvement. In some cases, myopathic changes were observed in the muscle biopsy and muscle imaging. Two patients had abnormal brain MRI with white matter abnormalities and one patient presented with dysmorphic features.
Conclusion: Biallelic variants in VWA1 may be responsible for up to 1% of hereditary motor neuropathy cases in the European population. Therefore, early molecular testing for VWA1 variants needs to be considered in patients with unexplained hereditary motor neuropathy. With the expected increase in newly diagnosed cases of VWA1-related neuropathy in the coming years, a foundation will be established to raise public awareness and support clinical collaboration and research in this field,.
Disclosure: HH was funded by the MRC (MR/S01165X/1, MR/S005021/1, G0601943), the National Institute for Health Research University College London Hospitals Biomedical Research Centre.

EPO-535

Identifying of circulating miRNAs as novel emerging biomarkers in Neurofibromatosis type 1

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Background and aims: In recent years is emerging the field of circulating miRNAs as tumor-associated biomarkers that reflect cancer dynamics, malignant potential and drug resistance. We investigated differentially expressed miRNAs (DEmiRNAs) to distinguish patients affected by Neurofibromatosis type 1 (NF1) with classical phenotype from NF1 patients showing a more severe clinical picture.

Methods: The study includes 126 NF1 patients, enrolled at Division of Neurology of AOU Luigi Vanvitelli and diagnosed based on the NIH Consensus Conference criteria of 1988. Clinical subgroups have been classified: NF1 patients with classical phenotype (G1); NF1 patients with G1 features plus systemic complications (G2); NF1 patients with G1 features with diagnosis of MPNST (G3); NF1 patients with G1 features plus multi-apparatus involvement and neurological malignancies (G4); NF1 patients with G1 features, plus multi-apparatus involvement and other tumours (G5). The miRNA expression levels were measured by small non coding RNA sequencing (sncRNA-Seq) using serum pooling approach, followed by RT-qPCR in the entire NF1 cohort.

Results: Our findings showed 87 DEmiRNAs involved in the neurological and psychological diseases, organismal injury, cancer, developmental, skeletal and muscular disorders. A concordance expression pattern between sncRNA-Seq and qRT-PCR data for seven DEmiRNAs was found.

Conclusion: NF1 is characterized by a highly clinical variability. Our results revealed novel and noninvasive potential circulating biomarkers of NF1 disease and related clinical complications. Further validation analysis in other NF1 patients are needed.

Disclosure: The research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-536

Real-world data from risdiplam treatment of SMA patients

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Background and aims: The latest novel disease-modifying therapy for spinal muscular atrophy is risdiplam, which is an orally bioavailable mRNA splicing modifier which increases systemic SMN protein concentrations by improving SMN2 gene transcription. In clinical trials, risdiplam improved motor functions with acceptable safety in SMA patients. The population treated with risdiplam in over 20 countries, up to age 60 represents real-world clinical practice.

Methods: In our centre we follow up 56 SMA patients. 30 of them receive nusinersen and 18 are treated with risdiplam through an early access program. In this cohort we follow 9 men and 9 women between ages 5 and 51 years (median 31,8 years, 22–28 months follow-up). 3 patients have SMA1, 14 SMA2 and 1 person has SMA3. In our cohort 16 patients have 3 SMN2 copies, 2 patients have 2 copies. All of them have severe kyphoscoliosis, 2 patients had spinal stabilization surgeries. Two patients use NIV, 2 have invasive ventilation. All patients are wheelchair-dependent, 3 are non-sitters. In 16 patients motor function was followed by RULM.

Results: RULM scores were between 0 and 28 and they increased or stayed stable in 11 cases (68.75%). Transient increases and decreases were also observed. Adherence is excellent and we also see a positive psychological effect. 6 patients had transient diarrhea, but we observed no significant side effects.

Conclusion: Risdiplam is well-tolerable and safe. In adult patients, even stagnating motor function is considered a positive result compared to natural history of disease. Further follow-up is necessary to detect clinically relevant changes.

Disclosure: At the point of abstract submission, I have nothing to disclose, but there might be an industrial sponsor.

EPO-537

Plasma miRNAs expression in a large family of healthy controls, presymptomatic and symptomatic TARDBP carriers

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease without effective treatment. The diagnosis of ALS includes the detection of early symptoms and, as the disease progresses, muscle weakness and atrophy spread to other parts of the body. Several studies highlight the miRNA's role in ALS pathology by describing their deregulation in various biological fluids, such as plasma.
Methods: In this study, we selected 15 tissue- and disease-specific circulating miRNAs involved in targeting TARDBP or binding TDP-43 during their biogenesis/mature form (Table 1) able to classify symptomatic (n=7), presymptomatic (n=8) TARDBP-G376D carriers and healthy members (n=13) belonging to a large ALS family. The differential expression of selected circulating miRNAs was verified by qRT-PCR in our cohort (Figure 1). Statistical analysis for comparing three groups was performed.

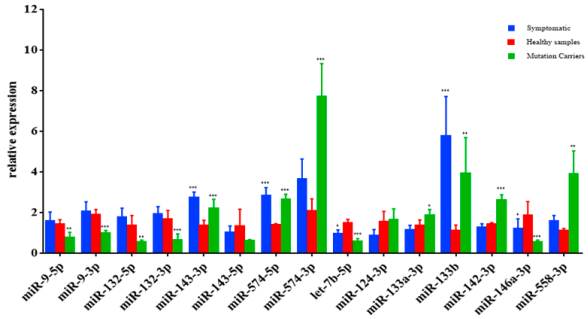

Figure 1

Results: Table 1 displays all miRNAs differentially expressed in family members. Five out of 15 miRNAs were significantly dysregulated between healthy control and patients. Furthermore, 13 out of 15 miRNAs were significantly dysregulated in presymtomatic carriers; eight miRNAs are deregulated exclusively in this group.

miRNA	Fold change (mean ± SD)	
	Symptomatic	Mutation Carriers
miR-9-5p	1.55 ± 0.48 p=0.57	**0,72 ± 0,30 p= 2*10⁻⁴**
miR-9-3p	2.03 ± 0.49 p= 0.40	**0.94 ± 0.18 p= 10⁻⁴**
miR-132-5p	1,74 ±0,48 p=0.09	**0.52 ± 0.13 p= 7*10⁻⁴**
miR-132-3p	1.88 ± 0.41 p= 0.37	**0.62 ± 0.32 p= 10⁻⁴**
miR-143-3p	**2.70 ± 0.31 p= 10⁻⁴**	**2.16 ± 0.49 p= 10⁻⁴**
miR-143-5p	1 ± 0.34 p= 0.57	0.57 ± 0.09 p= 0.12
miR-574-5p	**2.8 ± 0.43 p= 10⁻⁴**	**2.62 ± 0.28 p= 10⁻⁴**
miR-574-3p	3.61 ± 1.02 p=0.12	**7.65 ± 1.67 p= 10⁻⁴**

Table 1

Conclusion: This study shows miRNAs differentially expressed between clinical conditions suggesting that miRNA dysregulation may be used as an early prognostic biomarker for ALS. Interestingly, miR-574-3p, -133B and -558-3P were identified as significantly overexpressed in presymptomatic individuals compared with healthy members, suggesting that the expression of this miRNA is associated with TARDBP mutation. Additionally, -124-3p was significantly deregulated in patients when compared with presymptomatic carriers which supports the correlation of miRNA-133b expression with the progression of TARDBP-associated disease.
Disclosure: The authors disclose any conflicts of interest related to the manuscript.

EPO-538

Pathogenicity of mutation in MT-ND1 (m.3796A>G) in a family with "Leber Hereditary Optic Neuropathy Plus Phenotype"

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Background and aims: Leber Hereditary Optic Neuropathy (LHON) is a mitochondrial disease presenting with subacute loss of vision. Prevalence is around 1 in 30,000. Some patients suffer from a broader spectrum of symptoms such as movement disorders, neuropathy, ataxia, psychiatric disturbances, mental retardation, often named a Leber plus disease. The three most common pathogenic variants demonstrated in 90-95% of LHON are in MT-ND1 (m.3460G>A), MT-ND4 (m.11778G>A) and MT-ND6 (m.14484T>C). Counseling is complicated by the varying penetrance and influence of environmental factors such as tobacco smoking.
Methods: We present a family of 29 relatives, descending

from a woman who suffered from blindness, mental slowness and prominent cerebellar ataxia.
Results: Nine out of nineteen females (mean age 28y) and six out of ten males (mean age 25y) suffer from vision loss, compatible with LHON. Eight out of nineteen females and three out of ten males suffer from cerebellar ataxia. Seven out of nineteen females and two out of ten males complaint of muscle cramps. One patient has muscular fatigue with muscle biopsy showing a mitochondrial complex I deficiency. Four out of nineteen females and three out of ten males demonstrate mental slowness. Only one affected male family member has kids, all asymptomatic. In all affected, the m.3796A>G variant was found in MT-ND1, a mutation previously described in a patient with adult-onset dystonia, spasticity, and myopathy.
Conclusion: This family demonstrates the variability of symptoms, disease-severity and penetrance that is associated with the "LHON plus phenotype". We believe that the identified mutation m.3796A>G in MT-ND1 , an important subunit in complex I of oxidative phosphorylation that is involved in LHON, is likely pathogenic and explanatory for the observed phenotype.
Disclosure: Nothing to disclose.

EPO-539

Plasma neurofilament light chain concentration in RFC1-Related Disease: a multicentre cross-sectional study

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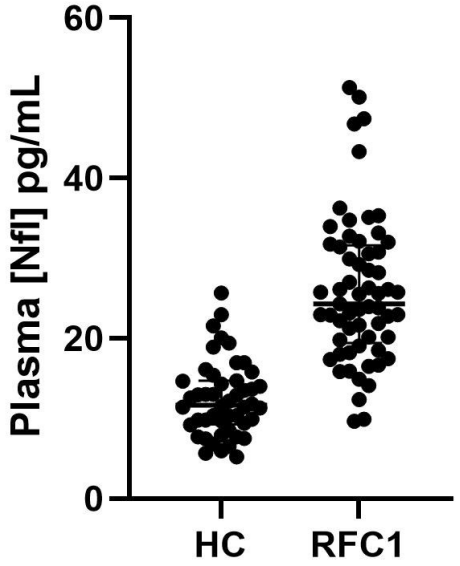
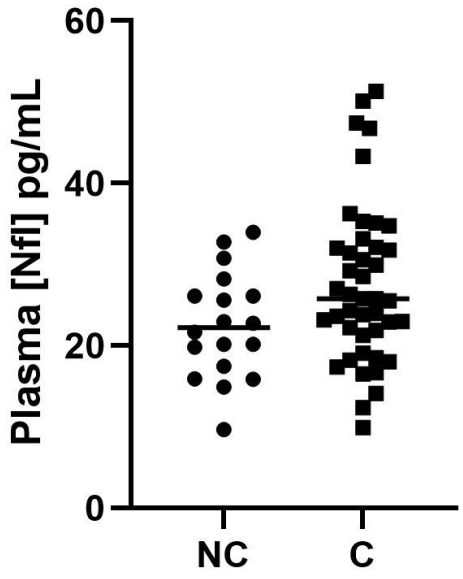
Background and aims: Recently, biallelic intronic AAGGG repeat expansions in the replication factor complex subunit 1 (RFC1) gene have been identified as the cause of cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS) and a frequent cause of late-onset ataxia and sensory neuronopathy. Disease severity and course appear to be highly variable and, given the lack of insight into the pathomechanisms of the disease, no potential biomarker has been identified yet. Neurofilament light chains (NfL) are a promising biomarker in both central



Significantly increased plasma NfL concentration in RFC1 CANVAS and disease spectrum patients compared to healthy controls (HC).



Significantly increased plasma NfL concentration in patients with clinical cerebellar involvement (C) compared to patients without cerebellar dysfunction (NC).

Conclusion: Serum NfL concentration was significantly higher in RFC1 CANVAS and disease spectrum patients than in HCs. Longitudinal studies are warranted to investigate the possible role of serum NfL in disease monitoring.
Disclosure: The authors have no relevant interests to disclose.

EPO-540

Diagnostic yield of whole-exome sequencing for dystonia patients: single tertiatry center experience

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Background and aims: Advent of next-generation sequencing has greatly impacted gene discovery and enabled more genetic diagnoses of dystonia than ever before. Our aim was to assess the clinical impact of whole-exome sequencing in our tertiary centre.
Methods: Our study cohort includes patients from the Clinic of Neurology at the Clinical Hospital Centre Rijeka, referred to genetic testing from 2020 to 2022. Exome sequencing was performed at the Clinical Institute of Genomic Medicine, UKC Ljubljana using standardized protocols and using a determined hereditary dystonia gene panel. Identified variants were classified according to the ACMG and AMP 2015 joint consensus recommendation, along with ACGS recommendations where applicable.
Results: We have performed exome sequencing in 20 patients. Causative pathogenic and likely pathogenic mutations have been confirmed in 7 patients (35%, GNAO, CHD8, GNAL, YY1, KMT2B and GNB1), while variants of uncertain significance (VUS) were found in 2 patients (10%, ADCY5 and SPG7). Additonally, one patient has confirmed carriership of classically recessive genes (5%, UPB1). Regarding dystonia type, the diagnostic yield for generalized dystonia was 77.7%, with one additional VUS finding (11.1%). In segmental dystonia there was one VUS and one carriership, while in focal dystonia there was no findings.
Conclusion: Genetic testing using whole-exome sequencing is recommended for dystonia patients, especially in generalized and segmental dystonia, which is in line with previous findings in the literature. This enables a complete and accurate genetic diagnosis in patients, which has real-life implications given the younger patient population.
Disclosure: There are no financial conflicts of interest to disclose for all authors.

EPO-541

Analysis of a new case of the IRF2BPL mutation syndrome: a rare neurological phenotype of a rare disease.

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Background and aims: Variants in interferon regulatory Factor 2-binding protein-like (IRF2BPL) gene are associated with neurodevelopmental delay, seizures, and other neurological manifestations, such as ataxia, dystonia, ocular disturbances and spasticity. We report a nonsense IRF2BPL variant in an individual with neurological impairments starting in adolescence with psychomotor regression.
Methods: Case report and non-systematic literature review.
Results: A 32-year-old male, presented appropriate cognitive and motor progression until the age of 12, when he quit school due to learning difficulties. At age 15 presented dysarthria and gait ataxia. At age 22 magnetic resonance imaging (MRI) revealed cerebellar atrophy. After 5 years of clinical stability, tendency to fall and dysarthria aggravated. At age 32, the deficits included proximal spastic paraparesis, hyperreflexia, mixed spastic and ataxic gait, dysmetric eye saccades, dysphagia, dysarthria, and progressively voider and scarcer speech. At this stage, MRI showed mild cerebellar atrophy. Genetic testing detected a nonsense c.499C>T (p.Gln167*) heterozygous variant of IRF2BPL gene, described as pathogenic, compatible with a dominant autosomal developmental regression syndrome with motor impairment, aphasia and seizures. A genetic consultation was required to examine the family members.
Conclusion: There are only 28 previously reported cases of pathogenic IRF2BPL mutations, and this case was never described before, to the extent of the authors knowledge. The nonsense variants are typical associated with more severe presentations. The IRF2BPL gene is involved in normal neuronal function, and may be important in other organ systems.
Disclosure: The authors declare no conflict of interests.

EPO-542

Identification of genetic networks highlights a risk trajectory linking Mild Cognitive Impairment to Alzheimer's disease

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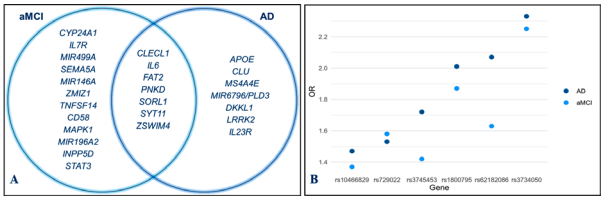
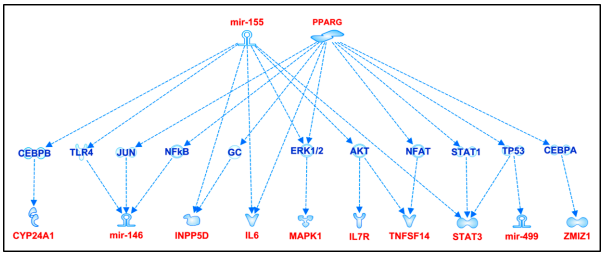
Background and aims: Mild Cognitive Impairment (MCI) and sporadic Alzheimer's Disease (AD) are multifactorial conditions resulting from a complex crosstalk among multiple molecular and biological processes. The study aimed at investigating genetic variants, which may represent susceptibility, prognostic biomarkers or multi-target treatment options for MCI and AD.

Methods: The study included 371 patients (217 amnesic MCI and 154 sporadic AD) and 503 control samples. Open Array technology was utilized to screen patients for a panel of 120 Single Nucleotide Polymorphisms (SNPs). Successively, the data were analysed by statistical, bioinformatics and machine-learning approaches.

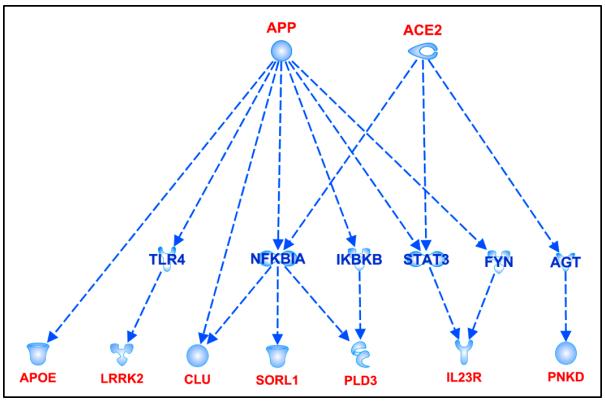
Results: As a result, 21 SNPs were associated with aMCI and 13 variants with sporadic AD. In particular, seven SNPs (rs10466829, CLECL1; rs1800795, IL6; rs3734050, FAT2; rs62182086, PNKD; rs11218343, SORL1; rs729022, SYT11; rs3745453, ZSWIM4) shared between both conditions, reported higher risk values in AD than in aMCI, suggesting the existence of a risk trajectory linking aMCI to AD. In addition, the study highlighted significant interactions among genes and miRNAs that participate in the signalling networks of APP (p=9.04*10–4), ACE2 (p=2.00*10–4), miRNA-155 (p=1.76*10–5) e PPARG (p=1.36*10–4), which have been involved in neuroinflammatory and neurodegenerative contexts underlying MCI and AD.



A. Venn diagram showing shared and specific genes associated with aMCI and sporadic AD. B. Illustration of the risk values (Odd Ratio, OR) of the variants that are slightly higher in AD patients with respect to the aMCI group.



Interaction among genes associated with AD and the APP and ACE2 signalling networks.



Interaction among genes and miRNAs associated with aMCI and the signalling networks of miR-155 and PPARG.

Conclusion: Overall, the present study identified several SNPs associated with aMCI and sporadic AD, among which seven SNPs were shared between both conditions and highlighted the existence of a risk trajectory linking aMCI to AD. These results may be relevant for the development of multi-target treatments and the evaluation of the individual risk for aMCI and progression towards AD.

Disclosure: Nothing to disclose.

EPO-543

A family from Turkey with congenital myasthenia and hereditary polyneuropathy

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Background and aims: Congenital myasthenia is caused by genetic defects of the neuromuscular junction proteins. The possible symptoms are, apnea attacks during feeding, weak crying, ptosis, in the neonatal period or exercise intolerance in childhood. Here, we report a large family with congenital myasthenia displaying heterogeneous neurological symptoms in affected family members, some of whom also have polyneuropathy.
Methods: The index case is a 44-year-old woman who was followed up for 15 years with ptosis in the neonatal period and fatigue in childhood. A detailed family history disclosed common occurrence of consanguineous marriages in the family. Three patients had complaints compatible with congenital myasthenia(IV-1,IV-6,V-5) and three patients had only neuropathic symptoms(III-12,IV-5,IV-7), one of whom(IV-6) had both complaints(Figure1). We performed a detailed electrophysiological and genetic analysis in this family.
Results: We determined decrement after repetitive stimulation of accessory and facial nerves, suggesting a postsynaptic type of neuromuscular junction disorder in patients with myasthenic symptoms and a demyelinating polyneuropathy with conduction blocks in patients with neuropathic symptoms. Two pathogenic variants were identified in the CHRNE gene of the index patient using WES analysis (c.1336del;p.Asp446ThrfsTr61, inherited from the father and c.1219+2T>G;splice region, inherited from the mother). The segregation results of Sanger analysis

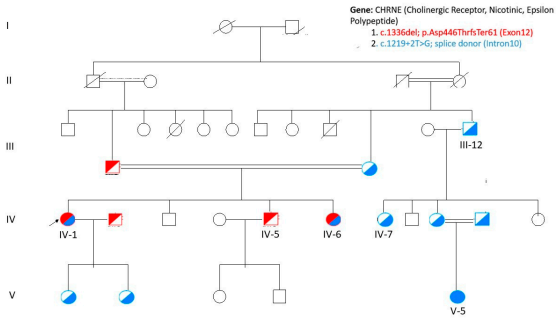

Figure1

Conclusion: The co-occurrence of congenital myasthenia and polyneuropathy is probably an incidental finding in this family due to high frequency of consanguineous matings on one hand and the high ethnic heterogeneity of the population under investigation on the other hand. The presence of conduction blocks in familial polyneuropathy is an interesting finding.
Disclosure: Electrophysiological study samples will be included in the final presentation.

EPO-544

The role of patient representatives in the optimization of Patient Care Pathways at European level: the PKU experience

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Background and aims: In defining and optimising patient care pathways (PCPs) the role of patient representatives (PRs) is very important; it is crucial in the contest of rare diseases where the complexity of the disorders is higher, co-morbidity and multi-organ involvement are present, multidisciplinary care is needed, and patients may experience inequality in the access to specialised diagnostic/treatment procedures. In this work we have analysed the role of PRs in the design and optimization of Phenylketonuria's (PKU) PCP.
Methods: We applied RarERN PathÓ methodology to PKU PCP within the Value of Treatment (VOT) for Rare Brain Disorders project (European Brain Council). PRs of PKU Associations of Ireland and Germany were involved. The PCPs in place in centers of excellence (COE) were analysed, and patients provided input through a semi-structured questions survey exploring organization of care and perception of criticalities when receiving healthcare services. A first draft of the optimized PCP for PKU was discussed in a plenary meeting attended by neurologists and PRs. Finally, PRs were requested to provide additional suggestions through a second ad-hoc survey.
Results: PRs contributed to the design of an optimized PCP, providing unique information on the main organizational challenges in COEs and on the coordination of care between COE and non-hospital care at European level.
Conclusion: To formally involve PRs in the co-design of the PCP is necessary because it allows to complement clinicians' perspective about "ranking" and "weight" of what really matters throughout the PCP. PKU case is particularly interesting in this respect.
Disclosure: The study received financial support from Biomarin.

EPO-545

RARS2-related encephalopathy: a case of ataxia-epilepsy due to a novel splicing variant and review of the literature

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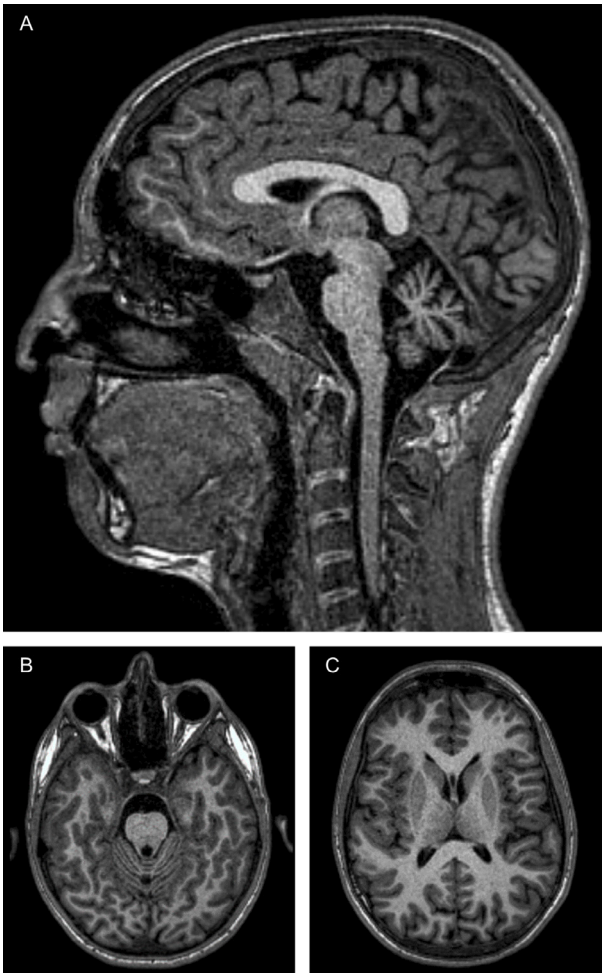
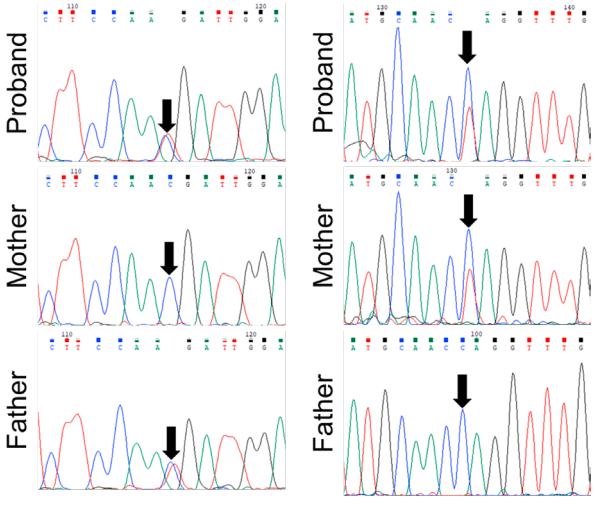
Background and aims: Biallelic RARS2 mutations cause a rare epileptic encephalopathy with 70 reported cases. We report a new case, notable for a novel splicing variant and a mild phenotype with late onset, ataxia, and mild epilepsy.

Methods: A 15 year-old-male patient was clinically evaluated by neurologists with additional training in pediatric neurophysiopathology and movement disorders. Electroencephalogram (EEG) and brain magnetic resonance imaging (MRI) were performed. A whole-exome sequencing (WES) was performed and followed by segregation analysis with Sanger sequencing. Respiratory chain activity (RCA) was assessed on peripheral lymphocytes.

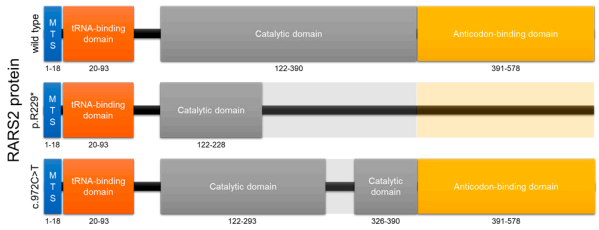
Results: The patient presented at 3 years with language delay and ataxia, and had a severe epileptic crisis at 13 years. He now displays mild intellectual disability, dysarthria, tremor, and ataxia. His EEG showed paroxysmal abnormalities at 3 Hz on fronto-temporo-occipital regions while his brain MRI showed isolated vermis cerebellaris atrophy. His RCA is normal. WES revealed two compound heterozygous mutations in RARS2: a nonsense (p.Arg229*) and a novel synonymous variant (c.972C>T) that determines the skipping of exon 11 (gnomAD allele frequency: 0.000004; ACMG criteria: PP3,PM2,BP6,BP7). Reviewing the literature on RARS2-related encephalopathy, we observed a strong correlation between the genotype and the phenotype severity including onset, survival, neurological and systemic involvement, neuroradiological and biochemical profiles, histopathological and functional characterizations.



T1-weighted brain MRI with a sagittal slice evidencing vermis cerebellaris atrophy (A), an axial slice evidencing cerebellar vermis and mesencephalon (B), and an axial slice evidencing conserved forebrain (C).



Sanger sequencing on DNA of the patient and his parents evidencing the c.685C>T (p.Arg229*) variant in the proband and his father and the c.972C>T variant in the proband and his mother.



Wild type and mutated RARS2 protein with the premature interruption of translation at the amino acid 228 due to the p.Arg229* nonsense mutation and the loss of the 32 amino acids of the catalytic domain of the enzyme encoded by exon 11.

Conclusion: A prompt genotypic characterization of patients with infantile-onset epilepsy and additional characteristics, such as ataxia and intellectual disability, may allow an early genetic diagnosis of RARS2-related encephalopathy and predict the phenotype, improving diagnostic counselling, follow-up, and assistance.

Disclosure: The authors declare no conflict of interest.

Cerebrovascular diseases 5

EPO-546

Tenecteplase in central retinal artery occlusion study (tencraos)

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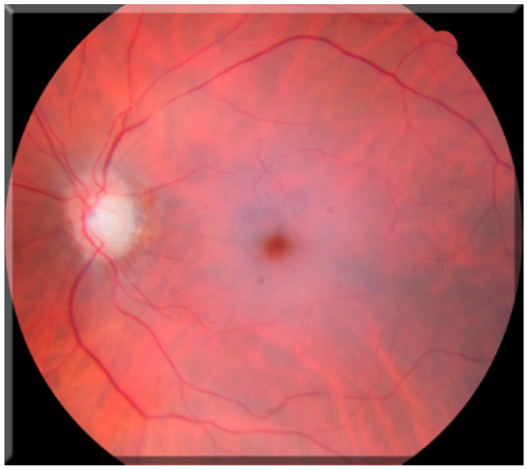
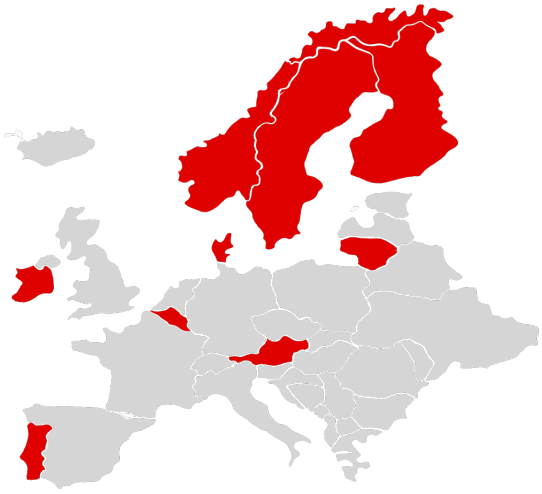
Background and aims: Central retinal artery occlusion (CRAO) is an ophthalmologic emergency that bears a high risk of permanent blindness. No evidence-based treatment is currently available. Whether prompt reperfusion with thrombolytic agents can improve the outcome in CRAO, as proved in ischemic stroke, remains unanswered. The main aim is to assess the effect of systemic tenecteplase within 4.5 hours of onset of central retinal artery occlusion.



Retina changes in a patient with CRAO

Methods: The trial is an ongoing prospective, randomised-controlled, double-dummy, double-blind phase 3 multi-centre trial of TNK 0.25 mg/kg + placebo vs. ASA + placebo (2 arms with 1:1 block randomisation). Patients are recruited after an ophthalmologist has confirmed CRAO and they can be treated within 4.5hrs. After observation in the stroke unit, patients will be re-examined by an ophthalmologist and a neurologist as an out-patient at 30 and 90-day follow-up. The primary outcome is the proportion of patients with ≤0.7 logMAR best-corrected visual acuity (BCVA) in the affected eye at 30 days after treatment, representing an improvement in BCVA of at least 0.3 logMAR.

Results: 9 countries are participating with more than 30 centres. Currently there are 6 countries activated for recruitment. We have recruited 29 patients so far, 6 in Norway and 2 in Finland. Updated figures will be presented.



European map of participating countries

Conclusion: Inclusion will continue until 78 patients have been randomised. All patients have been included within the strict parameters of the study without any serious adverse events.

Disclosure: Nothing to disclose.

EPO-547

Safety of tenecteplasa vs. Alteplasa in stent implantation in the acute ischemic stroke

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Background and aims: The use of intravenous fibrinolysis in patients who required stenting in the acute phase of the stroke with antiplatelet agents could increase the risk of bleeding. The objective of our study is to compare the safety of the use of tenecteplase (TNK) vs alteplase (rTPA) prior to stent implantation.
Methods: Retrospective observational single-center study. We evaluated patients between January 2021 and October 2022 treated by mechanical thrombectomy and stenting in the acute phase. They were subdivided into 3 groups based on whether they received intravenous fibrinolysis with TNK, rTPA, or without fibrinolysis.
Results: 34 patients with a mean age of 67.31 years (SD 17.16), 40% women, were included. 33.3% (12/34) received TNK, 20% (6/34) TPA, and 46.67% (16/34) did not undergo fibrinolysis. The NIHSS mean prior to treatment was 13 and the ASPECTS mean 8, with no significant differences between the groups. In 29/30 a satisfactory recanalization was achieved with TICI≥2b and in 19/34 an extracranial stent was placed. 3 patients treated with TNK and 1 with rTPA presented intracranial hemorrhage (OR=1.67, p=0.69), being symptomatic in the patient who received rTPA (OR=0.15, p=0.26). Among those treated with TNK vs those who did not receive fibrinolysis, there were no differences in asymptomatic hemorrhagic transformation (OR=1.44, p=0.69) or in symptomatic hemorrhage (OR=0.24, p=0.37).
Conclusion: In our series, the use of TNK prior to mechanical thrombectomy with stent implantation in the acute phase of stroke was shown to be safe and did not significantly increase the risk of symptomatic intracranial haemorrhage.
Disclosure: The authors did not receive funds, grants, or other support from any organization for the submitted work.

EPO-548

How Stressed Are the Patients and Caregivers Following an Acute Stroke? – A Study Protocol.

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Background and aims: Stroke is the third leading cause of death worldwide and a main cause of disability. Not only does it affect stroke survivors, but also their informal caregivers. Caregiver burden was previously associated with depression and low quality of life (QoL) of both, caregiver and the stroke survivor. However, a uniform methodology of assessment of caregiver burden has yet to be defined.
Methods: Aims: This study aims to evaluate stress, QoL, depression, anxiety as part of the overall caregiver burden following an acute stroke.
Results: We plan to conclude a longitudinal study of 150 stroke-survivor caregiver dyads. The assessments will be done immediately after stroke, at 3 and 12 months. To evaluate amount of stress, we will use the Perceived Stress Scale 10 (PSS-10) and combine that with the analysis of biological parameters that have been associated with chronic stress (hair cortisol. CRP, LDL, fasting glucose, HbA1c and blood pressure). Short form 36 (SF-36), Stroke Impact Scale (SIS-3.0) and EuroQol-5 (EQ5DL) will be used to determine QoL. Furthermore, we aim to assess anxiety (Hamilton Anxiety Scale / HAM-A), depression (Patient Health Questionnaire 9 / PHQ-9) and sexual behavior (Sexual Behavior Questionnaire SBQ-G) along with caregiver burden (Zarit Burden Interview / ZBI). Besides descriptive statistics, we aim to quantify the association between stroke parameters in patients and their caregivers' stress, thus multiple linear regression models will be fitted.
Conclusion: We aim to comprehend the burden of stroke patients and their caregivers, and establish prevention programs to reduce stress and enhance the QoL.
Disclosure: All authors have no financial conflicts to disclose. The financing of the project has yet to be defined.

EPO-549

Mitochondrial dysfunction in patients with cervical artery dissection: RNA-sequencing data analysis

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Background and aims: CeAD is the leading cause of ischemic stroke at a young age. It is based on undifferentiated connective tissue dysplasia. GWAS didn't establish significant genetic variants, which suggests epigenetic dysregulation. Research goal is to evaluate differentially expressed genes in peripheral blood in patients with CeAD relative to healthy volunteers.
Methods: Peripheral blood from 29 patients with CeAD (mean age 38.1±4.13; female-68.97%) and 18 healthy volunteers (mean age 30.1±6.65; female-66.67%) were collected into EDTA tubes, 1,500 µl aliquots were used for RNA extraction using the RNeasy Mini Kit. 1,000 ng of the RNA (RIN>7.0) were used to prepare each RNA-seq library with the TruSeq Stranded Total RNA Library Prep Gold kit. RNA-sequencing was performed on the Illumina© NovaSeq 6000. The depth of sequencing was 30-50 million paired-end reads per sample. 67%–82% of reads were aligned to the human reference genome using Hisat2. Counting reads in features is done with htseq-count. After TMM normalization, DE analysis was performed in EdgeR (CeAD vs Norma, adj.p-value <0.05, |logFC|>1.0). GSEA was conducted on the Reactome, KEGG and GO databases.
Results: DE analysis revealed >8,000 differentially expressed genes for CeAD relative to norma, LDHB was the most significant (LogFC - 3.6961, adj.p-value 7.1705e-17). GSEA determined the dysregulation of mitochondrial pathways (ATP-synthesis and heat production – adj.p-value 1.165896e-14, TCA-cycle and electron transport chain - adj.p-value 4.672472e-13) and cell-to-extracellular matrix signaling, RNA-processing, innate immunity.

Volcano plot demonstrates results of DE analysis for patients with CeAD relative to healthy volunteers

Conclusion: Mitochondrial metabolism, RNA processing and cell-to-ECM signaling play significant role in pathogenesis of CeAD and connective tissue dysplasia as its main cause.
Disclosure: Nothing to disclose.

EPO-550

Intensive lipid-lowering therapy for secondary stroke prevention: experience from a comprehensive stroke centre

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Background and aims: Updated guidelines for secondary ischemic stroke (IS) prevention suggest strict LDL cholesterol (LDLc) targets. The most established targets are <55 mg/dl for atherothrombotic stroke and <70 mg/dl for other subtypes. We present our lipid-lowering management experience in a comprehensive stroke centre.
Methods: Observational, descriptive study of a prospective cohort of patients with IS admitted to a Stroke Unit between July and October 2020. Demographic, clinical and laboratory data were collected at admission and after 5-month follow-up. Compliance with cLDL goals was assessed.
Results: A total of 152 patients (44.1% women, 70.9±13.9 years old) were included. 42 (27.6%) had TIA, and 110 (72.4%) IS. 30 were atherothrombotic, 46 cardioembolic and 57 of undetermined source. LDLc levels at admission were 97.1±38.0 mg/dl. 68 patients (44.7%) were receiving statin treatment (only 6 high-intensity statins, 15 Ezetimibe-combinations). Treatment was optimised in 120 patients (78.9%), including every atherothrombotic IS, prescribing 26.7% high-intensity statins, 50% Ezetimibe-combinations, and 1 PCSK-9 inhibitor in this group. LDLc was reduced by 31.2±37.9 mg/dl at follow-up (95% CI=22.9–34.8, p=0.0001). LDLc objective <70 mg/dl was achieved in 81.1% of patients, whereas 83.3% of atherothrombotic IS attained LDLc <55 mg/dl. There was 5.3% of poor treatment adherence and 9.8% of adverse effects.
Conclusion: Early use of high-intensity statins and Ezetimibe-combinations improved adherence to new cLDL targets. Low abandonment rates and few adverse effects were observed.
Disclosure: Nothing to disclose.

EPO-551

CAA and amyloid PET: quantitative analysis in a sample of patients with probable CAA

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Background and aims: The diagnostic criteria of CAA do not include the use of amyloid PET (a-PET). Being able to arrive at a diagnosis in advance of overt manifestations of CAA would be beneficial to avoid risk factors such as anticoagulation.
Methods: We recruited 7 patients who met the Boston Criteria 2.0 for probable CAA and underwent brain MRI, a-PET, and neuropsychological tests. Lumbar puncture and genetic analysis were also performed. We accomplished a quantitative analysis of the a-PET data after automated segmentation in 18 brain regions (Table 1).
Results: A total of 126 values expressing aβ burden were evaluated. If we exclude the cerebellum, only 9 brain regions (8%) have no pathological deposition (Table 2); 4 out of 9 were localised in the same area of post-hemorrhagic encephalomalacia. The occipital lobe showed variable amyloid load values, but 3 out of 14 occipital regions (21%) were also affected by encephalomalacia; in these same regions the lowest deposition was identified. The lateral temporal lobe (Figure 1) showed higher aβ load than the medial one. The prefrontal cortex, cingulate, precuneus and parietal lobe had bilateral uniform aβ deposition in excess of the norm.

	Sex	Age at diagnosis	Aβ 40 (CSF) (7755 - 16715)	Aβ 42 (CSF) (> 640)	Aβ 42 / Aβ 40 (CSF) (0.068 - 0.115)	p-tau (CSF) (21.5 - 56.5)	total tau (CSF) (146 - 404)	MMSE	Time between MMSE and a-PET
PT1	F	69	NE	NE	NE	NE	NE	20	173
PT2	F	70	5128	245	0,05	34.1	286	22	6
PT3	F	78	7019	234	0,03	114.8	781	24	55
PT4	M	74	3557	128	0,04	66.8	408	29	131
PT5	F	48	4355	270	0,06	36.4	337	29	42
PT6	F	74	NE	NE	NE	NE	NE	28	-7
PT7	F	79	NE	NE	NE	NE	NE	21	125
		70 ± 9.72 (mean ± SD)						25 ± 3.61 (mean ± SD)	75 ± 63.5 (mean ± SD)

Table 1. Demographic, clinical and biomolecular characteristics. Abbreviations: Aβ = amyloid beta; CSF = cerebrospinal fluid; MMSE = mini mental state examination; NE = not executed; p-tau = phospho-tau; PT = patient; t-tau = total-tau.'

Patient	Parietal lobe (right)	Parietal lobe (left)	Lateral temporal lobe (right)	Lateral temporal lobe (left)
PT1	9,57	7,89	7,96	7,15
PT2	5,56	5,18	6,21	7,2
PT3	6,19	6,41	8,01	8,05
PT4	6,85	5,18	1,62	5,93
PT5	8,76	8,49	9,65	6,67
PT6	4,78	4,71	6,67	5,13
PT7	6,19	6,05	9,58	10,2

ALG	N°	%	N°	%
grade 3	4	28,6	8	57,1
grade 2	10	71,4	5	35,7
grade 1	0	0,0	0	0,0
grade 0	0	0,0	1	7,1

Patient	Sensorimotor cortex (right)	Sensorimotor cortex (left)	Mesial temporal lobe (right)	Mesial temporal lobe (left)
PT1	8,43	7,57	2,36	2,85
PT2	2,95	2,91	3,24	3,52
PT3	1,44	2,46	1,43	2,63
PT4	4,04	3,44	-0,13	2,98
PT5	6,29	6,36	5,35	2,21
PT6	2,29	1,02	1,83	0,15
PT7	3,06	1,84	2,88	3,31

ALG	N°	%	N°	%
grade 3	2	14,3	0	0,0
grade 2	3	21,4	1	7,1
grade 1	6	42,9	9	64,3
grade 0	3	21,4	4	28,6

Patient	Occipital lobe (right)	Occipital lobe (left)	Cerebellum (grey matter)	Cerebellum (whole)
PT1	4,76	3,97	1,91	3,05
PT2	4,33	4,43	0,36	0,41
PT3	2,39	2,74	-0,86	0,15
PT4	-2,24	4,42	0,64	0,68
PT5	10,30	8,17	1,23	1,03
PT6	6,38	-0,54	0,30	0,53
PT7	4,99	5,82	-0,94	-0,73

ALG	N°	%	N°	%
grade 3	2	14,3	0	0,0
grade 2	7	50,0	0	0,0
grade 1	3	21,4	1	7,1
grade 0	1	7,1	13	92,9

Table 1. Values from quantitative a-PET analysis. The severity of amyloid load has been conventionally classified from grade 0 to grade 3, represented with different colours. Areas of recent or previous l-ICH are shown in red font.

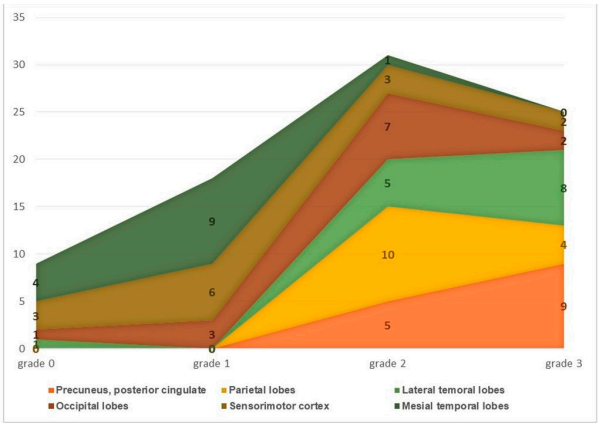

Figure 1. Distribution of severity of amyloid load at a-PET in six different brain regions according to ALG (Amyloid Load Grading): values below 2 (grade 0), values between 2 and 4 (grade 1), values between 4 and 7 (grade 2), values above 7 (grade 3).

Conclusion: Our preliminary results demonstrate concordance between diagnosis and a-PET quantitative results. However, due to the wide variability of CAA pathological and radiological phenomena, it is imperative to ensure a complementary qualitative analysis by a nuclear radiologist. Only a study with a large cohort of patients with clinically overt CAA may allow the adaptation of a-PET protocols to this pathology.
Disclosure: Nothing to disclose.

EPO-552

Effect of the extended thrombectomy time window on survival and quality of life – experiences from Szeged, Hungary

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Background and aims: The thrombectomy time window can be extended up to 24 hours. The aim of our research is twofold: to summarize the results of thrombectomies performed between 6–24 hours after the onset of symptoms, and to identify predictors that can predict the unfavorable outcome.
Methods: In 2020-2021, we processed the data of 90 patients who underwent thrombectomy at Szeged with stroke symptoms of 6–24 hours. Demographic and clinical data were analized, the 90-day mortality, the functional outcome, and the correlation of these parameters with the technical success of the thrombectomy. Correlation between the individual parameters and the outcome was peformed using SPSS and MatLab.
Results: The average age of the patients was 73.03 years (⌖11.85 SD), 48.88% of the patients were outside of the region of Szeged, tandem occlusion occurred in 13%. Sixtyeight percent of the thrombectomies were technically successful, the average score on the 90-day modified Rankin scale was 3 (⌖2 SD), the 90-day mortality was 30%. Higher age, previous stroke in medical history, severity of stroke, technical success of the thrombectomy, atrial fibrillation, lack of prior antiaggregant and thrombolysis treatment together can predict a poor clinical outcome with 93% specificity and 72% sensitivity.
Conclusion: While the practical application of the extended time window leads to more patients who can benefit from effective stroke care, our real world data analysis warrants further investigation to better identify a subgroup of patients to reduce mortality and further improve functional outcome.
Disclosure: Nothing to disclose.

EPO-553

Markers of damage to the blood-brain barrier and brain in cerebral small vessel disease and Alzheimer's disease

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Background and aims: It is believed that the comorbidity of cerebral small vessel disease (cSVD) and Alzheimer's disease (AD) is the cause of mixed cognitive impairments (CI). At the early stages, their comorbidity could not be confirmed by laboratory signs. This study was aimed at finding markers to differentiate cSVD and AD.
Methods: The study included 68 cSVD patients (61.0±8.6; m. 60.3%) with dysexecutive (26%), amnestic (7.2%) and mixed (66.8%) CI types and 17 AD patients (65.2±8.3; m. 35.3%). The following markers of damage to the blood-brain barrier and brain were investigated in blood serum (BS) and cerebral spinal fluid (CSF) with ELISA: matrix metalloproteinases (MMP) 2 and 9, tumor necrosis factor (TNF) alpha, tissue-type plasminogen activator (tPA), fibrinogen, neurofilament light chains (NEFL), glial fibrillary acidic protein (GFAP), neuron-specific enolase (NSE). Statistical analysis was performed with Mann-Whitney U test and receiver operating characteristic (ROC) curves analysis (SPSS v26).
Results: The levels of TNFalpha in BS and CSF and GFAP in CSF were significantly higher in cSVD patients ($p<0,001$) (Fig. 1). Differential markers of cSVD from AD were BS TNFalpha >9.95 pg/ml (0.99; CI 0.96-1.0), CSF TNFalpha >7.1 pg/ml (0.99; CI 0.99-1.0), CSF GFAP >1.03 ng/mL (0.92; CI 0.86–0.98) with sensitivity and specificity of threshold values >70% (Fig. 2).

Fig 1. The levels of TNFalpha in BS and CSF and GFAP in CSF in patients with cSVD (blue) and AD (orange)

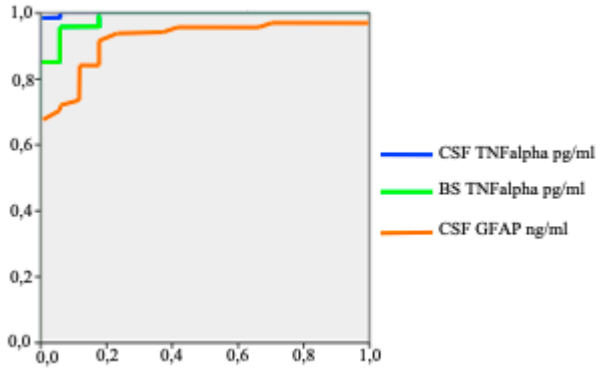

Fig 2. ROC curve analysis for markers of blood-brain barrier permeability and neurodegeneration in cSVD and AD

Conclusion: The established differential predictors indicate a high significance of TNFalpha-supported neuro-inflammation and astrocytic GFAP-reactivity in cSVD. Found threshold values can be used in AD with white matter hyperintensity to clarify isolated and mixed form with cSVD.

Disclosure: Supported by the Russian Foundation for Basic Research, project no.22-15-00183

EPO-554

Markers of blood-brain barrier permeability, lymphangiogenesis and neurodegeneration in cerebral small vessel disease

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Background and aims: This study aimed to calculate the predictive value of circulating markers associated with leading mechanisms of cerebral small vessel disease (cSVD).

Methods: The study included 68 cSVD patients (61.0±8.6; men 60.3%) with cognitive impairments of varying severity and 26 healthy participants (HP) (59.9±6.7; men 38.5%). The following indicators were determined in blood serum by ELISA: the markers of blood-brain barrier (BBB) permeability (matrix metalloproteinases (MMP) 2 and 9, tumor necrosis factor (TNF) alpha, tissue-type plasminogen activator (tPA), fibrinogen), lymphangiogenesis (vascular endothelial growth factor (VEGF) C) and neurodegeneration (neurofilament light chains (NEFL), glial fibrillary acidic protein (GFAP), neuron-specific enolase (NSE)). Statistical analysis was performed with Mann-Whitney U test, receiver operating characteristic (ROC) curves and Pearson's correlation analysis (SPSS v26).

Results: The level of all studied markers in cSVD patients was significantly different from HP. The highest areas under the ROC curve were determined for VEGF C (0.93, CI 0.87–0.98), MMP 2 (0.93, CI 0.87–0.98), MMP 9 (0.99, CI 0.99–1.00), TNF alpha (0.96, CI 0.91–1.00), GFAP (0.82, CI 0.73–0.90) with sensitivity and specificity of threshold values >70% for all of them (Fig. 1). The GFAP level correlated with the levels of TNF alpha (r=0.447), MMP 9 (r=0.554), VEGF C (r=0.430).

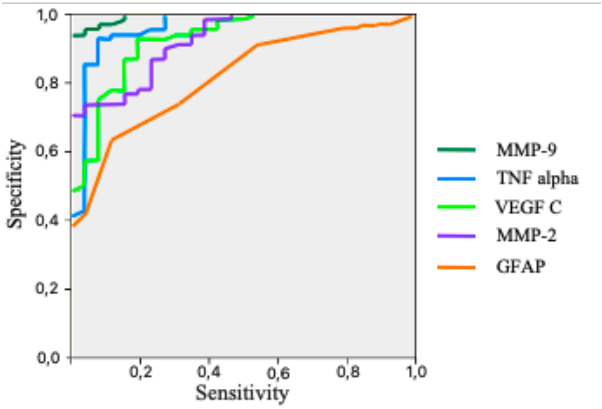
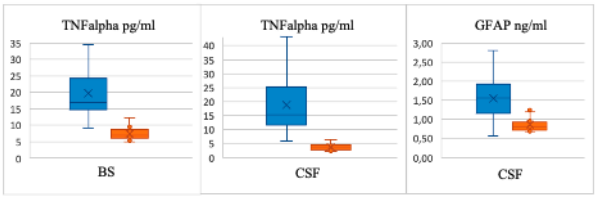


Fig 1. ROC curve analysis for markers of BBB permeability, lymphangiogenesis and neurodegeneration in cSVD

Conclusion: The analysis of GFAP associations suggests the determining role of TNF alpha, MMPs 2, 9 and VEGF C in damage and maintenance of high BBB permeability and GFAP-associated neuroinflammation and neurodegeneration and the possibility of using them in the cSVD diagnosis.

Disclosure: This study was supported by the Russian Foundation for Basic Research, project no. 22-15-00183.



EPO-555

Challenges Of Acute Ischemic Stroke Associated With Left Ventricular Thrombus: A Single-Center Experience.

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Background and aims: Left ventricular thrombus (LVT) is a known complication in patients with myocardial infarction (MI), mainly in anterior MI [1]. LVT is a rare cause of cardioembolic ischemic stroke (IS) and may remain undetected, as "embolic stroke of undetermined source (ESUS)"[2]. Transthoracic echocardiography (TTE) is the main investigation: intravenous contrast administration increases its sensitivity for LVT detection. Cardiac Magnetic Resonance Imaging (MRI) has a high sensitivity and specificity for the thrombus delineation [3].
Methods: A retrospective analysis of 2,792 consecutive patients with acute IS, admitted to the Stroke Unit of the University of Messina, between 2014 and 2022, LVT was reported in fifteen patients. 12 patients had a diagnosis of "cardioembolic IS", due to TTE LVT detection. Three patients were discharged with the ESUS diagnosis and underwent cardio-MRI.
Results: The cardiological assessment with TTE showed an apex hypo-akinesias and reduced left ventricular ejection fraction (LVEF<50%) in all patients. In twelve patients, TTE detected LVT; in three patients, TTE showed LVT risk factors, so they performed cardio-MRI, which revealed mural thrombosis. All patients were treated with vitamin K antagonists for a period of a minimum of 3–6 months up to thrombus resolution.
Conclusion: LVT is a rare cause of cardioembolic IS, and therefore a correct diagnostic-therapeutic pathway is of the utmost importance [4]. Whether there is high clinical suspect of LVT and TTE findings of left ventricular dysfunction, cardio-MRI should be performed when other methods are not diagnostic.
Disclosure: The authors have no financial interest to report and did not receive any fundings.

EPO-556

Thrombolytic and Endovascular Treatment Experience in Patients Over 85 Years of Age with Acute Ischemic Stroke

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Background and aims: Intravenous thrombolytic treatment(IVT) and endovascular treatment(EVT) are important in acute ischemic stroke(AIS). There is insufficient literature data regarding the safety of IVT and EVT in the elderly.We wanted to share our experiences with IVT and EVT in patients aged 85 years and older with aII.
Methods: 25 patients with acute ischemic stroke over the age of 85 were included in our study. Multiple risk factors,treatments used,admission and discharge NIHSS scores, door-to-needle and symptom-door times, complications after the procedure, discharge and 3rd month mRS scores were recorded.
Results: IVT was performed in 32% of the patients,EVT in 20% and both IVT and EVT in the remainder. Complications did not develop in 16 (64%) patients,asymptomatic intracranial hemorrhage (ICH) was observed in 5 (20%) and symptomatic ICH was observed in 2 (8%) patients.13 (52%) patients had a good outcome (mRS 0–2) at discharge.Hospital mortality rate was calculated as 24%. Our third month mortality rate at was 28%.Factors associated with poor outcome at 3 months (mRS 3–6); high entry NIHSS score (p=0.005), presence of symptomatic and asymptomatic ICH (p=0.048) and presence of more than one vascular risk factor (p=0.041). These results showed that aII can be effectively treated in this age group with IVT and EVT.It is noteworthy that third month mRS scores were found between 3–6 in all patients who developed symptomatic or asymptomatic ICH.

Relationship between patient characteristics and 3rd month mRS score

	3. month mRS 0-2	3. month mRS 3-6	P value
Symptom-Door Time	145,56±48,31	191±136,95	0,351
Admission NIHSS Score	9,11±5,33	15,87±4,01	**0,005**
Door-to-needle Time	89,22±43,16	109,67±71,35	0,63
Door-to-needle Time (categorical)			
≤60 minutes (n=9)	3	6	1
>60 minutes (n=15)	6	9	
Complication			
None (n=16)	9	7	
Asymptomatic bleeding (n=5)	0	5	**0,048**
Symptomatic bleeding (n=2)	0	2	
Other (n=2)	0	2	
Use of Antiaggregant er	4	5	0,671
Anticoagulant Drugs	5	11	
Var (n=9)			
Yok (n=16)			
Hypertension			
Var (n=19)	7	12	1
Yok (n=6)	2	4	
Diabetus Mellitus			
Var (n=5)	1	4	0,621
Yok (n=20)	8	12	
Atrial fibrillation			
Var (n=11)	3	8	0,677
Yok (n=14)	6	8	
Coronary artery disease			
Var (n=5)	1	4	0,621
Yok (n=20)	8	12	
Multiple risk factors			
Var (n=13)	2	11	**0,041**
Yok (n=12)	7	5	

Thrombolytic and Endovascular Treatment Experience in Patients Over 85 Years of Age with Acute Ischemic Stroke

Conclusion: In conclusion,it can be said that IVT and EVT applications are effective and safe in elderly patients with all.
Disclosure: We are of the opinion that IVT and EVT is safe in elderly patients and patient-based evaluation is important.

EPO-557

Aphasia due to acute stroke treated with the tablet-based speech therapy app Neolexon®: a randomized controlled trial.

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Background and aims: Aphasia is a common symptom in acute stroke patients, which has severe impact on both functional independence and quality of life. Current guidelines recommend face-to-face speech therapy as early as possible after stroke onset. Speech therapy smart devices are a promising approach to complement face-to-face logopaedics and are suitable for self-training purposes. We hypothesize, that speech therapy assisted by the tablet-based app Neolexon® is superior to standard logopaedics (NCT04080817).
Methods: We aim to enroll 180 adult German native-speaking patients with aphasia due to acute stroke and ≤13 points in the Language Aphasia Screening Test (LAST). Probands are dichotomized into three groups based on their LAST scale and randomly assigned (1:1) to receive either standard speech therapy or standard speech therapy and Neolexon®-therapy. Patients will be visited four times within three months during hospital stay and rehabilitation. Study visits comprise both comprehensive neurological and speech therapy examinations. Primary outcome is defined by a 10% mean difference in the change of percentile rank of the Bielefelder Aphasie Screening (BIAS) after three months. Secondary outcomes include quality of life, scale in Becks Depression Inventory and modified Rankin Scale after three months.
Results: From July 2021 up to now we enrolled n=62 patients, of which n=24 completed their last study visit. We aim to present preliminary results of ongoing analysis.
Conclusion: The Neolexon® application could be a beneficial complementary tool in speech therapy. This trial is suitable to provide evidence for computer-supported speech therapy in acute stroke patients with aphasia.
Disclosure: All authors report no conflicts of interest related to the presented research.

EPO-558

1-year outcome of mechanical thrombectomy in the oldest old

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Background and aims: Little is known about stroke treatment and one-year outcomes in the oldest old stroke population.
Methods: We analysed data from acute ischemic stroke (AIS) patients with large vessel occlusion treated by mechanical thrombectomy (MT) admitted to the Comprehensive Stroke Center at the University Hospital in Krakow, Poland, between 2019 and December 2021. The study was approved by the Ethical Committee. Only the patients who gave written consent were included. We studied 34 parameters readily available within 24 hours after AIS including demographics, stroke risk factors, thrombolytic treatment and several clinical and biochemical parameters. Outcome measure was the modified Rankin score (mRS) at 1-year after stroke. mRS≤2 defined good outcome and mRS=6 - death.
Results: During a study we registered 2,554 AIS patients, 1,788 (70%) patients agreed to participate of whom 593 (33.2%) received MT. IVT proceeded MT in 325 cases (54.8%). 1-year follow-up was available for 564 (95.11%) patients. We identified 16 patients aged ≥90 years. Oldest old patients as compared to others differed in gender distribution (females: 87.5% vs 45.1%, p<0.01) and had significantly more often atrial fibrillation (56.3% vs. 27.9%, p=0.014). 1-year mortality was similar between the studied groups (50% vs 30,1%, p=0.089), however, good outcome was noted less often the oldest old (31.3% vs. 61.7%, p=0.014).
Conclusion: MT in the oldest old as compared to others seems to be similarly effective in terms of 1-year mortality; still, 1/3 of the oldest old remains independent after 1-year follow up.
Disclosure: ERA-NET-NEURON/21/2020 iBioStroke grant

EPO-559

Comparison of characteristics and outcomes between acute ischemic stroke patients with different heart failure

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Background and aims: Acute ischemic stroke (AIS) can be complicated by heart failure involving preserved ejection fraction (HFpEF) or reduced ejection fraction (HFrEF), and whether prognosis differs between the two types of patients is unclear. We compared the clinical characteristics and outcomes of the two types of patients at 3 months after stroke.

Methods: We retrospectively analyzed patients who, between 1 January 2018 and 1 January 2021, experienced AIS that was complicated by HFrEF or HFpEF. All patients had been prospectively registered in the Chengdu Stroke Registry. Poor outcome was defined as a modified Rankin Scale (mRS) score of 2–6 at 3 months. Univariate and binary logistic regression was used to assess whether HFpEF was associated with significantly worse prognosis than HFrEF.

Results: Among the final sample of 108 patients (60.2% men; mean age, 73.08±10.82 years), 75 (69.4%) had HFpEF. Compared to HFrEF patients, those with HFpEF were older (p=0.002), were more likely to have chronic kidney disease (p=0.033) and to experience poor outcome (p=0.022). After adjustments, HFpEF was associated with significantly greater risk of poor outcome than HFrEF (OR 4.05, 95%CI 1.19–15.26, p=0.03). However, rates of hemorrhagic transformation or mortality at 3 months after AIS did not differ significantly between the two types of heart failure (all p>0.05).

Conclusion: Patients with AIS involving HFpEF may experience worse outcomes than those with HFrEF and therefore may require special monitoring and management. Our findings need to be verified in large prospective studies.

Disclosure: The authors declare no conflicts of interest.

EPO-560

Risk factors for osteoporosis in Korean adult stroke over 60 years old survivors

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Background and aims: Many studies examined the relationship between osteoporosis and stroke. However there are little study about risk factors of osteoporosis in stroke patients. We assumed that osteoporosis and stroke are more closely related beyond the previously known risk factors of osteoporosis. Therefore, we investigated the prevalence of osteoporosis among stroke survivors and analyze the risk factors for osteoporosis in an elderly Korean stroke population.

Methods: This study retrieved data contained in the 7th Korea National Health and Nutrition Examination Survey (KNHANES) for a population-based sample of stroke patients. Total 328 patients were included in this study and we compared two group, stroke with osteoporosis and without osteoporosis.

Results: The high prevalence of osteoporosis was observed among women, unemployed, low-educated people, and rheumatic arthritis patients. Contrary to our expectations, the study showed that those with higher average alcohol consumption and smokers had a lower prevalence of osteoporosis. After adjusting for sex and age, the study showed no statistical significance between the prevalence of osteoporosis in relation to education level and employment and smoking status. When adjusting for all variables, there was no statistical significance except for females and patients with rheumatic arthritis and cardiovascular disease.

Conclusion: The risk factor of osteoporosis in stroke patients may differ from that in non-stroke patients. Furthermore, stroke itself can be a more significant risk factor than other factors for osteoporosis. The main contributions of this study are this is the first study to evaluate the risk factors of osteoporosis in stroke patients using KNHANES data.

Disclosure: Nothing to disclose.

Higher cortical functions; Neuroinformatics; Neuro-oncology; Neurotoxicology/occupational neurology; Spinal cord and root disorders

EPO-561

Copper deficiency related myelopathy

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Background and aims: Myelopathy is a frequent reason for acute adult neurology admission and is an important cause of disability. The objective of this case report is to highlight a rare and treatable cause of non-compressive myelopathy. Acquired copper deficiency resembles subacute combined degeneration of the cord due to B12 deficiency and responds to copper replacement.
Methods: We present a case of a patient with progressive myelopathy who subsequently required admission. The biochemical and radiological features of acquired copper deficiency are discussed.
Results: A 74 year female presented to the outpatient clinic in February 2021 with slowly progressive distal sensory loss, poor balance and walking difficulty. Examination revealed a mild spastic quadriparesis with impaired distal sensation, marked proprioceptive loss and sensory ataxia. After 6 months, she was using a wheelchair. A microcytic anaemia with normal ferritin was noted. MRI spine showed a long segment of high T2 intrinsic posterior cord signal from C2-T3, therefore inflammatory and metabolic causes were considered. B12 level, CSF, EEG and nerve conduction studies were normal. An empirical course of intravenous methylprednisolone was given without improvement. Serum copper was low at 3.2 micromol/L (normal 12-26 micromol/L). Her walking improved with intravenous followed by oral copper replacement. She was later found to be using zinc containing denture cream which was stopped.
Conclusion: Serum copper levels should be checked early in the investigation of non-compressive myelopathy. Zinc containing denture cream affects copper absorption and can deplete serum copper levels.
Disclosure: The authors have no disclosures.

EPO-562

In the eye of the neurologist: distinct prognosis profiles in FND inpatients

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Background and aims: Functional neurological disorder is a frequent reason for neurology and psychiatry referrals and clinicians could be challenged by the management and follow-up of the disorder. FND patients represent a heterogenous population, however there has been little research whether there are different patient profiles, especially regarding adherence to the diagnosis and prognosis.
Methods: We developed a subjective, seven item clinician graded prognostic outcome score (POS) combining items relevant to diagnosis adherence and objective potential prognostic. We used latent class analysis with score items as indicators to examine patient profiles in a cohort of consecutive FND inpatients.
Results: Regarding diagnosis adherence and potential prognosis, we found the existence of two distinct FND patient profiles based on the proposed subjectively graded prognostic outcome score. In the neurologist's eye there is one profile of good diagnosis adherence and better potential prognosis and one profile of poor diagnosis adherence and potentially worse prognosis.

Table 1. Population characteristics			
		Count	% of total
Gender	Female	33	71,7%
FND manifestation	PNES	28	62,2%
	Motor or sensitive manifestation	14	31,1%
	Cognitive manifestation	3	6,7%
Neurological comorbidities	None	22	48,9%
	Epilepsy	9	20,0%
	Traumatic brain injury or stroke	3	6,7%
	Epilepsy due to brain damage	5	11,1%
	Headaches	3	6,7%
	Peripheral nervous system pathology	1	2,2%
	Intellectual deficiency	2	4,4%
Psychiatric comorbidities	None	29	64,4%
	Anxiety	7	15,6%
	Depression	6	13,3%
	Anxiety and Depression	3	6,7%
Term used for final diagnosis	No particular term	11	23,9%
	Psychogenic	27	58,7%
	Somatoform	3	6,5%
	Functional	5	10,9%
FND related ER visits in the previous year	No	40	88,9%
FND related hospitalizations in the previous year	No	43	95,6%

Table 1. Population characterics

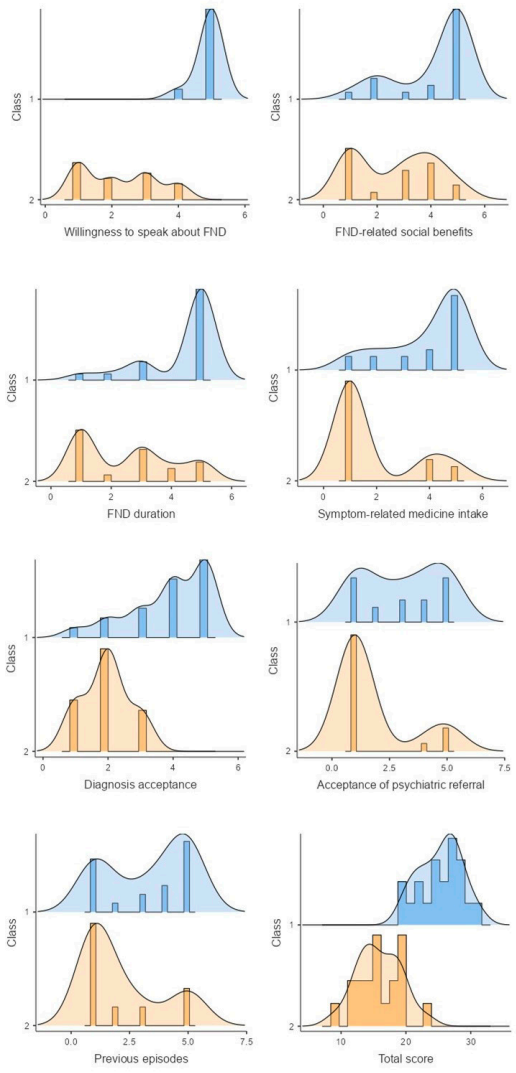

Figure 1. Histograms of LCA Indicators and total score between-class distribution

Conclusion: The POS score is a promising tool for the estimation of FND prognosis. Future research is needed to correlate patient profiles to the outcome and confirm the validity of the POS score in a larger, prospective cohort.
Disclosure: Nothing to disclose.

EPO-563

Vismodegib in Neoplastic Meningitis from Sonic Hedgehog (SHH)-Activated Medulloblastomas: a Case Report.

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Background and aims: Vismodegib is a SHH-inhibitor that proved to be effective in locally-recurrent SHH-activated medulloblastoma. However, whether vismodegib is effective in case of neoplastic meningitis (NM) as well has not been assessed so far. Here, we present a case of a patient with NM from SHH-activated medulloblastoma who showed a dramatic response to vismodegib.
Methods: (not applicable)
Results: A 34-year-old patient was diagnosed with a SHH-activated cerebellar medulloblastoma in 2015. He underwent gross-total resection, cranio-spinal radiotherapy (RT) and 5 cycles of lomustine, vincristine and cisplatin. Then, he remained disease-free until October 2021, when the MRI showed a new single contrast-enhanced nodule in the spine (T10), which was treated with stereotactic RT. However, the following MRI showed a diffuse leptomeningeal involvement, with new multiple linear and nodular lesions. The CSF cytology confirmed the presence of neoplastic cells. Therefore, in April 2022 vismodegib (150 mg daily) was started. The treatment was well tolerated, except for increased creatine phosphokinase (CTCAE v3.0 grade 1). After only 2 months of therapy, a reduction of the meningeal enhancement was seen on MRI, and after 4 months all nodular and linear lesions disappeared. Similarly, CSF cytology became negative after 4 months of treatment. Treatment is still ongoing, with an enduring response on MRI.
Conclusion: To our knowledge, this is the first report of an adult patient with NM from SHH-activated medulloblastoma achieving a complete response with vismodegib. Data from larger series are needed to confirm the effectiveness and safety of vismodegib in case of leptomeningeal spread.
Disclosure: I have no disclosures.

EPO-564

Posterior reversible encephalopathy syndrome in a COVID vaccine associated Guillain-Barré syndrome.

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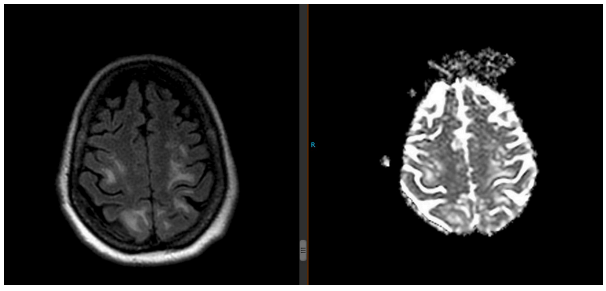
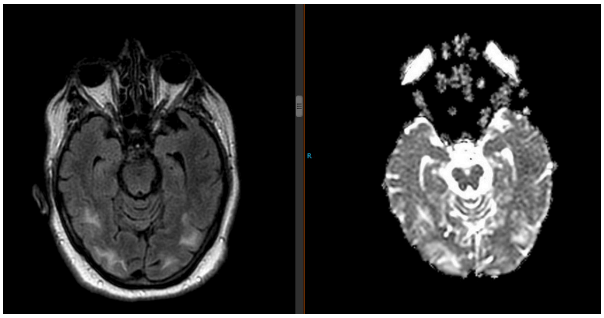
Background and aims: Posterior reversible encephalopathy syndrome (PRES) and Guillain-Barré syndrome (GBS) are two uncommon neurologic entities in the general population, and their overlap, although rare, has been reported. Most authors theorize that the dysautonomia observed in GBS patients might trigger blood pressure changes causing PRES, however forms and time of presentation vary amongst cases, blurring this linear causality.
Methods: We present a novel case admitted in our hospital and review the existing literature.
Results: We describe the case of a 67-year-old woman that three weeks after receiving the first dose of a viral vector COVID-19 vaccine presented with distal paraesthesia in all four limbs, dizziness, instability and altered gait. Six days before admission she experienced sharp back pain and had noticed high blood pressure in her residence. Initial neurological exam showed severe distal weakness, global hyporeflexia, sensory loss in glove and stocking pattern and autonomous gait was impossible. Additionally, our patient presented an altered mental status with tendency towards somnolence that fluctuated during her hospital stay and later developed visual hallucinations. GBS diagnosis was confirmed by CFS and neurophysiological tests. MRI showed symmetric subcortical vasogenic oedema in occipital, parietal, and frontal lobes, that suggested a concomitant PRES. During hospitalization she received intravenous immunoglobulins and physical therapy with partial motor improvement.



Parietal and frontal subcortical oedema suggestive of PRES; FLAIR and aADC sequences.



Occipital subcortical oedema suggestive of PRES; FLAIR and aADC sequences.

Conclusion: Although the physio-pathological base of the co-occurrence of these two neurologic syndromes still requires further analysis, our case adds to the existing evidence of the association between them and the need to consider PRES in GBS cases with atypical neurological manifestations.
Disclosure: None of the authors present any conflict of interest in this case.

EPO-565

Predicting brain metabolism in elderly patients with cognitive impairment using deep learning

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Background and aims: Image-to-image translation algorithms can generate highly precise synthetic images from real images. Usage of such methodology to predict brain development is currently uncharted territory. Regional decline in brain metabolism can aid in the differential diagnosei of neurodegenerative diseases. As such, FDG-PET, quantifying brain metabolism, presents a promising target for a proof-of-principle study of medical imaging time series prediction. Here, we aim to predict future FDG-PET scans from FDG-PET data acquired in year zero and year one using a convolutional neural network (CNN).
Methods: We identified elderly (≥55 years) participants from the Alzheimer's Disease Neuroimaging Initiative who received FDG-PET scans in three consecutive years. A CNN was implemented and trained on scans from year zero and year one to generate a prediction for the scan of the second year. The performance of the CNN was evaluated on a holdout sample using mean absolute error (MAE) and structural similarity (SSIM).
Results: Preliminary results suggest that second-year scans can be predicted with low reconstruction error (small MAE, high SSIM) when using data from individuals with high

likelihood of neurodegeneration-associated changes on FDG-PET, i.e., individuals with pending conversion to, or an existing diagnosis of Alzheimer's disease.
Conclusion: We report that future FDG-PET scans can potentially be predicted from existing FDG-PET data. If successful on a larger scale, our model may be relevant for data augmentation in scientific longitudinal studies, as well as provide insights into the development of brain metabolism in relation to neurodegenerative diseases.
Disclosure: Nothing to disclose.

EPO-566

Clinical-MRI Dissociation in Spinal Cord Sarcoidosis: A Case Report.

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Background and aims: The diagnosis of spinal cord sarcoidosis can be particularly challenging when not accompanied by clinically overt systemic involvement. Herein we describe a rare case of longitudinally extensive spinal cord sarcoidosis incidentally disclosed during the diagnostic work-up for intermittent diplopia.
Methods: The clinical presentation and diagnostic approach leading to the diagnosis of spinal cord sarcoidosis are presented.
Results: A 53-year-old man presented after one month of intermittent diplopia that resolved spontaneously. Neurological examination revealed diffuse hyperreflexia, bilateral Trömner sign, diplopia evocable after fatigability on the left gaze. Brain MRI revealed some abnormalities in the upper cervical spinal cord. Spinal cord MRI disclosed a longitudinally extensive T2-hyperintense lesion from C1 to D1, with patchy gadolinium enhancement. Negative testing for aquaporin-4 and myelin oligodendrocyte glycoprotein antibodies by cell-based assay (fixed and live, respectively). Lumbar puncture showed mild pleocytosis (12 white blood cells/mm^3), elevated proteins (70mg/dL; normal range, <40mg/dL). Chest CT revealed mediastinal lymphadenopathy, with associated intense FDG uptake on positron emission tomography. Transbronchial needle aspiration of a lymph node revealed non-caseating granulomatous inflammation, consistent with probable neuro-sarcoidosis. The patient was followed untreated for 3 months with stability of the spinal cord lesion on MRI. After he developed numbness in both hands and Lhermitte's phenomenon. Intravenous methylprednisolone was administered followed by slow tapering of oral, with prompt resolution of symptoms and marked improvement of the spinal cord abnormalities.

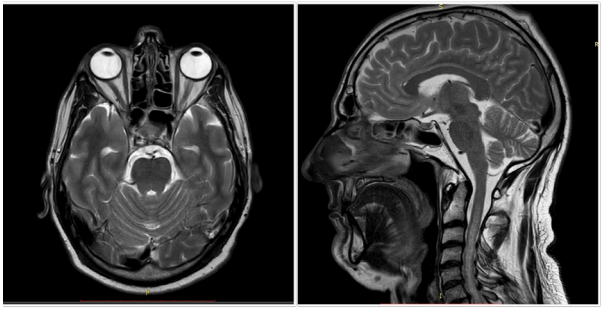


Figure 1. Axial (A) and sagittal (B) T2-weighted images of the brain did not show brain abnormalities, but reveal an extensive cervical spinal cord lesion.

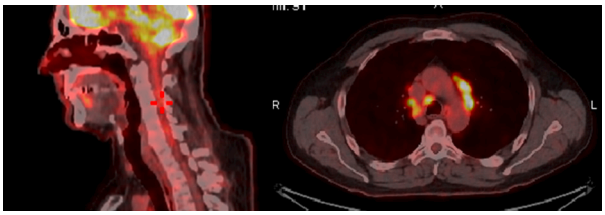
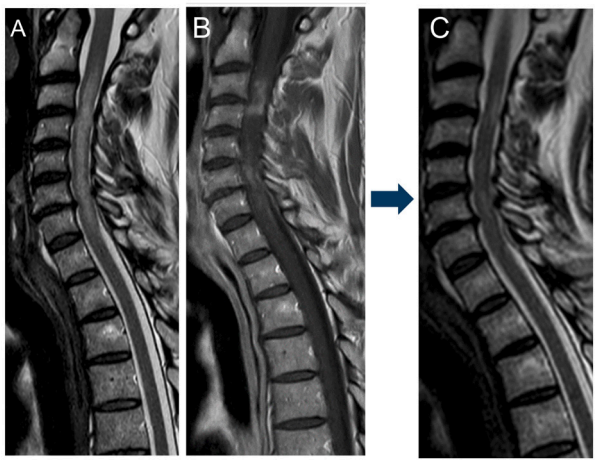


Figure 2. 18F-FDG PET/CT demonstrated hypermetabolic activity of the cervical spinal cord lesion (A), and mediastinal lymphnodes (B).

Conclusion: A marked clinical-MRI dissociation (i.e., extensive MRI abnormalities accompanied by only mild clinical manifestations) is a big clue for diagnosis.



On admission, a longitudinally extensive T2-hyperintense lesion (A), associated with patchy gadolinium enhancement (B). The spinal cord lesion resolved nearly completely after treatment with corticosteroids (C).

Disclosure: All authors had no disclosures.

EPO-567

Default mode network activity during attention switching in intracranial EEG

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Background and aims: The Default Mode Network (DMN) is one of the intrinsic brain networks playing a crucial role in many cognitive functions. First discovered as a resting state network, DMN was later shown to be activated not only during mind wandering but also in tasks requiring internally oriented attention. On the contrary, DMN is deactivated during external attention demanding tasks, thus its activity is often anti-correlated with other brain networks, such as Dorsal Attention Network (DAN). However, the neuronal mechanisms of DMN/DAN switching remain unclear.
Methods: We investigated the interplay between DMN and DAN during an attention switching task using intracranial EEG (iEEG) recorded in a large cohort of 25 epilepsy patients. The iEEG is a useful tool to study brain network dynamics, as it reflects the local neuronal activity in the vicinity of the intracerebral electrodes with millisecond precision.
Results: We found a robust representation of the attention switching in the alpha power (8–12 Hz) of the iEEG. In particular, the alpha power of DMN was strongly attenuated in the internal attention task and increased during the task requiring external attention, while the DAN showed exactly the opposite pattern of activations.
Conclusion: Given that the alpha power is often referred to as the idling rhythm, our results are thus in line with generally accepted concept of DMN/DAN dynamics. Uncovering the detailed neuronal mechanisms of attention switching may also have profound implications for various neurological and psychiatric diseases in which the network dynamics are compromised.
Disclosure: This research was supported by GACR grant 20-21339S and GAUK grant 272221

EPO-568

Scwannomas: Neuro-glial Interaction and Molecular Therapy

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Background and aims: Neurofibromatosis is a disease from the group of phakomatoses. This term unites group of three diseases: neurofibromatosis type I (NF1), neurofibromatosis type II (NF2), schwannomatosis, neurofibromas, and scoliosis. Schwannoma is a tumor that arises from the Schwann cells of the nerve sheath. It can be either malignant or benign. This type of oncology is diagnosed infrequently, in about 7% of cases of all soft tissue sarcomas. It is observed mainly in middle-aged people, more often in males. So far, there have been only surgical methods for removing these tumors. The aim of our work was to analyze the possibilities of treatment using molecular genetic methods for the treatment of schwannomas in animal genetic models.
Methods: Knock-out mice were obtained by disruption of Nf1 gene. Organ and tissues genesis were dependent of neurofibromin encoded by this gene. Glial fibrillar acid protein (GFAP) as marker of glial cells metabolite and neuron-specific enolase (NSE) as neuronal functions protein were evaluated.
Results: After development of shwannomas on mice legs we used adeno-associated serotype 1 virus (AAV1)-based vector delivering N-terminal of the TRK-fused gene. In result of 7 passages of virus vector delivering to experimental mice the sizes of 4 schwannomas were considerably reduced. After course of molecular treatment activity of GFAP and NSE was markedly decreased.
Conclusion: Mouse model of Neurofibromatosis I and II and schwannomatosis seems to be a good target for molecular therapeutic approaches.
Disclosure: Nothing to disclose.

EPO-569

Outcomes of tailored psychotherapy for dissociative seizures in a developing functional neurology service

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Background and aims: Dissociative seizures (DS) can cause distress and disability comparable to that caused by epileptic seizures. There is growing evidence to suggest psychological therapy can be effective in treating DS, although the treatment approaches are varied.
Methods: We analysed outcomes from a functional neurological disorders service in the North West of England offering short term psychotherapy to consecutive eligible patients with a diagnosis of DS. Patients were assessed for clinical and psychological variables before and after psychotherapy using the GAD-7 screening score for generalised anxiety disorder, the Work and Social Adjustment Scale (WSAS) to assess functional status, the PHQ-15 somatic symptoms scale, PHQ-9 depression score and PCLC PTSD symptom score.
Results: 86 patients (67 female) were referred for psychotherapy with a clinical diagnosis of DS. The mean number of therapy sessions was 5.94 (95% CI 5.04 to 6.84). Patients had significant improvements in GAD-7 sumscores ($Z=-2.549$, $p=0.011$), PHQ-15 ($p=0.028$), PHQ-9 ($Z=-3.202$, $p<0.001$) as well as PCLC PTSD symptom scores ($Z=-2.288$, $p=0.022$), comparing pre and post treatment values. Whilst there was a reduction in the median WSAS scores comparing pre and post treatment values (30 to 22.5), this difference was not significant ($Z=-1.932$, $p=0.053$). DS frequency improved in 67.4% of patients (95% CI 52.0% to 80.5%).
Conclusion: Although this is an observational study, findings support the notion that tailored psychotherapy is a clinically effective intervention to improve psychological status, quality of life and dissociative seizure frequency in a real-world clinical setting.
Disclosure: Nothing to disclose.

EPO-570

Manganism: a toxidrome to be remembered

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Background and aims: Manganese (Mn) is an abundant element in nature, but its neurotoxicity (manganism) is uncommon. It usually occurs after occupational or iatrogenic exposures to Mn. Manganism produces an extrapyramidal case that resembles Parkinson's disease due to a special tropism for the basal ganglia, with a typical brain magnetic resonance image (MRI): hypersignal on T1 sequence of both globus pallidus.
Methods: Description of a manganism's case.
Results: A 55 year old male was admitted with acute onset parkinsonism. Brain MRI showed basal ganglia ischemia and T1 hyperintensity of both globus pallidus, suggestive of Mn deposit. Accidental exposure to insecticide products containing Mn in a domestic greenhouse was verified, thus establishing the diagnosis of manganism. Parkinsonism was resolved within a few weeks, and later the patient developed an apathetic-abulic syndrome secondary to basal ganglia ischemia, showing a steady improvement after treatment with neuropsychological stimulation, fluoxetine and homotaurine.
Conclusion: We present a clinical case of manganism, epidemiologically atypical and showing infrequent and complex semiology. Manganism should always be considered in the differential diagnosis of a patient with acute parkinsonism, looking for a possible exposure to the toxin and having a high level of clinical suspicion. The most recent evidence suggests that Mn could have a molecular and neuropathological tropism on the basal ganglia and perhaps be related to the onset and development of Parkinson's disease.
Disclosure: Authors have no conflicts of interest to declare.

EPO-571

Spinal Arteriovenous Fistula (sAVF): An underrecognized cause of Longitudinally Extensive Transverse Myelitis (LETM)

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Background and aims: LETM causes acute paraparesis or paraplegia with a broad differential, including mainly inflammatory diseases. SAVF is a rare and potentially treatable cause of LETM, with devastating consequences if left untreated.
Methods: We present a case of LETM due to sAVF, along with a systematic review of the literature. We searched MEDLINE for LETM and sAVF cases, identifying 752 and 671 articles, respectively. Finally, 106 articles for LETM and 20 articles for sAVF were included.
Results: A 57-year-old previously healthy man, presented with subacute flaccid paraparesis, hypoesthesia below knees and urinary retention. Spine MRI revealed LETM from the 7th to the 12th thoracic vertebra, with concomitant dilated perimedullary vessels and T2 flow-voids. DSA depicted a sAVF at 3rd Lumbar artery level, which was subsequently embolized with excellent clinical response. In our review, we found 246 LETM cases (Mean age: 40 years, 129 Women-52%). The most common causes were NMOSD (32%), Infections (30%) and systematic Autoimmune diseases (13%). Only 3% of LETM cases were attributed to sAVF. Then, we searched for cases with sAVF, identifying 842 patients (Mean age: 58 years, 677 Men-80%). The most common clinical findings were sensory-71%, motor-60% and sphincter disturbances-31%. Myelopathy on MRI was found in 70% of patients. Surgery was the treatment of choice in 76%, while clinical improvement was established in 1/3 of the patients.
Conclusion: The diagnosis of sAVF is challenging and thus a high clinical and radiological suspicion is needed, especially among middle-aged men with LETM. Early diagnosis and minimally invasive intravascular interventions guarantee a favourable prognosis.
Disclosure: Nothing to disclose.

EPO-572

Mes-CoBraD: an open-source research platform for integrated data collection and analysis

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Background and aims: Complex brain disorders (CoBraD), as represented in Epilepsy, Neurocognitive and Sleep disorders, have high prevalence, individually and in combination, leading to disability and high socioeconomic burden. The "Multidisciplinary Expert System for the Assessment & Management of Complex Brain Disorders (MES-CoBraD)" is an international interdisciplinary project combining Real-World Data and developing a platform providing a comprehensive toolset with advanced functionalities for research and diagnosis. The main goal is to streamline and simplify the workflows of gathering, sharing and processing data, using existing mature tools, and organizing them in a common environment.
Methods: Nine Work Groups (WG) in four categories (Complex Brain Disorders, Real-World Data, Science of Science, and Socioeconomics) are working in tandem to ensure interoperability between clinical and technical requirements of the project.
Results: We structured a pilot data collection protocol including clinical history, neuroimaging, neurophysiology, neuropsychology and biomarkers (blood and hair). The platform supports data sharing by creation, sanitisation, anonymisation, harmonisation and upload of datasets on a common data-lake environment. Several open-source and tailormade tools are included, designed to address advanced research needs. The platform integrates several general statistics functions and machine learning algorithms, based on the acquired data, and used in a workflow management system, forming an expert system to support research and diagnostic processes.
Conclusion: The MES-CoBraD platform provides tools for harmonized data collection and analysis through a single unified environment. Users without significant technical experience or available computational resources will be able to share, review and analyze their data in a unified ecosystem.
Disclosure: Multidisciplinary Expert System for the Assessment and Management of Complex Brain Disorders (MES-CoBraD), is funded with a European Union's Horizon 2020 grant; ID: 965422

EPO-573

Tricky Feeding Artery in a Patient with Progressive Gait Disorder

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Background and aims: Dural arteriovenous fistulas (DAVF) are the most common type of vascular malformation of the spinal cord and may cause myelopathy through venous hypertension. The clinical evolution is slowly progressive and the diagnosis can be inferred from the Magnetic Resonance Imaging (MRI) appearance. The aim of our report is to present the case of a patient with progressive gait disorder in which DAVF was suspected.
Methods: A 62 years old patient, known with a history of back injury five years prior, was admitted for gait disorder and bilateral asymmetric lower limb weakness and paresthesia with onset in the past two years and slow progression. Spinal MRI revealed T2 bright signal enlargement of the spinal cord at the level of T9–T12 vertebrae and conus medullaris with para-medullary flow voids suggestive of venous hypertensive myelopathy. Thus, a spinal DAVF was suspected. An MR angiography of the spinal cord showed enlarged serpiginous peri-medullary vessels, as well as one enlarged vessel around left L5 nerve root. Digital subtraction angiography with selective catheterization of the internal iliac arteries was performed showing DAVF at L5-S2 level with arterial feeder originating in the right iliolumbar artery.
Results: Super-selective microcatheterization permitted endovascular occlusion of the supplying artery through injection of embolic material. Upon discharge seven days later there was marked improvement of the symptoms.
Conclusion: The feeding artery of a DAFS can be elusive and MR angiography can guide the endovascular management of such vascular malformations, which may require injection of arteries as far as internal iliac branches.
Disclosure: I make no disclosures.

Headache 4

EPO-574

Microvascular involvement in migraine: an optical coherence tomography angiography study

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Background and aims: The aim of this study was to evaluate the microvasculature of the macula and the optic nerve by optical coherence tomography angiography (OCTA) in patients affected by migraine with aura (MA) and without aura (MO), compared to healthy controls (HC).
Methods: We collected data from ocular and orthotic examinations, including eye motility, intraocular pressure, best-corrected visual acuity, objective refraction, fundus examination, macular and optic disk OCTA examination. The following OCTA parameters were recorded: macular, inside disc, peripapillary, disc whole image, fovea choriocapillaris, fovea, parafovea vessel densities (VD); peripapillary, fovea, parafovea and macular full retinal thickness, and foveal avascular zone (FAZ) parameters. Clinical and demographical data were collected.
Results: We included 56 eyes from 28 patients with a diagnosis of MO, 32 eyes from 16 patients with a diagnosis of MA, and 32 eyes from 16 HC. The FAZ area was 0.230 ±0.099 mm^2 in the MO group, 0.248±0.091 mm^2 in the MA group and 0.184±0.061 mm^2 in the control group. The FAZ area was significantly larger in the MA group than in the HC group (p=0.007). The foveal choriocapillaris VD was significantly lower in MA patients (63.6±2.49%) when compared with MO patients (65.27±3.29%) (p=0.02).

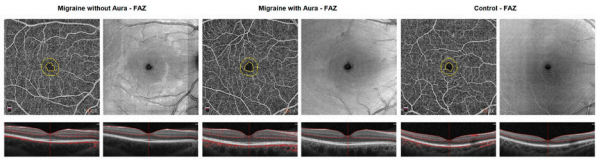

Figure 1: Representative macular optical coherence tomography angiography (OCTA) scans of migraine with aura (MA), without aura (MO), and healthy controls (HC) participants. The foveal avascular zone (FAZ) area is circled in yellow. The mean FAZ area was

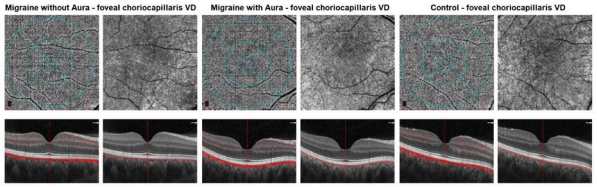

Figure 2: Representative macular optical coherence tomography angiography (OCTA) scans of migraine with aura (MA), without aura (MO), and healthy controls (HC) participants. The foveal choriocapillaris vessel density (VD) decreased in MA patients.

Conclusion: An impairment of retinal microcirculation can be detected in patients with MA, as demonstrated by the enlargement of FAZ. The study of choroid circulation may reveal microvascular damage in MA patients. OCTA is a useful non-invasive screening tool for the detection of microcirculatory disturbance in patients with migraine.
Disclosure: Nothing to disclose.

EPO-575

Neuralgias of trigeminal terminal branches in a headache unit

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Background and aims: International Classification of Headache Disorders, III Edition (ICHD-III) did not include neuralgias of trigeminal terminal branches previously considered in ICHD-II: nasociliary, supraorbital or other terminal branch neuralgias. We aim to analyse incidence and characteristics of these disorders in a headache registry.
Methods: Prospective observational study evaluating patients diagnosed as nasociliary neuralgia (code 13.5 in ICHD-2), supraorbital neuralgia (13.6) or other terminal branch neuralgias (13.7) attended in a headache unit from January-2008 to January-2023. We collected demographic and clinical data.
Results: We included 108 patients (71 females, 37 males) out of 8,728 attended in our unit during the inclusion period (1.2%). Age at onset was 47.4±18.7 years (6–89). Latency between onset and diagnosis was 34.4±68.5 months (1–420). Among the entities independently considered in ICHD-2, we diagnosed 5 nasociliary and 43 supraorbital neuralgias. Among those included among other terminal branches, most frequent neuralgia was auriculotemporal (28 cases). We also identified patients with supratrochlear (9 cases), infraorbital (8), lacrimal (8), mental (6), and infratrochlear (1) neuralgias.
Conclusion: Neuralgias of trigeminal terminal branches are not uncommon in a headache unit. Diagnostic delay observed in our series indicates a need for increasing their understanding, which, in our opinion, has not been facilitated by having been withdrawn from ICHD-3. We suggest that supraorbital and auriculotemporal neuralgias are considered independently in next editions of ICHD and that the entity "neuralgia of other terminal branches" is reintroduced.
Disclosure: No potential disclosures related to this work.

EPO-576

Head-to-head study on efficacy and safety of Monoclonal Antibodies Against Calcitonin Gene-Related Peptide for Migraine

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Background and aims: Monoclonal antibodies targeting the CGRP pathway (mAbs) have shown effectiveness, safety and tolerability in clinical trials both episodic and chronic migraine. However, there are no prospective real-world studies intending to compare their efficacy and safety. Aim of the study is to compare the effectiveness and safety of Galcanezumab, Fremanezumab and Erenumab for the treatment of chronic and episodic migraine, through real world data.

Methods: This is a prospective observational study comparing the effective and safety of Galcanezumab, Fremanezumab and Erenumab for the treatment of 140 chronic and episodic migraine patients. Framenezumab, Erenumab or Galcanezumab were administered for 12 months. The mean monthly days with headache, MIDAS score, and adverse events were evaluated during the run-in period and every three months by reviewing standardized paper patient headache diaries.

Results: We found a mean reduction of migraine monthly days from baseline of -12.152 (-9.821,-14.482) in the Galcanezumab group, -13.021 (-10.806,-15.237) in the Fremanezumab group, -11.784 (-9.440,14.127) in the Erenumab group (for all p<0.001). We found a mean reduction of MIDAS score of -33,273 (-26,857,- 39,689) in the Galcanezumab group, -36,542 (-30,563,- 42,520) in the Fremanezumab group, -31,946 (-25,631, 38,261) in the Erenumab group (for all p<0.001). We found no significant differences between mAbs in the reduction of mean monthly days with headache, and MIDAS score.

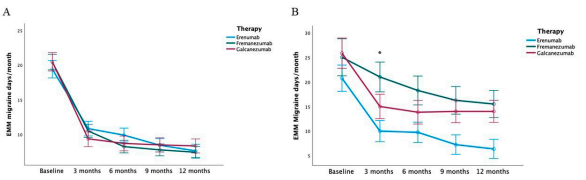

Figure 1 Monthly migraine days in Erenumab, Fremanezumab and Galcanezumab patients (A) and in Medication Overuse Headache patients (B)

	Total patients	Galcanezumab	Fremanezumab	Erenumab	P value	t/X²
Number of patients	140	41 (29.3%)	54 (38.6%)	45 (32.1)	0.630	
Age, years	42.2 ± 10.5	42.2 ± 11.7	40.9 ± 9.8	43.7 ± 10.2	0.444	0.816*
Sex						
Female	111 (79.2%)	32 (78.1%)	43 (83.3%)	34 (75.6%)	0.519	1.313*
Male	29 (20.8%)	9 (21.9%)	9 (16.7%)	11 (24.4%)		
Disease duration, years	16.8 ± 9.7	16.4 ± 9.8	17.3 ± 9.5	17.1 ± 9.9	0.9371	0.064*
Concomitant preventive treatments	63 (45.0%)	17 (41.5%)	26 (48.1%)	20 (44.4%)	0.974	0.052*
Monotherapy	47 (74.6%)	13 (76.5%)	20 (76.9%)	14 (70%)	0.984	0.386*
Polytherapy	16 (25.4%)	4 (23.5%)	6 (23.1%)	6 (30%)		
Headache diagnosis						
Chronic migraine	89 (64.0%)	27 (65.8%)	34 (63.0%)	28 (62.2%)	0.940	0.124*
Episodic migraine	51 (36.0%)	14 (34.2%)	20 (37.0%)	17 (37.8%)		
MOH	20 (14.2%)	6 (14.6%)	4 (7.4%)	10 (22.2%)	0.083	5.524*
Comorbidities	57 (40.7%)	17 (41.4%)	22 (40.7%)	18 (40.0%)	0.983	4.981*
Headache days per month	21.0 ± 8.0	21.4 ± 6.8	20.5 ± 8.0	21.1 ± 7.6	0.916	0.088*
MIDAS score	56.0 ± 20.0	57.8 ± 18.5	53.6 ± 21.6	57.2 ± 20.6	0.909	0.095*

Values are mean ± standard deviation (SD) or number (%)
* χ2 test
* t-test
MOH = medication overuse headache
MIDAS = Migraine Disability Assessment scale

Table 1 Baseline demographic and clinical characteristics

A

	3 months	6 months	9 months	12 months
Galcanezumab	- 11.184(-9.525,-13.045)*	-11.711(-9.452,-13.780)*	-12.475(-10.376,-14.585)*	-12.152(-9.821,-14.482)*
Fremanezumab	-9.593(-7.825,-11.360)*	-11.319(-9.470,-13.167)*	-12.327(-10.128,-14.524)*	-13.021(-10.806,-15.237)*
Erenumab	-7.933(-6.138,-9.709)*	-8.889(-6.850,-10.928)*	-10.850(-8.581,-13.119)*	-11.784(-9.440,-14.127)*
Total patients	-9.489(-8.448,-10.530)*	-10.708(-9.523,-11.893)*	-11.832(-10.616,-13.048)*	-12.385(-11.088,-13.681)*

B

	3 months	6 months	9 months	12 months
Galcanezumab	- 30.289(-23.284,-37.295)*	-31.974(-26.428,-37.519)*	-33.944(-28.181,-39.708)*	-33.273(-26.857,-39.689)*
Fremanezumab	-27.958(-21.158,-34.685)*	-31.095(-25.536,-36.654)*	-35.449(-29.896,-41.109)*	-36.542(-30.588,-42.520)*
Erenumab	-21.489(-16.681,-26.281)*	-25.165(-19.611,-30.714)*	-28.660(-23.138,-34.062)*	-31.946(-25.631,-38.261)*
Total patients	-25.879(-22.870,-28.888)*	-29.452(-26.235,-32.613)*	-32.040(-28.830,-35.210)*	-34.186(-30.830,-37.714)*

Values are mean (95% Confidence Interval)
* p < 0.001

Table 2 Monthly migraine days and MIDAS score reduction compared to baseline

Conclusion: Our results confirm the therapeutic benefits of anti-CGRP mAbs. There is no evidence that suggests that one antibody may be superior to the others in terms of effectiveness, both in chronic and episodic patients.

Disclosure: Cinzia Valeria Russo received personal compensation from Sanofi Genzyme and Merck Serono.

EPO-577

Anti-Calcitonin Gene-Related Peptide Monoclonal Antibodies for the Treatment of Vestibular Migraine.

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Background and aims: Vestibular Migraine (VM) is considered the most common cause of recurrent vertigo for which specific treatments are missing. Monoclonal antibodies against CGRP, are effective in preventing migraine. Since CGRP is also detected in human cochlear and vestibular organs it may also play a role in vestibular physiology.

Methods: This is a prospective observational cohort study, aiming at evaluating the efficacy of Erenumab, Framenezumab or Galcanezumab for the treatment of fifty VM patients. We assessed mean monthly days with headache and dizziness/vestibular symptoms, pain intensity and migraine-related clinical burden occurring for 18 months.

Results: Response to treatment was excellent as 90% of patients had at least a 50% reduction in vertigo frequency, 86% had at least a 50% reduction in headache frequency, and 80% a MIDAS reduction of at least 50%. Overall, 78% of patients had a concomitant reduction of all three parameters. Mean monthly days with dizziness/vestibular symptoms showed an overall significant decrease from a mean of 10.3 at baseline to 0.8 days (CI 95% 0.1, 1.5; p<0.001) after twelve months (F=27.588; p<0.001).

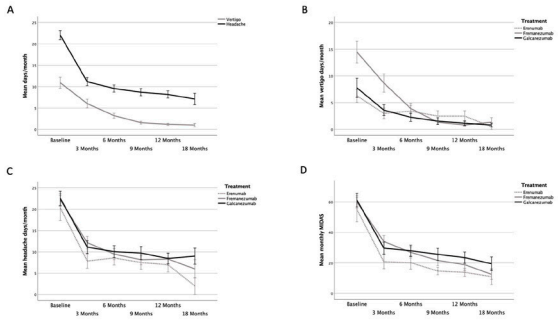

Figure 1 Mean monthly days with vestibular symptoms and headache (A) and differences in vertigo (B), headache (C) and MIDAS (D) in three different anti CGRP Mab

Patients	N = 50
Age	45.0 ± 13.3
Gender	
Famale	39 (78.0)
Male	11 (22.0)
Disease duration, years	18.7± 10.9
Concomitant oral preventive treatments	18 (36.0)
Monotherapy	13 (72.0)
Polytherapy	5 (28.0)
Previous preventive classes failure	2.3 ± 0.8
Vertigo (days per month)	10.3 ± 9.2
Headache (days per month)	20.9 ± 7.3
MIDAS	52.8 ± 19.9
Values are mean ± standard error (SE) or number (%)	
MIDAS migraine disability assessment scale	

Table 1 Demographic and baseline headache characteristics of patients

Conclusion: We show that anti-CGRP mAbs may be effective in the treatment of Vestibular Migraine. Their use should be encouraged early in the disease course to allow for a better symptom control and quality of life improvement.

Disclosure: Cinzia Valeria Russo received personal compensation from Sanofi Genzyme and Merck Serono.

EPO-578

Chasing the smoking gun without success – no evidence of cortical spreading depression in migraine without aura

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Background and aims: There is uncertainty about whether the cortical spreading depolarization (CSD) causes the migraine headache. The susceptibility weighted imaging (SWI) is the part of magnetic resonance imaging (MRI) protocol that depicts the cerebral veins and likely reflects the CSD. The aim was to assess the frequency of SWI changes in migraine without aura and compare it to migraine with aura and controls.
Methods: 300 patients were included when they (i) presented with an acute neurological deficit or headache, (ii) had a brain MRI, and (iii) had a discharge diagnosis of migraine aura, migraine without aura or controls (n=100 per group).
Results: In the migraine with aura group, SWI asymmetry was found in 26% (95%CI 18–35), significantly more than in patients with migraine without aura (3%, 95%CI 1–8, p<0.001). There was no difference between patients with migraine without aura and controls (7% (95%CI 3–14), p=0.19). After adjusting for age, sex, arterial hypertension and hyperlipidemia, the SWI asymmetry was still significantly more frequent in migraine with aura compared to pooled migraine without aura and controls (adjustedOR 6, 95%CI 1.98–19, p=0.001).
Conclusion: Our findings argue against the notion of CSD as part of the pathophysiology of migraine without aura.
Disclosure: No relevant disclosures to the abstract.

EPO-579

Weather impact on migraine: an Emergency Department retrospective study

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Background and aims: Migraine is a relapsing, remittent pleomorphic disorder characterized by recurrent attacks that may be triggered or precipitated by several factors. About half of migraineurs identified weather conditions changes as a trigger for the headache onset, or as a cause of worsening of ongoing headache symptoms. Aim of the present study was to assess the influence of some meteorological parameters on migraine attacks.
Methods: We retrospectively evaluated the clinical data of all patients with headache who presented to the Emergency Room (ER) of Policlinico Gemelli from 20th March 2010 to 20th March 2012. Primary and secondary headaches were classified according to the International Headache Society (IHS) criteria. Weather data were obtained from the Italian National Weather Service, analyzed, and correlated with clinical data, using Spearman's correlation coefficients.
Results: During the 24 months period, 1,615 patients with migraine without aura and 127 with migraine with aura were admitted to the ER. Number of emergency admissions were directly correlated with the increase of temperature compared to the previous day and the humidity level two days before the attack, and inversely correlated with the atmospheric pressure two days before.
Conclusion: Our data confirm that a subgroup of migraineurs is highly sensitive to variations of meteorological factors. We could hypothesize that any variation of weather parameters may interfere with neuronal excitability of the trigeminal-vascular system directly, or with structures to it correlated, facilitating the onset of attacks. Alternatively, it could be possible that quantitative variations of trigger factors may enhance the response of migraineurs to environmental stimuli.
Disclosure: The authors report no disclosures relevant to the manuscript.

EPO-580

Headache location and response to greater occipital nerve block – is posterior location required? A real-world study

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Background and aims: Selection criteria for greater occipital nerve block (GONB) for migraine are unclear. The present study aims to report the relationship between headache location and efficacy of GONB.
Methods: We included consecutive migraine patients treated according to clinical indication with GONB in the Headache Center of Avezzano-L'Aquila. Patients received bilateral local injections of methylprednisolone 40 mg/lidocaine 10 mg. We reported the median decrease in monthly migraine days (MMDs) and headache intensity (HI) (ranging 0–10) during the month following the first-ever GONB compared with the previous month. We performed chi-squared or Wilcoxon-Mann-Whitney tests to assess outcomes according to migraine pain location.
Results: We included 52 patients (84.6% female). Pain location was anterior (frontal/temporal) in 32 patients (61.5%), posterior (parietal/occipital) in 9 (17.3%) and diffuse in 11 (21.2%). Overall, median MMDs decreased from 20 (95% CI, 10–30) to 9 (IQR 6–20; p=0.006) while median HI decreased from 8 (IQR 7–9) to 6 (IQR 5–8; p<0.001). MMD decrease was not different in patients with anterior location (-5 median days, IQR -14 to -0.5) than in those with posterior (-2; IQR -5 to 0) or diffuse location (0 median days, IQR -1.5 to +1; p=0.164). Median HI decrease was -1.5 (IQR -3 to 0) in patients with anterior, -1 (IQR -3 to 0) in those with posterior, and -2 (IQR -3 to -1.5) in those with diffuse location (p=0.737).
Conclusion: According to our data from a limited population, the decrease in MMD and in HI after GONB is independent from pain location.
Disclosure: No disclosure to declare.

EPO-581

Infodemiology of cluster headache seasonality: A proof of concept by a Google Trends analysis

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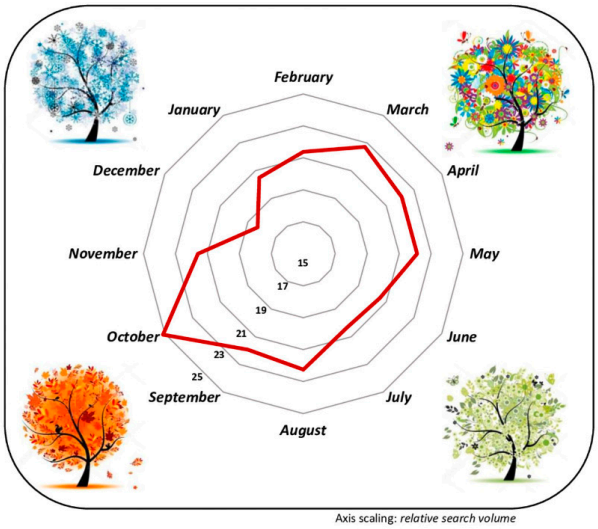
Background and aims: Cluster headache is commonly reported to follow an annual pattern with a peak in the spring and a second peak in autumn. Patients with headache frequently use search engines, such as Google, to look for terms related to their disease, creating trend data that can be analyzed with Google Trends. Indeed, Google Trends has been used for surveillance studies and can provide indirect estimates of the burden of diseases and symptoms. The present cross-sectional study investigated the seasonality of searches for "cluster headache" in the northern and southern hemispheres using 10 years of Google Trends data.
Methods: The term "cluster headache" or its translation in the 10 most spoken languages in the world was searched on Google Trends to obtain relative search volumes, in order to compare variations in searches across periods. Twentyeight countries were selected according to the following criteria: (1) a relative search volume of >40 for the term for cluster headache; and (2) a population of at least 5 million inhabitants. For statistical purposes, countries were grouped in relation to hemisphere. Relative search volumes were extracted from January 2012 to January 2022 and analyzed according to two subgroups based on meteorological seasons.
Results: A seasonal trend for in searches for cluster headache was found worldwide exhibiting higher relative search volumes in spring and autumn compared with summer and winter.



Radar chart showing the seasonality of Google Trends search volumes for the term "cluster headache," with two peaks in spring and autumn.

Term	Country	Search volume	Inhabitants
Cluster headache	United Kingdom	76	68.7 million
Cluster headache	South Africa*	69	61.0 million
Cluster headache	Australia*	68	25.8 million
Cluster headache	Philippines	62	112.9 million
Cluster headache	Nepal	61	29.9 million
Cluster headache	Canada	57	38.5 million
Cluster headache	United Arab Emirates	56	9.3 million
Cluster headache	New Zealand*	53	5.1 million
Cluster headache	Pakistan	47	230.9 million
Cluster headache	Jordan	46	10.8 million
Cluster headache	Singapore	40	5.6 million
Cluster headache	United States	40	335.4 million
Cefalea en racimos	Cuba	100	11.2 million
Cefalea en racimos	Costa Rica	59	5.1 million
Cefalea en racimos	Spain	51	46.8 million
Cefalea en racimos	Mexico	45	132.4 million
الصداع العنقودي	Saudi Arabia	100	35.8 million
Cefaleia em salvas	Brazil*	100	216.0 million
Cefaleia em salvas	Portugal	92	10.3 million
Sakit kepala cluster	Indonesia*	100	280.2 million
Sakit kepala cluster	Malaysia	52	33.3 million
Algie vasculaire de la face	France	64	65.6 million
Céphalée de Horton	Canada	100	38.5 million
Céphalée de Horton	France	87	65.6 million
Céphalée de Horton	Belgium	87	11.5 million
群発頭痛	Japan	100	125.6 million
Кластерные головные боли	Russia	100	146.0 million
Кластерные головные боли	Kazakhstan	60	19.7 million
Cluster-Kopfschmerz	Germany	100	84.3 million

Relative search volumes for the term "cluster headache" for each selected language, extracted from January 2012 to January 2022.

Conclusion: Higher search volumes for the term during the meteorological seasons of spring and autumn clearly reflect a circannual pattern of cluster headache occurrence, representing new evidence for its seasonality.
Disclosure: I have no disclosure.

EPO-582

Fremanezumab adherence & persistence along with past & concomitant migraine medication use: PEARL 3rd interim analysis

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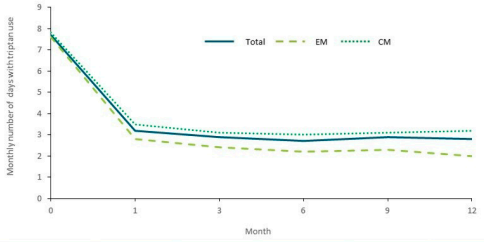
Background and aims: Suboptimal adherence to oral migraine preventive treatments is common. Consequences include patients cycling across various preventive treatments and reduced treatment effectiveness. This analysis provides real-world data on patient adherence to and persistence with fremanezumab for migraine prevention.

Methods: PEARL (EUPAS35111) is an observational, prospective, Phase IV study, evaluating the effectiveness of fremanezumab for migraine prevention in adults with episodic or chronic migraine (EM, CM). This third interim analysis was conducted when all patients had completed ≥6 months of treatment. Patient data included past-preventive and concomitant migraine medication use, fremanezumab adherence (administration within ±5 days of due date) and persistence (continued administration, unless required to discontinue) using daily headache diaries.

Results: Among 968 patients (EM, 33.1%; CM, 66.9%), the most common past-preventive migraine treatments were anticonvulsants, beta-blockers, and tricyclics (Table 1). Most patients (64.7%) used concomitant migraine medication; 51.3% used acute and 33.2% preventive - tricyclics (6.0%), beta-blockers (6.0%), and anticonvulsants (5.6%) being the most common. The mean number of days with concomitant triptan use decreased within one month of treatment and persisted over time (Figure 1). Over time, the proportion of patients receiving their fremanezumab dose within +/–5 days of their due date decreased progressively, but persistence was largely maintained (Figure 2).

Past-preventive medication class	Total use			Mean duration of use, months, n
	Total patients (N=968), n (%)	EM patients (N=320), n (%)	CM patients (N=648), n (%)	
Anticonvulsants	665 (68.7)	256 (80.0)	409 (63.1)	11.0
Beta-blockers	590 (61.0)	187 (58.4)	403 (62.2)	9.2
Tricyclics	552 (57.0)	163 (50.9)	389 (60.0)	10.0
Calcium channel blockers	371 (38.3)	168 (52.5)	203 (31.3)	6.9
Onabotulinumtoxin A	344 (35.5)	37 (11.6)	307 (47.4)	17.8
Angiotensin II receptor antagonists	149 (15.4)	10 (3.1)	139 (21.5)	9.1
Valproic acid	135 (13.9)	48 (15.0)	87 (13.4)	9.1
Erenumab	85 (8.8)	21 (6.6)	64 (9.9)	11.6
Galcanezumab	4 (0.4)	1 (0.3)	3 (0.5)	4.0

Table 1: Past-preventive medication in patients with migraine. CM, chronic migraine; EM, episodic migraine.



Total, n	968	953	893	691	475	314
EM patients, n	320	314	291	223	134	87
CM patients, n	648	639	602	468	341	227

At cut-off, not all data for this endpoint were available and missing data have been excluded. The number of patients prematurely discontinuing the study and the number of patients that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers. CM, chronic migraine; EM, episodic migraine.

Figure 1: Monthly number of days with concomitant acute migraine medication (triptans) use by migraine type.

Patients, n	897	726	508	372

Patients are classified as non-adherent if a dose of fremanezumab treatment is not taken within +/–5 days of their monthly or quarterly dosing regimen (compared to the previous injection) for at least one injection up to the relevant time-point. From the time of the first injection occurring outside the +/–5 days dosing regimen onwards, the patient is classified as non-adherent from that time-point even if the patient becomes adherent in the follow-up. At cut-off, not all data for this endpoint were available and missing data have been excluded. The number of patients prematurely discontinuing the study and the number of patients that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers.

Figure 2: Adherence to and persistence with the fremanezumab treatment schedule over Months 3, 6, 9 and 12 post-initiation.

Conclusion: The proportion of patients receiving their fremanezumab dose for migraine prevention within their ±5-day administration window decreased over time, while treatment persistence was more stable. Sustained reductions in concomitant triptan use suggest patients maintain efficacy with fremanezumab despite fluctuations in adherence (as defined in this study).

Disclosure: Funded by Teva Pharmaceuticals.

EPO-583

Impact of fremanezumab on headache intensity and duration of remaining migraine attacks: PEARL 3rd interim analysis

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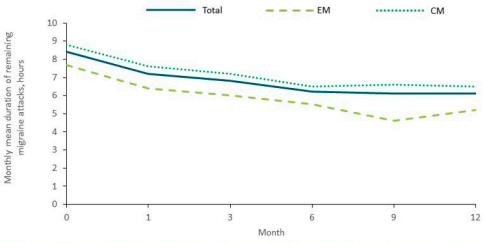
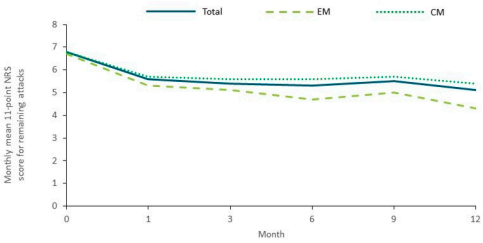
Background and aims: The duration and pain intensity of migraine attacks can directly impact patient outcomes, including quality of life and healthcare resource utilisation.
Methods: PEARL (EUPAS35111) is an observational, prospective, Phase IV study, evaluating the effectiveness of fremanezumab for migraine prevention in adults with episodic or chronic migraine (EM, CM). This third interim analysis was conducted when all enrolled patients had completed >=6 months of treatment. Daily patient headache diaries were used to record patient data, including the impact of fremanezumab initiation on monthly migraine days (MMD, primary outcome), and headache severity and duration of remaining migraine attacks over 12 months (secondary outcomes). Headache severity was measured using an 11-point Numerical Rating Scale (NRS, 0=no pain; 10=worst pain possible).
Results: The full analysis set included 968 patients (EM, 33.1%, CM, 66.9%). In patients with available data, mean MMD decreased from 14.6 days at baseline to 6.1 days at Month 12 after fremanezumab initiation. The monthly mean duration of the remaining attacks decreased from 8.4 hours at baseline to 6.1 hours at Month 12 (7.7 to 5.2 hours for EM; 8.8 to 6.5 hours for CM [Figure 1]). The monthly mean NRS score decreased from 6.8 at baseline to 5.1 at Month 12, with a similar trend in patients with EM and CM (Figure 2).



Total, n	730	650	636	468	308	193
EM patients, n	262	223	214	158	88	53
CM patients, n	468	427	422	310	220	140

At cut-off, not all data for this endpoint were available and missing data have been excluded. The number of patients prematurely discontinuing the study and the number of patients that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers. CM, chronic migraine; EM, episodic migraine.

Figure 1: Monthly mean duration of remaining migraine attacks, by migraine type.



Total, n	375	335	334	256	163	100
EM patients, n	140	116	111	82	42	31
CM patients, n	235	219	223	174	121	69

At cut-off, not all data for this endpoint were available and missing data have been excluded. The number of patients prematurely discontinuing the study and the number of patients that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers. CM, chronic migraine; EM, episodic migraine; NRS, Numerical Rating Scale.

Figure 2: Monthly mean 11-point NRS score for peak headache severity, by migraine type.

Conclusion: This analysis demonstrated that, in addition to reducing MMD, fremanezumab treatment reduced the duration and mean pain intensity of migraine attacks in patients with EM and CM.
Disclosure: Funded by Teva Pharmaceuticals.

EPO-584

Trpa1 gene polymorphism involvement in migraine pathogenesis

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Background and aims: TRPA1 expressed in trigeminal neurons are one the key receptors in migraine pain, same as TRPV1, which single nucleotide polymorphism (SNP) rs8065080, as we previously found, may serve as a potential biomarker of migraine chronification risk. Recent studies suggested that SNPs rs11988795, rs920829, rs13255063 of TRPA1 gene have a protective function against neuropathic pain. However, TRPA1 SNPs has not been tested in migraine yet. Here was evaluated the genotype frequency distribution of rs11988795, rs920829, rs13255063 in the TRPA1 gene in healthy individuals and patients with episodic (EM) and chronic migraine (CM) to test the influence of the SNPs on susceptibility to these forms of migraine.

Methods: The study included 127 patients with migraine (40 EM and 31 CM) and 56 healthy controls. DNA from peripheral blood was used to test TRPA1 SNPs using allele-specific PCR.

Results: The distribution of genotypes of the rs13255063 TRPA1 in EM and in CM differed significantly from control (p=0.003 and p=0.0002), (Table 1). Notably, both in EM and CM groups in contrast to control one, the frequency of AA genotype associated with higher pain threshold doubly decreased, while TT genotype emerged, known as a risk factor for neuropathic pain (Fig.1). Two other SNPs did not show any significant differences.

SNP, genotypes	Control n (%)	Episodic migraine, n (%)	Chronic migraine n (%)
rs11988795			
GG	20 (36)	24 (60)	15 (48)
GA	32 (57)	16 (40)	16 (52)
AA	4 (7)	0	0
rs920829			
GG	32 (57)	31 (78)	23 (74)
GA	20 (36)	9 (22)	8 (26)
AA	4 (7)	0	0
rs13255063			
AA	45 (80)	19 (48)	16 (52)
AT	11 (20)	15 (37)	11 (35)
TT	0	6 (15)	4 (13)

Table 1. Genotypes distribution of rs11988795, rs920829, rs13255063 in TRPA1 gene in the control group, episodic and chronic migraine patients

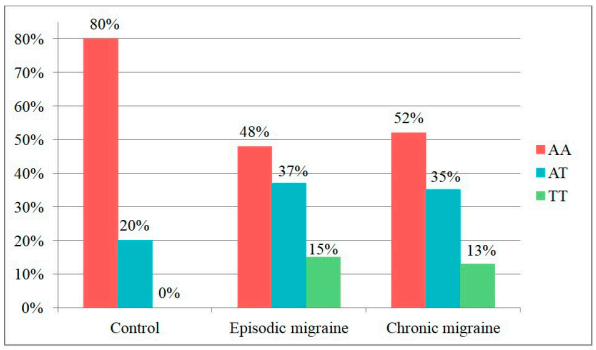

Fig. 1. TRPA1 rs13255063 genotypes distribution in the control group, episodic and chronic migraine patients

Conclusion: This study confirms an association of TRPA1 gene with migraine and indicates an involvement of TT genotype of rs13255063 in pathogenesis of disease, both in case of episodic and chronic forms.

Disclosure: This work was supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030).

EPO-585

Pain-modulation system in patients with episodic migraine and medication overuse headache: offset analgesia paradigm

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Background and aims: The offset analgesia (OA) phenomenon refers to the disproportionately large decrease in the perceived pain following a slight decrease in intensity of a noxious warm stimulus, as expression of activation of the endogenous pain-modulation system, whose dysfunction is supposed to be involved in the pathophysiology of migraine and medication overuse headache (MOH). Aim of this study was to investigate pain processing mechanisms in patients with episodic migraine (assessed during the different phases of the migraine cycle) and MOH by using the OA paradigm,

Methods: 40 patients with episodic migraine, 10 patients with MOH, and 15 healthy control subjects were enrolled. All subjects underwent an experimental paradigm (3 stimulus offset trials and 3 constant temperature trials based on the individual heat pain threshold). Both the trigeminal area (supraorbital region) and an extratrigeminal site (ipsilateral hand) were tested.

Results: An absent OA phenomenon was observed in patients with MOH when testing the trigeminal area. No significant differences in the OA phenomenon were observed between patients with episodic migraine. Group comparisons during the constant trial showed a significant difference between episodic migraine patients evaluated in the interictal vs peri-ictal phase: marked habituation to the stimulus was observed only in patients in the ictal and pre-ictal phase.

Conclusion: A dysfunction in the endogenous pain-modulation system could play a pathophysiological role in patients with MOH. Changes in habituation and sensitization phenomena in response to thermal stimuli were also observed throughout the migraine cycle, suggesting a complex interplay between different aspects of painful sensations processing in migraine.

Disclosure: Nothing to disclose.

EPO-586

Effectiveness And Safety Of Monthly Versus Quarterly Fremanezumab For Migraine Prevention: A Real-Life Pilot Study

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Background and aims: Fremanezumab, an anti-CGRP monoclonal antibody, is available in two dosing options for migraine prevention: 225 mg monthly and 675 mg quarterly. This study aimed to compare the effectiveness and safety of monthly versus quarterly fremanezumab in a real-life setting.

Methods: 48 migraine patients were prospectively enrolled. All participants completed a three-month treatment period, receiving fremanezumab monthly or quarterly (25 versus 23, respectively); 44 completed a six-month treatment period (26 versus 18). Two patients switched from quarterly to monthly fremanezumab after three months. Demographic data were collected at baseline. Clinical variables, including monthly headache days (MHD) and migraine days (MMD), monthly acute medication days (AMD) and pills (AMP), headache intensity on NRS, HIT-6, and MIDAS scores were recorded at baseline and after three (M3) and six (M6) months of treatment. Adverse events (AEs) were also investigated at M3 and M6. Within and between-group differences in treatment effectiveness were assessed at M3 and M6 using Wilcoxon and mixed-effect ANOVA tests.

Results: After 3 months of treatment as well as after 6 months, both groups had a significant reduction of MHD, MMD, AMP, AMD, NRS, HIT-6 and MIDAS scores. AEs were reported by three patients of the quarterly group at M3 and by one patient of the monthly group at M6. Between-group differences in clinical outcomes at each time-point were not statistically significant.

Conclusion: Both monthly and quarterly fremanezumab resulted to be effective for migraine prevention; no significant difference between the two dose regimens emerged. Also, a similar safety profile was observed.

Disclosure: The authors declare no competing interests.

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EPO-587

Light sensitivity in myasthenia gravis: frequency, clinical characteristics and impact on the quality of life

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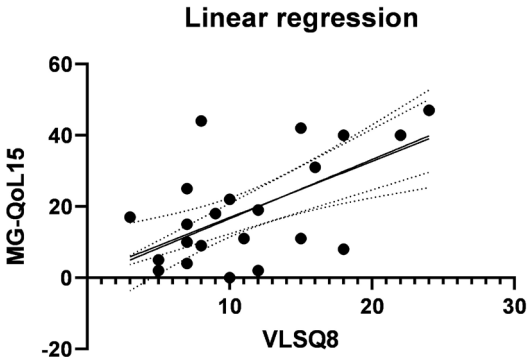
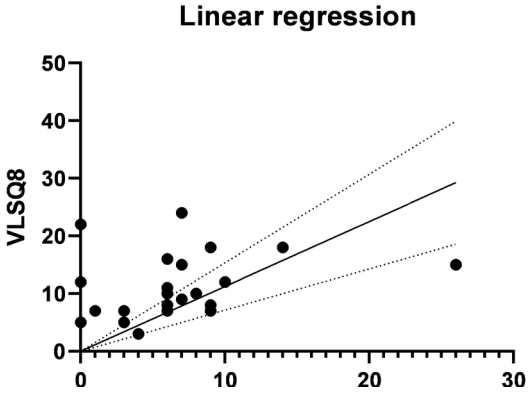
Background and aims: Dysfunction of extraocular muscles is common in myasthenia gravis (MG) and most patients develop ptosis and/or diplopia during the disease course. Light sensitivity (LS) (a.k.a. photophobia) is a frequently reported symptom among patients with MG, but it has not been thoroughly investigated. The aim of this study was to assess the frequency, the clinical characteristics and the impact on the quality of life of LS in MG patients.
Methods: In this prospective observational study, we enrolled patients with diagnosis of MG, consecutively admitted at the Fondazione Policlinico Universitario A. Gemelli in Rome from December 2021 to December 2022. Inclusion criteria were age ≥18 years, diagnosis of MG with Acetylcholine Receptor antibodies and ocular involvement. Exclusion criteria were migraine, ophthalmological and psychiatric comorbidities. The severity of LS was assessed by the Visual light sensitivity Questionnaire-8 (VLSQ-8). Each patient with MG was evaluated with the QMG, MG-ADL and MG-QoL-15 scales.
Results: 59 patients with MG (males=40, 67.7%) and 50 healthy subjects (males=24, 48 %) were recruited. The frequency of photophobia was higher in MG patients (23/59, 38.9%), compared with controls (0, 0%) ($p<0.0001$). Linear regression analysis showed that the severity of LS of MG patients was associated with a lower health-related quality of life and a more severe disease as assessed by both MG-ADL ($p<0,0001$) and QMG scores ($p<0,0001$).





Conclusion: LS represents a frequent and disabling symptom of MG, it has an impact on the quality of life of patients. The cause of LS in MG warrants further investigation.
Disclosure: The authors declare tey have no relevant or material financial interests that relate to the research.

EPO-588

Detection of Potential Pathogenicity of Glutamate Decarboxylase Antibodies in Patients with Stiff Person Syndrome

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Background and aims: Stiff-person syndrome (SPS) is a rare autoimmune disease characterized by painful spasms and rigidity. Antibodies (abs) to the intraneural enzyme glutamate decarboxylase (GAD) are most frequently found in SPS. Their pathogenic significance is discussed controversially. If GAD abs are pathogenic, they should reach their intracellularly located antigen. With the following experiments, we investigated whether GAD abs can be internalized in GAD65 transfected HEK293 cells.

Methods: We performed internalization assays on fixed HEK293 cells. HEK293 cells were transfected with plasmids containing GFP-tagged GAD65-DNA, incubated with commercial GAD abs, fixed with 4% formaldehyde and permeabilized with triton X-100. After incubation with secondary antibodies, fluorescence signals were detected. We then performed internalization assays on living HEK293 cells without fixation. Instead, living HEK293 cells were pre-treated with chloroquine to influence membrane permeability.

Results: An average of 31±0.8 % of the HEK293 cells were successfully transfected. We then quantified the colocalization of GAD-DNA and GAD abs of the overall GAD plasmid transfection rate: In fixed HEK293 cells, the colocalization rate was 11%, and 37% when permeabilized with triton. In living HEK293 cells, GAD abs were internalized into 21% of cells with, and in 0% of cells without chloroquine pre-treatment.

Conclusion: GAD abs were only internalized and reacted with GAD65 in fixated and permeabilized cells but not in living, untreated cells. Further investigations are necessary to find out whether GAD abs can be internalized into live neurons and linked to the impairment of GAD and GABAergic neurons to provide more effective therapeutic approaches.

Disclosure: No conflict of interest.

EPO-589

Use of fluid biomarkers in ongoing Clinical Trials on Multiple Sclerosis (MS)

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Background and aims: The present study aimed to describe the state of art of fluid biomarkers use in ongoing MS clinical trials.

Methods: A review of 600 ongoing protocols in the clinicaltrials.gov database was performed. The trials enrolled subjects with a diagnosis of RRMS, SPMS and/or PPMS according to Revised McDonald Criteria 2017 or RMS according to Lublin et al. 2014. The presence of CSF (c) or blood (b), either plasma (p) or serum (s), biomarkers among the primary and/or secondary study outcomes was assessed.

Results: Overall, 5% of ongoing studies on MS adopted CSF or blood biomarkers. They were mostly adopted as secondary outcomes in phase 3–4 clinical trials to support the potential disease modifying properties of the intervention. Most studies evaluated sNfL, some considered pNfL or cNfL. A small number considered novel biomarkers of neuroinflammation and neurodegeneration as sGFAP/cGFAP, bIL-6, sChi3L1, and/or inflammatory biomarkers: sVCAM, sMAdCAM, sCXCL13.

N.	PATIENTS NUMBER	PHASE	MOLECULE	AGE	DIAGNOSIS	EDSS	MAIN CRITERIA	DIAGNOSTIC CRITERIA	PRIMARY OUTCOME	SECONDARY OUTCOME	NAME
1	44	1	METFORMINE	30-65	PPMS SPMS	0-9.5	stable in the last 6 months	McDonald 2017	-	NfL levels at baseline and after 12 months	
2	150	1-2	IMCY-0141 vs DIMETHYLFUMARATE vs PLACEBO	18-45	RRMS	0-5	treatment naive disease duration ≤ 3 years	McDonald 2017	-	sNfL at baseline and after weeks 2, 4, 6, 8, 10, 12, 24 and 36.	IMCY-MS-001
3	200	3	RITUXIMAB 500mg /6 months vs. RITUXIMAB 500mg /12 months	20-52	RRMS CIS	0-5,5	completed the RIFUND-MS trial	McDonald 2017	-	mean change of sNfL concentration between the two dosing arms	RIDOSE-MS
4	168	2	SAR443820 vs PLACEBO	18-60	MS	2-6	untreated/stable patients	McDonald 2017	sNfL levels at 48, 96 weeks		-
5	264	3	RITUXIMAB vs MAVENCLAD	18-65	RRMS		disease activity in the last 12 months	McDonald 2017	-	sGFAP at week -1, 51 and 96 weeks sNfL at week -1, 51 and 96 weeks	NOR-MS
6	865	3	OCRELIZUMAB 1200/1800 mg /24 weeks vs OCRELIZUMAB 600 mg /24 weeks	18-55	RRMS, aSPMS	0- 5.5	≥2 clinical relapses within the last 2 years or ≥1clinical relapse in the last year no relapse 30 days prior to screening	McDonald 2017	-	bNfL from baseline up to 4.3 years bIL-6 from baseline up to 4.3 years	-
7	800	3	REMIBRUTINIB vs TERIFLUNOMIDE	18-55	RRMS	0-5.5	≥1 relapse within the previous year or ≥2 relapses within the previous 2 years neurologically stable within 1 month	McDonald 2017	-	sNfL levels from baselineand up to years	-
8	699	3	OCRELIZUMAB 1200/1800 mg /24 weeks vs OCRELIZUMAB 600 mg /24 weeks	18-55	PPMS	0-5.5	neurologically stable within 1 month	McDonald 2017	-	bNfL from baseline up to 4.3 years bIL-6 from baseline up to 4.3 years	-
9	180	3	OFATUMUMAB vs FINGOLIMOD vs SIPONIMOD	10-17	RRMS	0-5.5	≥1 relapse within the previous year or ≥2 relapses within the previous 2 years	McDonald 2017	-	sNfL at day 1, and after 3,6,12,18,24 months	-
10	200	3	CLADIBRINE vs. PLACEBO	> 18	AMS	6.5-8.5	deterioration of upper limb function in the 2 years previous baseline no relapse within 6 months	McDonald 2017	-	sNFL at baseline, 6 and 24 months association between sNFL and memory B count and upper limb function	ChariotMS

Description of selected clinical trials in which fluid biomarkers were evaluated as primary or secondary outcome (part 1).

N.	PATIENTS NUMBER	PHASE	MOLECULE	AGE	DIAGNOSIS	EDSS	MAIN CRITERIA	DIAGNOSTIC CRITERIA	PRIMARY OUTCOME	SECONDARY OUTCOME	NAME
11	900	3	TOLEBRUTINIB vs TERIFLUNOMIDE	18-55	RRMS	0 - 5.5	≥1 relapse within the previous year or ≥2 relapses within the previous 2 years	McDonald 2017	-	pNFL from baseline and after 36 months sChi3L1 from baseline and after 36 months	GEMINI 1 e 2
12	10	3	OFATUMUMAB	18-60	RRMS	0 -5.5	≥1 relapse within the previous year or ≥2 relapses within the previous 2 years	McDonald 2017	-	sGFAP at 5, 28 90, 273 days and correlation with microglial activity sNFL at 5, 28 90, 273 days and correlation with microglial activity	-
13	736	3	FENEBRUTINIB vs TERIFLUNOMIDE	18-55	RRMS	0 -5.5	-	McDonald 2017	-	sNfL from baseline and after 48 weeks	FENhance
14	50	4	CLADRIBINE	18-65	RRMS	0 -5.5	at least 1 relapse or 1 GD or 1 new or enlarged T2 lesion in the last 12 months	McDonald 2017	-	cNfL at 5 weeks, 10 weeks, 1 year, or 2 years	CLOCK-MS
15	3526	4	RITUXIMAB vs other DMTs	> 18	CIS RRMS	0-9.5	treatment naive or second DMTof a different class	McDonald 2017	-	sNFL at baseline, 3, and 9 years	COMBAT-MS
16	296	4	B-cell tailored OCRELIZUMAB vs standard OCRELIZUMAB	18-60	RRMS	0-6.5	treatment with ocrelizumab for a minimum of 48 weeks	McDonald 2017	-	sNFL at baseline and 96 weeks	BLOOMS
17	234	3	OCRELIZUMAB SC vs OCRELIZUMAB IV	18-65	RRMS PPMS	0-6.5	neurological stability for ≥30 days	McDonald 2017	-	sNfL at day 1, weeks 12, 24, 48	Ocarina II
18	990	3	TOLEBRUTINIB vs PLACEBO	18-55	PPMS	2-6.5	disease duration <15 years if EDSS >5.0 or <10 years if EDSS≤5.0. CSF OB + and/or elevated IgG index	McDonald 2017	-	pNfL from baseline up to 48 months pChi3L1 from baseline up to 48 months	PERSEUS
19	1290	3	TOLEBRUTINIB vs PLACEBO	18-60	SPMS	3-6.5	documented disability progression within 12 months no clinical relapses for at least 24 months	McDonald 2017	-	pNfL from baseline up to 48 months pChi3L1 from baseline up to 48 months	HERCULES
20	2060	3	OFATUMUMAB	18-100	RRMS	0-9.5	completed a selected Novartis MS study which dosed ofatumumab every 4 weeks	McDonald 2017	-	sNfL from baseline up to 5 years	ALITHIOS
21	156	3	AHSCT vs. BMT	18-55	RRMS SPMS	0-6	≥ 2 episodes of disease activity in the 36 months prior ≥ 1 episode of disease activity must occur following ≥ 1 month of treatment with an oral DMT	McDonald 2017	-	sNfL from baseline up to 72 months	BEAT-MS

Description of selected clinical trials in which fluid biomarkers were evaluated as primary or secondary outcomes (part 2).

N.	PATIENTS NUMBER	PHASE	MOLECULE	AGE	DIAGNOSIS	EDSS	MAIN CRITERIA	DIAGNOSTIC CRITERIA	PRIMARY OUTCOME	SECONDARY OUTCOME	NAME
22	594	3	RITUXIMAB vs OCRELIZUMAB	18-65	MS	0-6.5	treatment naive RRMS or previously treated RRMS or PMS patients with clinical/radiological activity in the last year for PMS also s/cNfL elevation considered	McDonald 2017	-	sNfL from baseline up to month 24	DanNORMS
23	898	3	EVOBRUTINIB vs TERIFLUNOMIDE	18-55	RMS	0-5.5	≥1 documented relapses within the 2 years before screening	McDonald 2017	-	sNfL at baseline and after 12 weeks	EvolutionRMS 1 e 2
24	132	3	OCRELIZUMAB	18-55	RMS	0-5.5	documented relapse in the past year	McDonald 2010	cNfL at baseline and after 12, 24, 52, 144, or 240 weeks	-	
25					PPMS	3-6.5	elevated IgG index or OCBs		-	cNfL in CSF baseline and after 12, 24, 52, 144, or 240 weeks	
26	30	4	CLADRIBINE	21-65	SPMS	2-7	neurologically stable for > 30 days prior	Lublin 2014	s/c NfL values from pre-treatment to week 48	cGFAP from baseline up to 96 weeks cNfL and sNfL antibody baseline and 96	-
27	45	4	CLADRIBINE after antiCD20 vs. antiCD20	> 18	RMS	0-7	treatment with antiCD20 for ≥18 months	Lublin 2014	-	changes in sNfL from baseline to 12 months	-
28	150	4	OFATUMUMAB after DMT vs. DMT	18-50	RRMS	0-5.5	on a DMT for at least 6 months no relapse reported within 6 months	McDonald 2017	-	% of participants with baseline NfL≥10pg/ml and NfL<10pg/ml achieving NEDA-3	SOSTOS
29	10	4	interruption of NATALIZUMAB vs. maintenance of NATALIZUMAB	21-65	RRMS	0-9.5	clinically stable with pre-planned annual dose interruption of 2 consecutive doses	McDonald 2017	b/c NfL at interruption and after 6 months	sVCAM sMAdCAM at interruption and after 6 months	-
30	15	4	CLADRIBINE	45-55	RRMS	0-9.5	N	McDonald 2017	-	sNfL at baseline and 18 months sGFAP at baseline and 18 months	CLADPET
31	100	4	OCRELIZUMAB	18-40	RIS	0	diagnosis established within last 5 years	McDonald 2017	-	sNfL baseline and after 24, 48, 72, 104, 130, 156, 182, 208 weeks	CELLO
32	50	1-2	MELATONIN + OCRELIZUMAB vs. OCRELIZUMAB alone	18-65	PPMS	2-7	no immunomodulatory treatment in the prior 9 months no melatonin during the month prior to participation	McDonald 2010	-	sCXCL13 at baseline and after 48 weeks aNfL at baseline and after 48 weeks	-

Description of selected clinical trials in which fluid biomarkers were evaluated as primary or secondary outcomes (part 3).

Conclusion: Considering the numerous ongoing clinical trials in MS, still a small number considers fluid biomarkers as outcome measures, thus testifying the distance from clinical practice. Fluid biomarkers were prevalently considered in studies evaluating the effectiveness of approved second line therapies. Almost all clinical trials evaluating new drugs, particularly BTK-inhibitors considered fluid biomarkers, suggesting a future clinical utility in assessing the effectiveness of these treatments. Nevertheless, the cost-effectiveness in the "real word" remains to be clarified. NfLs have been also used to monitor disease progression after natalizumab suspension in stable patients, cladribine efficacy after anti-CD20 discontinuation, and the efficacy of AHSCT compared to medical treatment.
Disclosure: Nothing to disclose.

EPO-590

Anti-adenylate kinase-5 autoimmune encephalitis - the important role of clinical suspicion

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Background and aims: Anti-adenylate kinase-5 (anti-AK5) encephalitis is a recently described non-paraneoplastic autoimmune limbic encephalitis, characterized by severe amnesia, psychiatric symptoms, and rarely seizures. It is poorly responsive to immunotherapy.
Methods: Clinical case description.
Results: A healthy 72-year-old man presented with a two-week history of progressive confusion and disorientation. Neurological examination revealed severe anterograde amnestic syndrome with marked short-term memory impairment. Brain MRI showed bilateral temporal lobe T2/FLAIR hyperintensities, relatively symmetric, with heterogeneous contrast-enhancement (Figure 1). EEG showed diffuse slow-wave activity, without epileptiform activity. CSF evaluation revealed five nucleated cells, hyperproteinorrachia, and intrathecal oligoclonal band synthesis; bacteriological and virological analysis were negative. Routine panels of CSF/serum antineuronal antibodies were negative. There was no evidence of malignant neoplasm or autoimmune comorbidities. Considering the diagnosis of autoimmune encephalitis, the patient was started on IV corticosteroid, followed by IV immunoglobulin. Despite initial improvement, there was clinical and imagiologic worsening six weeks later. Since imagiological and clinical features were compatible with anti-AK5 encephalitis, immunofluorescence antibody studies were reviewed and a pattern suggestive of anti-AK5 antibodies was identified in rat tissue (Figure 2). Anti-AK5 antibodies in CSF and serum were later confirmed by immunoblot. Despite treatment with plasmapheresis and rituximab, severe memory impairment persisted. Brain lesions evolved to mesio-temporal atrophy.

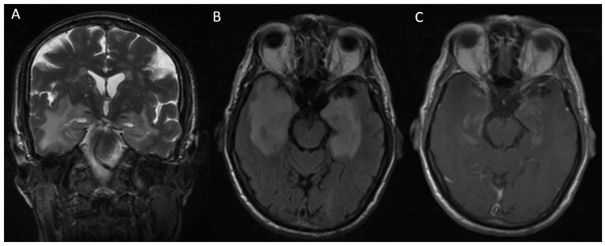

Fig. 1 Coronal T2 (A) and axial FLAIR (B) brain MRI showing bilateral hyperintense medial temporal lobes, and axial T1 brain MRI with gadolinium (C) showing bilateral heterogeneous contrast enhancement.

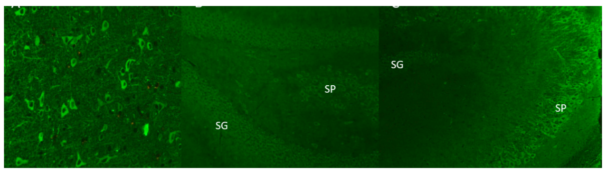

Fig. 2 Indirect immunofluorescence, serum sample. (A) Monkey cerebrum - cytoplasmic positivity of cortex neural (x400) (B, C) Rat hipocamppus, immunofluorescence localized to the granular neurons of the dentate gyrus (SG) and pyramidal cells (SP) (x100).

Conclusion: We report a new case of anti-AK5 encephalitis with the typical clinical course of severe subacute amnestic syndrome. We want to emphasize the importance of expanding antibodies' investigation in presumed autoimmune encephalitis, particularly for the detection of recently described antibodies that might be absent from routine panels.
Disclosure: Nothing to disclose.

EPO-591

Anti-DPPX encephalitis: clinical characterization and outcome of 11 new patients

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Background and aims: Anti-dipeptidyl-peptidase-like protein-6 (DPPX) encephalitis was first described in 2013 and, since then, only 65 cases have been reported. We aimed to characterize a new series of patients with anti-DDPX encephalitis from a clinical and outcome perspective.
Methods: Retrospective nationwide study of patients tested positive for anti-DPPX antibodies in the French referral centre.
Results: Of 11 identified patients, 7(63%) fulfilled the typical triad of weight loss, cognitive impairment and hyperexcitability. Additionally, 9(82%) had cerebellar involvement, 3(27%) diarrhea, 7(64%) mood disorders, 3(27%) brainstem involvement, 3(27%) sleep disorders and 2(18%) dysautonomia (Figure 1). 5(45%) cases had an abnormal brain MRI, mainly cerebellar atrophy (3/5, 60%). CSF analysis revealed pleocytosis in 2(18%), high protein levels in 4(36%) and positive oligoclonal bands in 6/8(75%). All patients except a recent diagnosis (10/11, 91%) were treated with immunotherapy: 8(72%) patients received first line immunotherapy (IT) (median delay from onset 18 months, range 2–180) and 8(72%) received second line IT (median delay from onset 15 mohs, range 8–181). Four patients (36%) experienced relapsntes during follow-up. Figure 2 depicts the evolution of the modified Rankin score (mRS) of 10 patients with disability information between onset and last visit. Improvement of at least one mRS point was observed in 4/10(40%) and stabilization in 3/10(30%) patients. The median follow-up was 45 months (2-219).

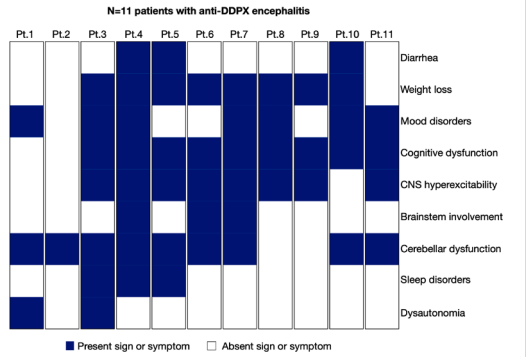

Figure 1. Distribution of signs and symptoms in the cohort of patients with anti-DPPX encephalitis.

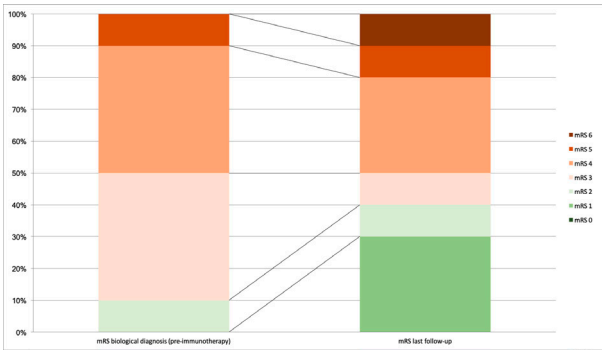

Figure 2. Evolution of the modified Rankin score from neurological onset to last visit.

Conclusion: Anti-DPPX encephalitis recognition is crucial as we observed that, even in cases of delayed administration, most patients improved or stabilized following immunotherapy.
Disclosure: Macarena Villagrán-García received a research fellowship grant from the Spanish Foundation Alfonso Martín Escudero.

EPO-592

Therapeutic Plasma Exchange and Double Filtration Plasmapheresis in neuroimmune diseases as the first treatment option

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Background and aims: Therapeutic plasma exchange (TPE) and double filtration plasmapheresis (DFPP) are therapeutic modalities that are used in the management of severe neuroimmune disorders. High-dose intravenous immunoglobulins is an alternative treatment for these patients but it's significantly more expensive. The American Society for Apheresis accepted TPE as first line treatment for some severe neuroimmune conditions, like: acute Guillain-Barre Syndrome, Myasthenia Gravis and chronic inflammatory demyelinating polyneuropathy.
Methods: We reviewed medical records of 82 patients with severe autoimmune neurological diseases requiring TPE or DFPP, treated in our hospital during a 4-year period (from 2019 to 2022). We analysed the efficacy, side effects and complications of these procedures on specific scales.
Results: The prevalent neuroimmune conditions treated in our centre, were: Guillain-Barre Syndrome (47%), Myasthenia Gravis (25%), neuromyelitis optica (5%) and chronic inflammatory demyelinating polyradiculoneuropathy (5%). The mean number of TPE sessions/patient and DFPP sessions/patient was 3.8 (range 3–5) and 2.5 (range 2–4), respectively. The most common systemic complications of plasma exchange were: dyselectrolytemia (48% of patients), hypocalcemia (38% of patients), and hypotension (8% of patients). Infection/sepsis, produced by prolonged immobilization, developed in 20% patients. These systemic complications were completely reversible. No mortality was directly generated by these therapeutic procedures. After completing the plasma exchange sessions, 80% of the patients had clinical neurological improvement, 20% had no improvement.
Conclusion: Based on the results of our center, we conclude that plasmapheresis represents a first option in the treatment of autoimmune diseases, being a relatively safe procedure with mild complications and good clinical outcome.
Disclosure: Nothing to disclose.

EPO-593

Quality of Life in patients with Susac Syndrome – Identifying themes and pitfalls

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Background and aims: Susac syndrome (SuS) is a neuroimmunological disease characterized by encephalopathy, hearing impairment and visual disturbances. This may have an impact on the patients' quality of life (QoL). To date, no studies have investigated QoL in SuS. This study aims to investigate generic and disease specific QoL and to map disease related themes in patients with SuS.
Methods: 10 patients (3 men, 7 women, average age 38 years) were recruited via the Neurology department of the Antwerp University Hospital. After obtaining written informed consent, patients filled in two questionnaires: EQ-5D-5L and NeuroQoL. Results were analysed using a t-test. Patient's experiences during daily life were explored in a semi-structured interview to identify relevant themes. Questionnaires and interviews were triangulated within the epistemological concept of pragmatism.
Results: Preliminary results show that responses from the questionnaires were comparable to the general population (EQ-5D-5L) and were less severe than the average response in a neurological population (NeuroQoL). The following themes were influential: Emotional Health, Social Network and relatives, Financial burden, Impact on activities, Symptoms and Treatment.
Conclusion: SuS has a considerable impact on the patient and their environment during the diagnosis phase, the follow-up and in case of relapse. Triangulation shows that the included questionnaires underestimate the burden placed upon these patients. Improving QoL may be possible via interventions focusing on the aforementioned themes.
Disclosure: No specific conflicts of interest to disclose.

EPO-594

Extracellular vesicles from Peripheral B cells may contribute to pathogenesis and be a biomarker of Multiple Sclerosis.

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Background and aims: To investigate whether extracellular vesicles (EVs) mediate exchange of myelin autoreactive antibodies from peripheral B cells to the CNS and analyze whether myelin antibodies could act as diagnostic biomarker in MS.
Methods: Circulating B cell-derived EVs from blood and cerebrospinal fluid (CSF) of MS patients were isolated by precipitation and immunoisolation, their anti-myelin antibody content was analyzed by Elisa. The effect of circulating EV-derived autoantibodies on demyelination was studied in vitro. Whether myelin antibodies carried EV reach oligodendrocytes in patients was also evaluated. Influence of disease activity and disease-modifying therapies in the content of antibodies in blood B cell-derived EVs of MS patients was examined.
Results: This study enrolled 136 MS patients and 39 healthy controls. EV-autoreactive myelin antibodies released by peripheral B cells were identified in the blood of MS patients, but not in the CSF. We also have identified a cut-off value of 3.95 ng/ml of MBP autoantibodies in EVs derived from blood peripheral B cells with a 95.2% sensitivity and 88.2% specificity which allow to differentiate MS patients from healthy controls. These myelin antibody-loaded vesicles induced demyelination in oligodendrocytes in vitro. EV-derived myelin antibodies were found in oligodendrocytes from MS patients. Disease activity nor disease-modifying therapies did not affect the antibody content in blood peripheral B cells-derived EVs of MS patients.
Conclusion: Blood peripheral reactive immune cells could contribute in remote to the pathogenesis of MS by using EVs as antibody delivery nano-system. Furthermore, EV-derived myelin antibodies could have a role as minimally invasive diagnostic biomarker in MS.
Disclosure: This work was sponsored by the FIS PI21/00918 project from the Spanish Ministry of Health—Carlos III Health Institute (ISCIII) and the European Regional Development Fund (FEDER Funding), Miguel Servet (CP20/00024 to Laura Otero-Ortega) Miguel Servet (CPII20/00002 to María Gutiérrez-Fernández), a predoctoral fellowship (FI17/00188 to Mari Carmen Gómez-de Frutos; FI18/00026 to Fernando Laso-García), a Río Hortega (CM20/00047 to Elisa Alonso-López) from the Carlos III Health Institute Health Care Research Fund and was co-funded by the European Regional Development Fund (ERDF).The authors declare that they have no competing interests.

EPO-595

Neural and lymphocyte-derived extracellular vesicles as biomarkers for treatment response in Multiple Sclerosis.

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Background and aims: The benefit of each disease modifying treatment (DMTs) for individual patients in MS is unknown, which makes clinical decision-making a complex process. Previous studies of our group showed that DMTs alter circulating Extracellular Vesicles (EVs) in MS patients. Here, we aim to investigate whether circulating EVs could show potential for therapeutic response monitoring in MS treated patients.
Methods: EVs specifically derived from neurons, oligodendrocytes, B and T lymphocytes were isolated from blood of 36 MS patients before DMT initiation and after 3 months. Over the course of 12 months, treatment response was monitored by: 1) disease activity by clinical relapses and new lesions in magnetic resonance; 2) motor and cognitive progression independent of relapse activity (PIRA) 3) relapse-associated worsening (RAW). Motor and cognitive progression was measured using the Expanded Disability Status Scale (EDSS) and symbol digit and 9-hole peg test (9HPT).
Results: Patients with no evidence of disease activity (NEDA) showed higher size of B cell-derived EVs compared to those with activity of disease (p=0.015). Analyzing motor progression, patients with EDSS-associated RAW showed lower levels of B cell-derived EVs (p=0.05) and patients with 9HPT-associated PIRA had smaller size oligodendrocyte-derived EVs (p=0.001). Patients showing cognitive progression had lower levels of T cell-derived EVs (p=0.018). While bigger size B-cell derived EVs were found in patients cognitive PIRA (p=0.041), smaller B-cell derived EVs were associated to those patients with cognitive RAW (p=0.028).
Conclusion: Circulating EVs derived from oligodendrocyte, B and T cells may play an important role as biomarkers for treatment response in MS patients.
Disclosure: This work was sponsored by the FIS PI21/00918 project from the Spanish Ministry of Health—Carlos III Health Institute (ISCIII) and the European Regional Development Fund (FEDER Funding), Miguel Servet (CP20/00024 to Laura OteroOrtega) Miguel Servet (CPII20/00002 to María Gutiérrez-Fernández), a predoctoral fellowship (FI17/00188 to Mari Carmen Gómez-de Frutos; FI18/00026 to Fernando Laso-García) from the Carlos III Health Institute Health Care Research Fund and was co-funded by the European Regional Development Fund (ERDF). The authors declare that they have no competing interests

EPO-596

Neuropathological findings in CASPR2-encephalitis. Report of 2 cases.

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Background and aims: Antibodies against contactin-associated protein-like 2 (CASPR2) are associated with phenotypically heterogeneous autoimmune encephalitis. Detailed neuropathological studies have been reported in only two patients, and in one of them, the findings were unclear due to severe hypoxic changes.
Methods: We describe the neuropathological findings of two patients with CASPR2-encephalitis who died at 3 months and 3 years from disease onset, respectively. Antibodies were determined by immunohistochemistry and in-house cell-based assays in a reference laboratory.
Results: Patient 1: a 48-year-old male developed Morvan's syndrome progressing over 3 months. Both CASPR2 and LGI1 antibodies were found in serum and CSF, and brain MRI showed bilateral mesotemporal abnormalities. Despite immunotherapy with methylprednisolone and IVIg, the patient died of cardiac arrest in the context of severe dysautonomia. Autopsy revealed a malignant thymoma and pontine and cortical tauopathy involving neurons and astrocytes, without overt inflammatory changes. Patient 2: a 68-year-old man with cardiomyopathy, developed rapidly progressive short-term memory deficits. CSF and MRI studies were unremarkable except for the presence of CASPR2 in CSF and serum. Steroids led to transient cognitive improvement, followed by clinical fluctuations that ultimately stabilized for 2 years under rituximab treatment. He died from heart failure, and the autopsy revealed selective atrophy in hippocampal CA1, without inflammatory infiltrates, and stage III of argyrophilic grain disease in mesotemporal regions.
Conclusion: Neuropathological findings in these 2 different stages of CASPR2-encephalitis do not reveal prominent inflammatory changes. In contrast, different patterns of tauopathy were found. Whether these findings are causally related or purely coincidental remains unknown.
Disclosure: Nothing to disclose.

EPO-597

Hu-antibodies autoimmunity in patients without detectable cancer

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Background and aims: Anti-Hu paraneoplastic neurological syndromes are almost invariably associated to lung cancer. However, up to 3% of cases may present without an underlying malignancy. We aimed to characterize this non-paraneoplastic subset in a cohort of anti-Hu patients.
Methods: Retrospective nationwide study of patients tested positive for Hu-antibodies in the French Reference Centre.
Results: Among 466 included patients, 54 (12%) had a previously known cancer at the onset of neurological symptoms, 295 (63%) had a subsequent oncological diagnosis, 84 (18%) did not but had less than 2 years follow-up and 33/466 (7%) remained cancer-free 2 years after onset (Figure 1). We compared 295 patients developing a proved cancer versus 33 cancer-free patients after 2 years follow-up. Cancer-free patients had a lower median age (54 vs 64 years, p=0.002), a less frequent history of smoking (77% vs 97%, p=0.001), coexistent neural antibodies (3% vs 20%, p=0.01) and hyperproteinorrachia (38% vs 73%, 0.0001). They also had a longer median delay to Hu-antibodies detection (12 vs 3 months, p<0.001), more common involvement of limbic (51% vs 25%, p=0.003) and myenteric areas (33% vs 13%, p=0.003; Figure 2), more frequent modified Rankin score <4 at diagnosis (45% vs 21%, p<0.001) and longer survival (Figure 3). Imaging findings suggestive of a possible regressed tumour were observed in 13/33 (39%).

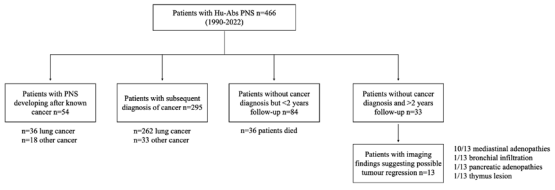

Figure 1. Flowchart of the study.

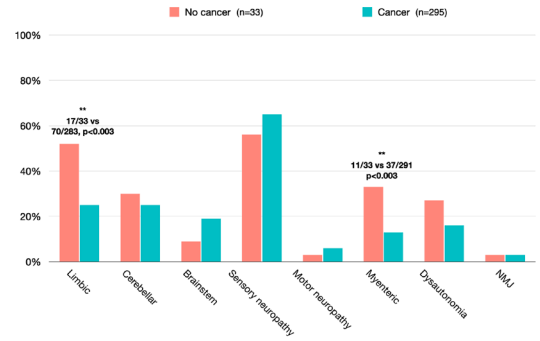

Figure 2. Clinical area involvement in patients with or without cancer.

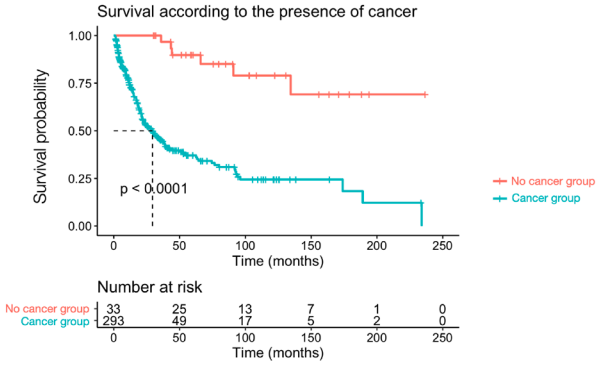

Figure 3. Survival analysis according to the presence of a cancer.

Conclusion: Patients with Hu-antibodies remaining cancer-free after a long follow-up have distinct features despite not presenting with a specific clinical phenotype. However, whether these patients had a regressive cancer or represent truly idiopathic cases remains unknown.

Disclosure: Macarena Villagrán-García received a research fellowship grant from the Spanish Foundation Alfonso Martín Escudero. Antonio Farina received a research fellowship grant from the European Academy of Neurology.

EPO-598

Myelin Oligodendrocyte Glycoprotein antibody associated disorder in neuro-Behçet's disease: differential diagnosis

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Background and aims: Myelin oligodendrocyte glycoprotein associated disorder (MOG-AD) diagnosis could be difficult when other autoimmune comorbidities can mimick its presentation.

Methods: We hereby report the case of a 54 years-old woman with a history of Behçet's disease (HLA-B51 positivity, recurrent oral aphthosis, skin ulcers and positive pathergy reaction) since adolescence.

Results: In September 2013 she developed paraparesis, urinary retention, headache and emesis. She was admitted to a Neurology Department, where Magnetic Resonance Imaging (MRI) showed T2-hyperintense brainstem lesions with contrast enhancement, and a transverse myelitis from T2 to T11. Cerebrospinal fluid (CSF) analysis revealed elevated leukocytes and protein and one oligoclonal band. Excluded infectious CNS diseases, high-dose intravenous methylprednisolone (IVMP) was administered, with partial recovery. A diagnosis of probable neuro-Behçet's disease (NBD) was made. The patient was stable until 2020, when she experienced a new clinical (nausea and speech disturbances) and MRI (cortical lesions with mild oedema in left temporal lobe) relapse. She was admitted to our Neurology Department: the complete diagnostic workup was unremarkable, except for MOG-IgG positivity, detected using fluorescence-activated cell sorting. She was diagnosed as MOG-AD. At the subsequent two-year follow-up, serum MOG-IgG were constantly detected.

Conclusion: NBD occurs in less than 10 % of patients with Behçet's disease, and its parenchymal type can manifest with clinical and MRI findings similar to MOG-AD. The recurrence of MOG-IgG positivity, longitudinally extensive spinal cord lesions and partial response to IVMP, guided, over time, our diagnosis. Distinguishing MOG-AD from other CNS inflammatory diseases is mandatory for treatment decision-making.

Disclosure: Dr. Vitobello, Dr. Oggiano and Dr. Bianco have nothing to disclose. Dr Manni has served on scientific advisory boards for Merck Serono, Sanofi Genzyme and Roche. Prof. Trojano received honoraria for consultancy or speaking from Biogen, Sanofi Aventis, Merck Serono, Novartis, Genzyme, TEVA, and Bayer-Schering and research grants from Merck Serono, Biogen, and Novartis. Dr. Iaffaldano A., Prof Paolicelli and Prof Iaffaldano P. have served on scientific advisory boards for Biogen, Novartis, Roche, Merck and Genzyme, and they have received speaker honoraria from Biogen Idec, Merck, Roche, Teva, Sanofi-Genzyme and Novartis.

Neuroimaging; Neurosonology

EPO-599

Impact of rater experience on detecting MRI features of idiopathic intracranial hypertension

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Background and aims: In idiopathic intracranial hypertension (IIH), MRI features (empty sella (ES), optic nerve sheath distension (ONSD), optic nerve tortuosity (ONT), posterior globe flattening (PGF) and transverse sinus stenosis (TSS)) are promising diagnostic markers.

Methods: In patients with definitive IIH and routine cranial MRI performed during diagnostic work-up, we compared ratings in real-world setting by radiologists with unknown awareness of IIH-MRI-features with a junior neuroradiologist aware of features but without special training and a senior neuroradiologist with experience in IIH imaging (gold-standard).

Results: In 84 IIH patients (88% female, mean age 33.5 years), 78.6% had ≥1 IIH-MRI-feature and 60% had ≥3 features with ONSD most frequent (64.3%) followed by TSS (60.0%), ONT (46.4%), ES (44.4%) and PGF (23.8%). Compared to gold standard, IIH features were described significantly less frequently in routine MRI reports (≥1 feature 64.3%, ≥3 features 15.7%, ONSD 28.6%, ONT 13.1%, PGF 4.8%, TSS 42.9%, p<0.01 respectively) except for ES (42.9%, p=0.9). Specific referral question regarding IIH increased detection rates in routine reports, but ONSD, ONT and PGF were still significantly lower than by gold standard. Contrary, rating by a neuroradiologist without special training produced significantly higher frequencies of ≥1 / ≥3 MRI features (95.2% and 72.5%, p<0.01 respectively), ONSD (81.0%, p<0.01) and ONT (60.7%, p<0.01), but not ES (47.6%), PGF (29.8%) and TSS (68.1%).

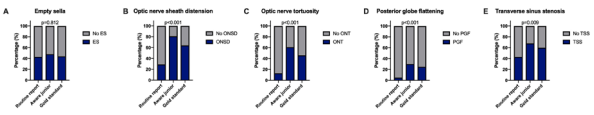

Figure 1

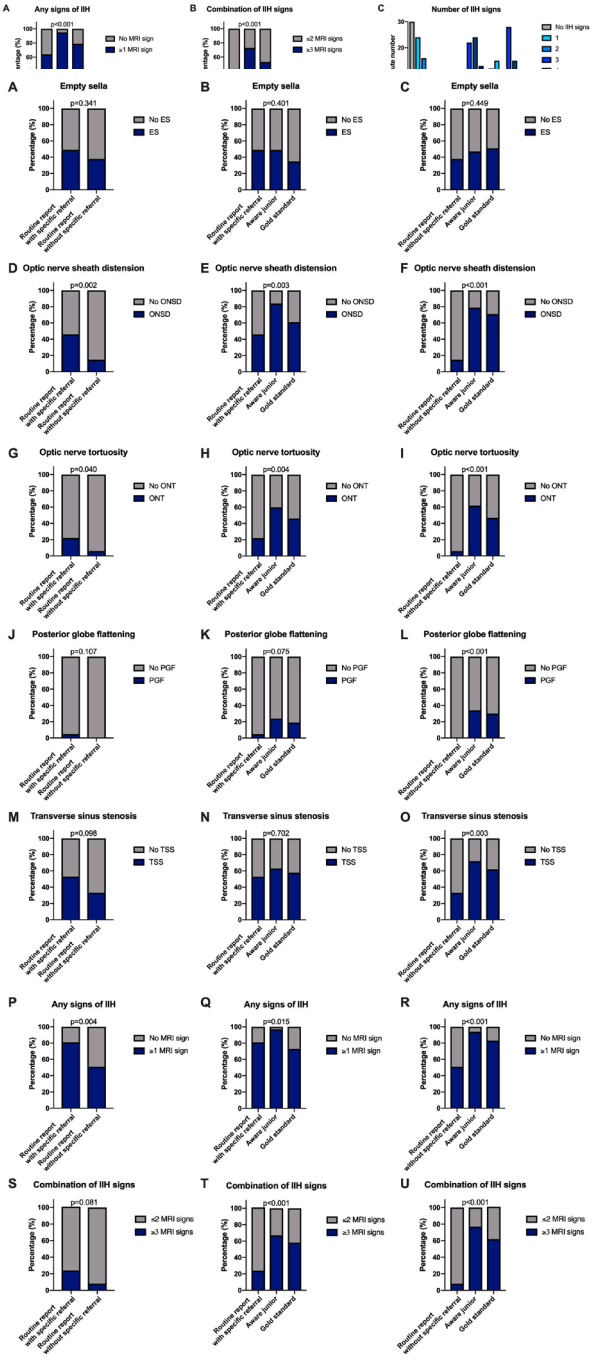

Figure 3

Conclusion: MRI features are underestimated in routine MRI reports and partly overestimated by less experienced neuroradiologists. Reevaluation of MRI scans by an

experienced rater (and to a lesser degree specific referral question) improves diagnostic accuracy.
Disclosure: GB: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

EPO-600

Frailty is associated with hippocampal atrophy in cognitively unimpaired older individuals

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Background and aims: Frailty (FI)has been associated with an increased risk of dementia (1)(2).The aim of the present study was to investigate the association between frailty, operationalized through a FI and hippocampal volume in cognitively intact subjects.
Methods: Sociodemographic, clinical, biological and neuroimaging data of 291 cognitively unimpaired individuals were obtained from the Alzheimer's Disease neuroimaging Initiative (ADNI) database phase 2. Clinical variables collected at screening and baseline visits were used to develop a 40-items FI (3). A linear regression model was then performed to explore the association between FI and hippocampal volume, adjusting for age, sex, education, ApoE status, CSF Aβ-42 and CSF P-tau. Sensitivity analyses were conducted using a modified 28-items FI
Results: Participants included in the study had a mean age of 73 (SD 6.0) years, mean education of 16.6 (SD 2.5) years, and 54% of them were women.The mean score of the 40-items FI was 0.18 (SD 0.08). In the multi-adjusted model, a statistically significant association between the 40-items FI and the reduction of hippocampal volume was observed (ß -0.15, 95%CI -0.28, -0.02, p=0.02). The association remained significant even considering the 28-items FI (ß -0.11, 95%CI -0.20, -0.01, p_0.03).
Conclusion: The results show that FI correlates with a reduction of hippocampal volume, an in vivo biomarker of neurodegeneration, independently from chronological age and traditional pathological lesions. Frailty contributes to hippocampal atrophy. Further studies are needed to clarify the relationship between frailty, neurodegeneration, and other biomarkers of dementia
Disclosure: Nothing to dislose.

EPO-601

Biochemical pathways involved in higher resilience in Parkinson's disease

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Background and aims: The emerging concept of resilience in Parkinson's disease (PD) aims to explain variations in symptom severity and progression rates in patients with a comparable extent of neurodegeneration. While several lifestyle factors and neurobiological underpinnings have recently been associated with slower disease progression, the biochemical basis of higher resilience is still unknown.
Methods: Using data from the PPMI database, high and low resilience groups were defined by residuals derived from a regression model predicting the motoric symptom severity by the dopamine transporter signal. In a preliminary gene set enrichment analysis (GSEA) we used protein abundances, quantified by slow off-rate modified aptamers, of 40 low and 50 high reserve patients. Gene sets were considered as of interest by an FDR<25%. We aim to apply an unsupervised machine learning algorithm in a bigger cohort to further investigate and validate the identified pathways of interest. Before clustering patients based on metabolome and proteome data, we will apply a feature selection algorithm. Finally, the difference in cluster expression scores across motor reserve categories and their influence on motor symptom progression will be investigated.
Results: Or preliminary results suggest higher resilience to be related to upregulated iron transport and homeostasis as well as inflammatory pathways. Low reserve, in contrast, seems to be associated with increased apoptotic processes. Further, cytochrome C was identified as a potential metabolite of interest.
Conclusion: In conclusion, identifying altered metabolites, proteins, or whole biochemical pathways might help to point out novel interventional targets.
Disclosure: I have nothing to disclose.

EPO-602

Effects of deep brain stimulation on functional connectivity in Parkinson's disease

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Background and aims: Deep-brain stimulation in the subthalamic nucleus (STN-DBS) is a prosperous surgical treatment for Parkinson's disease (PD). Research findings indicate that STN-DBS affects functional brain connectivity, however, with diverse results (Mueller 2013, Zhang 2021). Using a relatively large cohort, we inspected the impact of DBS in brain connectivity of PD patients.

Methods: Connectivity of 104 PD participants (age 59.5±7.9 y; 34 fem, disease duration 15.1±6.3 y) was measured with functional magnetic resonance imaging (fMRI) in STN-DBS ON and OFF state. Eigenvector centrality (EC) and global correlation (GCOR) maps were estimated using LIPSIA software and CONN toolbox, respectively, for each individual in both states. The contrast of STN-DBS ON-OFF was computed with SPM12 across all subjects as well as for female and male patients independently.

Results: Significant STN-DBS ON-OFF EC increase was found in male participants confirming the findings of Mueller 2013 (Fig 1). The contrast was shown in left and right premotor and parietal cortex, and right insula. No significant connectivity differences were found in females. The reversed contrast across all 104 PD patients demonstrated brain network centrality decrease in the left and right entorhinal cortex with both centrality measures EC and GCOR (Fig 2).

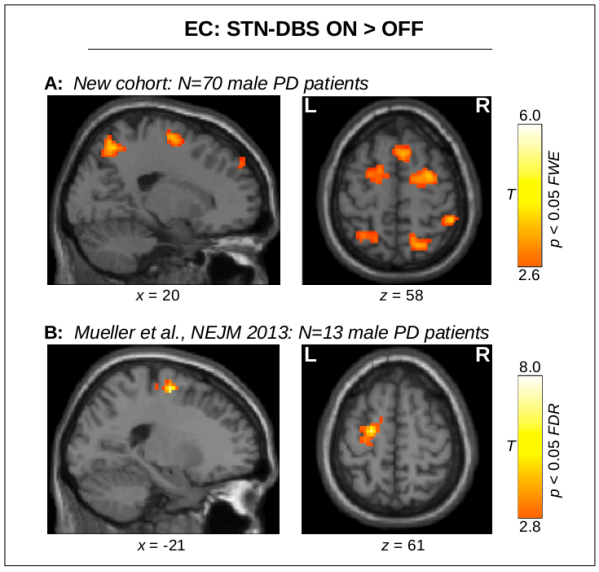

Figure 1. Significant STN-DBS ON-OFF EC increase in a group of male PD participants. The new cohort (A) is verifying the former finding (B).

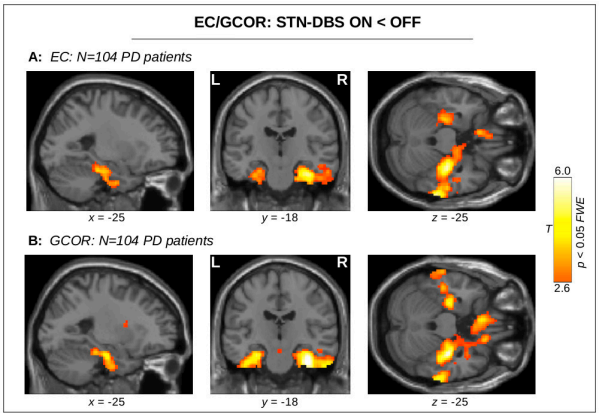

Figure 2. Significant STN-DBS ON-OFF EC decrease illustrated in brain slices of all PD participants (n=104). EC and GCOR results are aligned.

Conclusion: The analysis illustrated EC increase in several cortical regions of male individuals. Profound centrality decrease was shown in all groups indicating an association between STN-DBS and hippocampal connectivity.

Disclosure: Supported by a grant of the National Institute for Neurological Research, Czech Republic, Programme EXCELES (ID project No. LX22NPO5107) and the Charles University: Cooperatio Program in Neuroscience.

EPO-603

Paramagnetic rim lesions lead to pronounced diffuse periplaque white matter damage in multiple sclerosis

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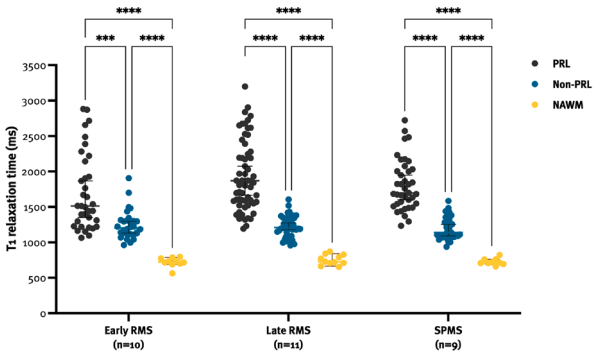
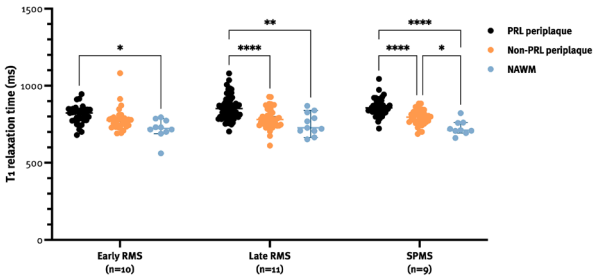
Background and aims: Paramagnetic rim lesions (PRLs) are a novel imaging biomarker, indicating a more severe disease course and earlier conversion to secondary progressive multiple sclerosis (SPMS).
Methods: We performed a cross-sectional, retrospective study on MS patients who underwent 3T MRI. Patients were grouped into early relapsing MS (eRMS) (disease duration (dd) ≤1 year), late RMS (lRMS) (dd ≥10 years), and clinically definite SPMS by Lorscheider et al. (dd ≥10 years). T1 relaxation times were measured by the quantitative "SyMRI" technology in PRLs and non-PRLs, their corresponding periplaque areas, and normal-appearing white matter (NAWM).
Results: Thirty patients were included (mean age 39.5 years [SD 11.0], 73.3% female, median EDSS 2.3 [range 0–6.0]). 135 PRLs and 107 non-PRLs were identified, 5 (16.7%) patients having no PRLs (2 eRMS, 2 lRMS, 1 SPMS). T1 relaxation times in PRLs were significantly longer compared to non-PRLs (eRMS: 1,705 vs. 1,245, lRMS: 2,011 vs. 1,223, SPMS: 1,811 vs. 1,200; p<0.001) (Figure 1). The PRL periplaque area showed significantly longer T1 relaxation times compared to the non-PRL periplaque area and NAWM in lRMS (857 vs. 789, p<0.0001; 857 vs. 752, p=0.0043) and SPMS (864 vs. 792; 864 vs. 727; p<0.0001). In eRMS, longer T1 relaxation times were observed only between the PRL periplaque area and NAWM (811 vs. 720, p=0.0124) (Figure 2).



PRLs showed longer T1 relaxation times compared to non-PRLs and NAWM.



The PRL periplaque area showed longer T1 relaxation times compared to the non-PRL periplaque area and NAWM.

Conclusion: PRLs are more destructive than non-PRLs and lead to pronounced diffuse periplaque WM damage which explains the more rapidly progressive clinical disability in patients with PRLs.
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

EPO-604

Quantification of Thalamic Volume in Multiple Sclerosis: From the Multicenter INNI Dataset Towards Clinical Application

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Background and aims: Thalamic atrophy has been found since the earliest phases of multiple sclerosis (MS). Aim of this study was to obtain a reliable segmentation of the thalamus in MS by comparing existing automatic methods.
Methods: 141 relapsing-remitting MS and 69 healthy controls (HC) with baseline and 1-year 3D T1-weighted, T2-weighted and diffusion weighted (DW) MRI were collected from the Italian Neuroimaging Network Initiative. From DWI, fractional anisotropy (FA) maps were derived for the FSL-MIST multimodal segmentation. FSL-FIRST v5.0.9 and Freesurfer v6.0 were also compared. The agreement among the results of the pipelines and the effect sizes in differentiating between MS and HC were assessed. In patients, correlations with age, disease duration, EDSS and T2-hyperintense lesion volume (LV) were evaluated.
Results: At baseline, FIRST and MIST showed the highest significant agreement for thalamic volumes ($R=0.87$, $p<0.001$), with the highest effect size for MIST (Cohen's $d=1.11$). At baseline, FIRST showed the highest significant correlations with age (-0.36, $p<0.001$), EDSS ($R=-0.3$, $p<0.001$), T2-hyperintense LV ($R=-0.4$, $p<0.001$) and disease duration ($R=-0.2$, $p=0.02$). At follow-up, MIST showed the lowest variability in estimating thalamic volume changes (TVC) for HC (standard deviation=1.07%) in comparison to the other pipelines, and the highest effect size (Cohen's $d=0.21$). In MS, only MIST TVC showed a significant correlation with T2-hyperintense LV change ($R=-0.22$, $p=0.01$).
Conclusion: We found that the use of a multimodal approach increased robustness of the longitudinal results and a better capability to detect small variations of thalamic volumes, as shown by the results for MIST.
Disclosure: This study was partially supported by Fondazione Italiana Sclerosi Multipla with a research fellowship (FISM 2019/BR/009) and a research grant (FISM2018/S/3).

EPO-605

MRI abnormalities in stiff person syndrome

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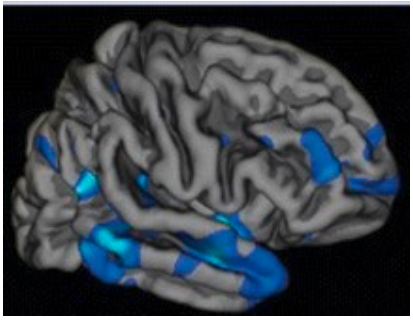
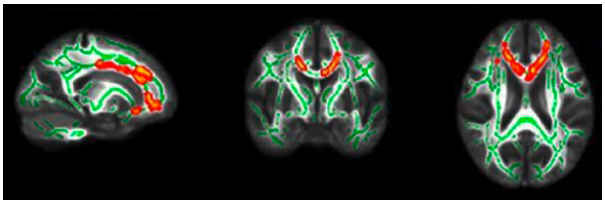
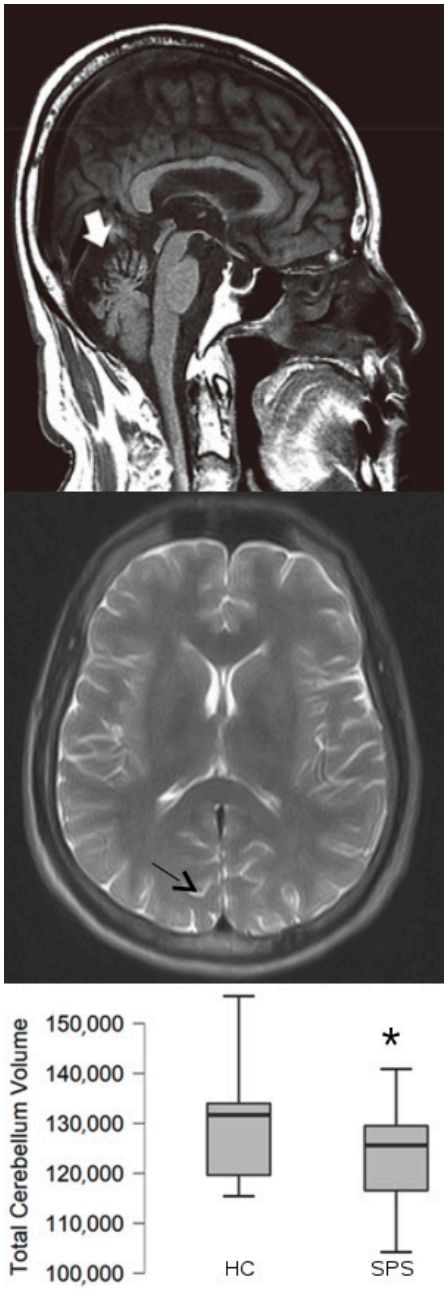
Background and aims: Stiff-person-syndrome (SPS) is a chronic autoimmune disease which mainly affects the central nervous system with spasms and stiffness, pain and psychological comorbidities. The diagnosis remains challenging due to the variety of symptoms, and conventional brain imaging contribution to the diagnosis is often limited. Magnetic resonance imaging (MRI) studies on SPS are lacking so far.
Methods: 25 SPS patients were examined by a neurologist, underwent questionnaires about chronic pain and were compared to 25 sex and age matched healthy controls (HC). MRI was performed at 3 Tesla. For each participant we included a structural sequence, diffusion tensor imaging, resting-state functional MRI and proton magnetic resonance spectroscopy in the insular cortex.
Results: SPS patients had lower cortical thickness bilaterally in the prefrontal cortex in the region of superior frontal gyrus (SFG) in comparison to healthy controls. SPS patients indicated chronic pain in the GCPS. There was a negative correlation between the individual extent of pain according to the GCPS and cortical thickness in the bilateral SFG. GABA spectroscopy in the insular cortex revealed lower GABA in the SPS cohort compared to the HCs.



SPS patients show lower prefrontal and temporal cortical thickness



SPS patients had lower fractional anisotropy bilaterally in the prefrontal cortex



SPS patients with higher GAD antibody titer show more cerebellar atrophy

Conclusion: This study provides a comprehensive radiological description of the pain pathology associated with GAD positive SPS, using advanced MRI analyses. The findings of the SPS patients in cortical thickness match those of patients with chronic pain and social anxiety disorder. The radiological peculiarities of the patients in our cohort, by identifying the precise structures affected, can provide a better understanding of the pathophysiology and the development of the chronic pain.

Disclosure: Nothing to disclose.

EPO-606

Multishell diffusion-weighted MRI characterization of chronic active lesions in Multiple Sclerosis

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Background and aims: Chronic active Multiple Sclerosis (MS) lesions, seen on susceptibility-weighted MRI as Paramagnetic Rim Lesions (PRL), are associated with increased clinical disability and axonal damage. Diffusion MRI (dMRI) can characterize in vivo PRL's tissue damage, however the tissue microstructure specificity of dMRI models is limited. Here, we characterized PRL's microstructure using 4 different models, including one novel dMRI model: Microstructure Fingerprinting (MF).

Methods: 367 lesions (202 PRL and 165 non-PRL) were segmented in 44 MS patients (27 relapsing-remitting, 11 secondary progressive, 6 primary progressive). For each lesion, we calculated volume, quantitative T1 values and diffusion parameters (Table 1) derived from 4 dMRI models: Diffusion Tensor Imaging (DTI), Neurite Orientation Dispersion and Density Imaging (NODDI) and DIstribution of Anisotropic MicrOstructural eNvironments in DWI (DIAMOND) and MF.

Results: PRL were bigger ($p<0.001$) and featured higher T1-values ($p<0.001$) vs non-PRL. DTI and DIAMOND models showed lower fractional anisotropy, higher mean diffusivity and radial diffusivity in PRL vs non-PRL ($p<0.001$). NODDI and MF models showed lower neurite density index and weighted fibre volume fraction ($p<0.001$), suggesting overall impaired axonal integrity/density in PRL vs non-PRL (Table, Figure).

	PRL *Mean ± SD*	**non-PRL** *Mean ± SD*	*p*
Volume, mm^3	228,673 ± 290,301	102,998 ± 112,540	< 0,001
T1, ms	1529,872 ± 284,678	1236,189 ± 217,452	< 0,001
DTI_AD, mm^2/s	0,00101 ± 0,00018	0,00096 ± 0,00019	< 0,001
DTI_FA	0,35872 ± 0,11089	0,44450 ± 0,12704	< 0,001
DTI_MD, mm^2/s	0,00074 ± 0,00014	0,00064 ± 0,00013	< 0,001
DTI_RD, mm^2/s	0,00060 ± 0,00015	0,00047 ± 0,00014	< 0,001
NODDI_fExtra	0,58044 ± 0,10657	0,48462 ± 0,10705	< 0,001
NODDI_NDI	0,27335 ± 0,08745	0,33077 ± 0,10099	< 0,001
NODDI_fIso	0,14599 ± 0,10826	0,18461 ± 0,09603	< 0,001
NODDI_odi	0,25121 ± 0,08352	0,23366 ± 0,07619	0,097
DIAMOND_wAD, mm^2/s	0,00182 ± 0,00029	0,00175 ± 0,00028	0,018
DIAMOND_wFA	0,54310 ± 0,12855	0,63083 ± 0,13551	< 0,001
DIAMOND_wMD, mm^2/s	0,00107 ±0,00016	0,00095 ± 0,00017	< 0,001
DIAMOND_wRD, mm^2/s	0,00070 ± 0,00018	0,00054 ±0,00020	< 0,001
MF_frac_CSF	0,26621 ± 0,15471	0,20683 ± 0,14503	< 0,001
MF_frac_ftot	0,73357 ± 0,15500	0,79317 ± 0,14503	< 0,001
MF_fvf_tot	0,14803 ± 0,06889	0,20792 ± 0,08798	< 0,001
MF_wfvf	0,19508 ± 0,06413	0,25581 ± 0,08374	< 0,001

Table: Mean volume, T1 times and diffusion parameters of DTI, NODDI, DIAMOND and MF models for PRL and non-PRL lesions. Abbreviations: DTI_AD: DTI Axial Diffusivity DTI_FA: DTI Fractional Anisotropy DTI_MD: DTI Mean Diffusivity DTI_RD: DTI Radial Diffusivity NOD

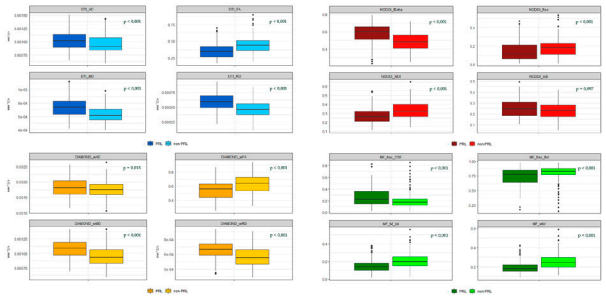

Figure: Boxplot of average DTI (blue), NODDI (red), DIAMOND (yellow) and MF (green) dMRI model parameters in PRL and non-PRL lesions. Abbreviations: DTI_AD: DTI Axial Diffusivity DTI_FA: DTI Fractional Anisotropy DTI_MD: DTI Mean Diffusivity DTI_RD: DTI Radial D

Conclusion: Consistent with previous data, we show that PRL are characterized by higher axonal damage when compared to non-PRL. Results derived from the MF model are in line with those obtained with DTI, NODDI and DIAMOND, suggesting that this novel dMRI model can be used to study MS lesion pathology. As an advantage, the MF model framework allows further methodological improvement, using more accurate white matter-diffusion simulations.

Disclosure: Authors have no relevant disclosures related to this submission.

EPO-607

Retinal ischemia due to different stages of atherosclerosis

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Background and aims: Ischemic stroke (IS) and retinal ischemia (IR) share similar vascular risk factors, but differ in response to intravenous thrombolysis and the risk for subsequent stroke or restroke. High resolution orbital color-coded sonography (OCCS) is an easy to use diagnostic tool in the diagnosis of this small vessel. This study characterized the cardiovascular risk profiles of patients with central retinal artery occlusion (CRAO).

Methods: We performed a retrospective analysis on the detailed cardiovascular risk factors and neuroimaging data in 94 patients with IR. CRAO were further divided based upon their appearance on OCCS as hyperechoic, termed ssCRAO ("spot sign") or hypoechoic (heCRAO). Statistical analyses were performed with Kruskal-Wallis, Mann-Whitney-U and $\chi 2$ testing. P-values were corrected for multiple testing and considered significant if < 0.05.

Results: 26 patients were diagnosed as heCRAO and 68 as ssCRAO. Patients with ssCRAO were significantly older. Male patients were overrepresented in the cohort as whole. ssCRAO was associated with more severe atherosclerosis whereas heCRAO patients had more echolucent atherosclerosis. The presence of atrial fibrillation did not differ statistically significant between the subgroups and most patients with atrial fibrillation were on ongoing oral anticoagulation while suffering CRAO.

Conclusion: Based upon these findings, we postulate that emboli in atherosclerosis may be one of the most important, if not the main embolic source, for IR. By contrast, the contribution of atrial fibrillation in IR etiology remains questionable. These findings have implications for secondary stroke prevention suggesting more intense treatment of atherosclerotic risk factors.

Disclosure: Nothing to disclose.

Movement disorders 4

EPO-608

Extensor dystonia in young-onset Parkinson's disease

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Background and aims: Extensor dystonia (ED), in the form of retrocollis or extensor truncal dystonia (ETD), has been scarcely reported in idiopathic Parkinson's disease (PD). Studies suggest an increased presence in advanced stages of PD but its exact prevalence remains unknown (Kashihara et al. 2013; Thiel et al. 2022). We describe three cases of ED in young-onset PD.
Methods: A search was conducted in our outpatient database for PD patients who presented ED at any point during their follow-up.
Results: Three female patients (of ages 65, 66, and 69) with PD onset at ages 44, 47 and 52, respectively, fulfilled above criteria. The first two underwent bilateral subthalamic deep brain stimulation (DBS) at 11 and 14 years from PD onset. One had retrocollis only during off periods and responded to oral dopaminergic drugs and later to DBS. The other had continuous ETD that worsened during off periods with a clear tendency to arching the back but was able to walk unassisted. The third patient had painful ETD that conditioned severe postural instability and multiple falls. Botulinum toxin injection in mainly affected muscles showed only partial response. She needed a walking frame and was dependent for basic activities.

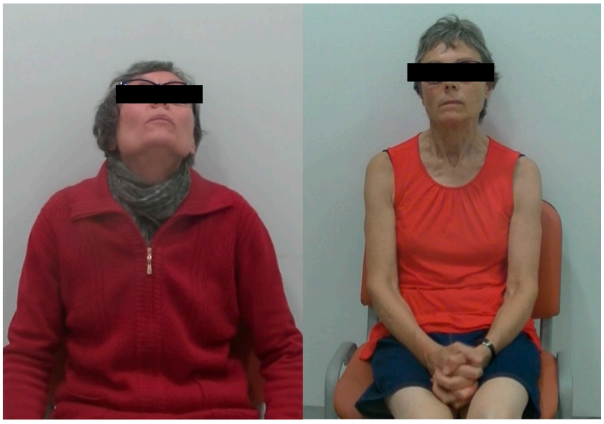

Figure: 66 year old female patient with off period retrocollis.

Conclusion: ED significantly affects quality of life and motor function of PD patients. Most reported cases are from young-onset PD but systematic studies to determine prevalence and associations are lacking. As these cases suggest, different mechanism might be involved, and treatment should be individualized.
Disclosure: We have no actual or potential conflict of interest in relation to this presentation.

EPO-609

Abstract withdrawn

EPO-610

Enrolment characteristics for patients entering a Phase 3 study of subcutaneous levodopa/carbidopa infusion with ND0612

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Background and aims: The BouNDless study (NCT04006210) compared the efficacy, safety, and tolerability of subcutaneous levodopa/carbidopa (LD/CD) as an investigational ND0612 24-hour infusion versus oral immediate-release (IR)-LD/CD in patients with Parkinson's disease (PwP) experiencing motor fluctuations. Here we report patient enrollment characteristics; primary results will be available in 2023.
Methods: Following screening, PwP on ≥4 doses/day of oral LD/dopa-decarboxylase inhibitor (LD ≥400mg/day) and experiencing ≥2.5h daily OFF-time were consented and enrolled. They entered a 4-6 week open-label adjustment period during which oral LD formulations and COMT inhibitor doses were converted to equivalent doses of IR-LD/CD and then adjusted to optimal clinical effect.

Patients then entered an 4-6 week open-label ND0612 conversion period in which IR-LD/CD was replaced by ND0612 (LD/CD dose up to 720/90mg/day) with adjunct IR-LD/CD, as required, and adjusted until this combination regimen was optimal. Patients then entered a 12-week, double-blind, double-dummy period, during which they were randomized (1:1) either to their optimized regimen of ND0612 infusion (plus IR-LD/CD), or to the optimized IR-LD/CD-only regimen.

Results: Enrollment characteristics of randomized patients (n=259) were similar to other clinical trials in PwP experiencing motor fluctuations refractory (mean±SD age: 63.5±9.0y; 63.7% male; diagnosed 9.6±4.3y; motor fluctuations 4.5±3.3y, mean OFF time 6.1±1.7h). Levodopa equivalent daily doses at enrollment were 1029mg; 86% patient were receiving adjunct Parkinson's medications, mainly dopamine agonists (63%).

Conclusion: Enrollment characteristics of patients randomized in the BouNDless trial are consistent with those observed in other clinical studies in PwP experiencing motor fluctuations.

Disclosure: Funded by NeuroDerm. Olivier Rascol, Alberto Albanese, Aaron Ellenbogen, Joaquim Ferreira, Tanya Gurevich, Sharon Hassin, Jorge Hernandez-Vara, Stuart Isaacson, Karl Kieburtz, Peter LeWitt, Lydia Lopez Manzanares, C. Warren Olanow, Rajesh Pahwa, Werner Poewe, Harini Sarva, Fabrizio Stocchi, Alberto Espay, and Navin Giladi are members of the BouNDless study group. Tami Yardeni, Liat Adar, Laurence Salin, Nelson Lopes, Nissim Sasson, and Ryan Case are employed by NeuroDerm.

EPO-611

Dystonia management in four European countries: evaluation of patients' experience

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Background and aims: A long time for diagnosis and treatment of dystonia was reported. The aim of present study was to evaluate dystonia management from patients' own experience in four European countries with different health care systems regarding the delivery of services and education.

Methods: Dystonia survey was undertaken using a structured on-line questionnaire to assess patients' own experience of dystonia management and treatment in Croatia, Italy, Germany and the UK. The questionnaire was composed of 30 questions divided into three parts: part I. general questions part II. specific questions as disease duration, type of DS, experience with a first initial visit to GP etc.; part III. type of therapy, satisfaction/discontinuation of therapy.

Results: A total of 1,645 patients responded to survey: 379 (12.2%) from Croatia, 340 (10.9%) from Germany, 175 (5.6%) Italy and 751 (24.1%) from UK. Women outnumbered men in all countries cervical dystonia was the most prevalent type. Most patients (around 50%) from all countries were 41-50/51-60 years old. Although most patients across countries were diagnosed within 2 years since the first symptoms, significant number waited more than 10 years (7–15%). In comparison to UK participants Italian and Croatian patients reported shorter time to diagnosis. Croatian patients have experienced a 'more adequate' initial GP assessment.

Conclusion: Sub-analysis of Germany, Italy and the UK did not show significant differences in the current state of dystonia management among countries, although significant difference exists in the healthcare system.

Disclosure: Nothing to disclose.

EPO-612

CACNA1A variant can be associated with generalized dystonia

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Background and aims: Mutations in the CACNA1A gene have been correlated with episodic ataxia type 2, spinocerebellar ataxia type 6, and familial hemiplegic migraine type 1. Dystonia is not enlisted among the typical clinical manifestations of CACNA1A mutations. We report the case of a patient with a novel missense mutation of the CACNA1A gene presenting headache, head and arm tremor, slowly progressive dystonia associated with episodic painful focal dystonic attacks.

Methods: A 57-year-old woman was referred because of neck dystonia associated with head and arms tremor since the age of 15 years. At the age of 47, in 2012, she presented an increase in tremor amplitude led to suspect of essential tremor. In 2019 she showed mild dysarthria, right torticollis with dystonic head tremor and both arms, and gait with dystonic head posture. Moreover, she reported paroxysmal dystonia attacks (3–4 per week) of the lower extremities, occurring without apparent provoking factors.

Results: Dystonia's genetic panel showed a heterozygous mutation in the CACNA1A gene (NM_023035.2:c.1630C>T p.(Arg544Trp). In 2020 due to worsening dystonia,, she underwent evaluation for Gpi-DBS surgery. However, a brain MRI showed cortical atrophy, and she was excluded.

Conclusion: CACNA1A mutations are associated with a broad spectrum of neurological manifestations, with a frequent overlap of headache and neurological signs related to the involvement of the cerebellum. Few dystonic symptoms have been reported so far; however, the link between dystonia and CACNA1A mutations is increasingly evident, although the prevalence, incidence, and pathogenesis still need to be elucidated.
Disclosure: Nothing to disclose.

EPO-613

Au nanoclusters loaded with GLP-1 agonist as a potential treatment for Parkinson's Disease

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Background and aims: Parkinson's Disease (PD) is the second most common neurodegenerative disease worldwide. To date, the drugs used for PD are only designed to treat symptoms and ultimately, patients will develop a cumulative disability and neuronal loss. In previous studies exendin-4, a glp1 agonist tested in PD mice models was found to improve neurotoxin-induced motor alterations and chronic inflammation in the brain. In order to aim for success in drug transportation and take advantage of the neuroprotective effects of previously reported effects of gold nanoparticles we treated SH-SY5Y cells with Au loaded -4 nanoclusters with exendin on a PD cell model.
Methods: To evaluate the effect of the nanosystem four groups were tested and treated for 72 hours. DAPI staining, Neurite length measurements, and LDH assays were performed on the groups. XRD, TEM, and FTIR microscopy were used for nanoparticle characterization.
Results: When analyzed with TEM and XRD techniques, the gold nanoparticles showed a 1–3 nm size. The nanosystem exendin-nanoparticle reversed the oxidative damage in a PD SH-SY5Y cell model. Following light microscopic analyses, the stained cells with DAPI showed similar cell survival compared to the control cell group. The nanosystem displayed neuronal protection on the 6-OHDA PD model.
Conclusion: GLP-1 agonists combined with nanotechnology have not yet been studied in Parkinson's Disease before, we hope to open a new research perspective into the treatment options for PD. Targeting mitochondrial and oxidative stress relief while using nanotechnology might improve the therapeutic treatment for PD patients and help provide better medical results.
Disclosure: Nothing to disclose.

EPO-614

Absent significant association of oral levodopa with polyneuropathy in Parkinson's disease

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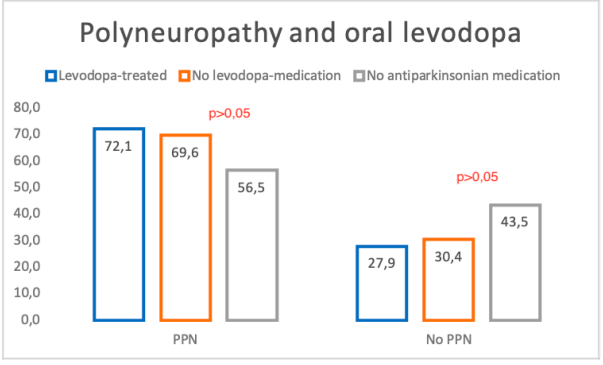
Background and aims: Peripheral polyneuropathies (PPN) have a prevalence of about 8–10% in the elderly in general population. Some studies suggest an increased prevalence of PPN in patients with Parkinson's disease (PD) and an association of PPN with oral levodopa treatment.
Methods: We assessed clinical and electrophysiological data of 692 consecutive patients with idiopathic PD, admitted to our clinic between 2016 and 2019.
Results: Of 692 patients, 73,26% had clinically PPN, mostly a sensory or sensorimotor axonal, moderate or severe one. Of 623 patients (90.02%) received diverse antiparkinsonian medication, 567 (91.0%) had oral levodopa. Of 69 patients with no antiparkinsonian medication, 57 (82.61%) had PPN. Of the patients receiving oral levodopa, 409 (72.13%) had PPN ($p>0.05$). Of the 56 patients, receiving diverse antiparkinsonian medication other than levodopa, 39 (69.4%) had PPN. ´Vitamin B12 blood levels below 300pg/ml were more common in PPN-positive PD patients (40.62% at the time point of PPN first diagnose) than in PPN-negative PD patients (23.78%). 40.0% of levodopa-naive PD patients had low blood level of the vitamin B12, compared to 40.46% of levodopa-treated PD patients ($p>0.5$). In tested patients without antiparkinsonian medications at all, 38.18% patients had low vitamin B12 blood level.
Conclusion: Peripheral polyneuropathy is very common in Parkinson's disease patients. Typically, it is a moderate or severe, sensory or sensorimotor axonal polyneuropathy. A low vitamin B12 blood level was more common in PPN-positive PD patients. No significant association between oral levodopa or other antiparkinsonian medication and PPN in PD patients was found.
Disclosure: Nothing to disclose.



EPO-615

Challenges in Wilson´s disease therapy: therapy initiation, compliance, comorbidities and survival

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Background and aims: The aim of the study is to highlight the challenges in long-term treatment of patients with Wilson´s disease occurring during their entire life-span.
Methods: In a combined retrospective and cross-sectional mono-centric study demographical, treatment related and clinical and biochemical data were extracted from the charts of 110 patients with Wilson´s disease.
Results: Rapid recovery of liver dysfunction and prolonged recovery of neurological symptoms were observed after initiation of WD-specific therapy with up to 900mg DPA and up to 1,200mg Trientine during the first two years of treatment. During the course of treatment about one third of the patients presented with compliance problems reaching from low adherence to medication regimens to complete cessation of medication with lethal outcome. More than 20% of the patients had mild to moderate side effects of WD-specific treatment and more than 70% of the patients developed neurological and non-neurological comorbidities interfering with WD. About 4% of the patients developed malignancies as hepatocellular carcinoma. In contrast to previous reports life-expectancy in WD appears to be reduced.
Conclusion: Throughout their entire life-span patients with WD have to face a variety of challenges and need careful therapy monitoring.
Disclosure: The authors declare no conflicts of interest associated with this research work.

EPO-616

First-year Treatment Intensity and Prognosis in Early Parkinson's Disease: A Retrospective, Longitudinal Study in Israel

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Background and aims: Given Parkinson´s disease (PD) heterogeneity, it is challenging to find associations between patients' characteristics and prognosis. We compared long term disease prognosis among people with Parkinson's Disease (PwPD) by treatment intensity in the first year after PD diagnosis.
Methods: This population-based, retrospective cohort study utilised data from a large health plan in Israel. Members were included if they had ≥1 PD diagnosis between 2005–2010. Index date was defined as the earliest PD diagnosis or anti-PD therapy initiation. PwPD were required to have ≥5 years' membership in the health plan prior to index date and up to 10 years of follow-up. Study population was divided into low and high treatment intensity groups based on levodopa-equivalent daily dose status during the first year post-index date (low [mild], <600 mg; high [intensive], ≥600 mg). Survival, comorbidities, and symptoms were evaluated and compared.
Results: We identified 2,525 eligible PwPD (mean [SD] age, 74.5 [10.7] years; males, 55.9%). Of those, 292 (11.6%; mean age, 75.4 [8.8] years; males, 65.1%) were intensively treated during the first year post-index date; 2,233 (88.4%, mean age, 74.4 [10.9] years; males, 54.7%) were mildly treated (Table). Compared with mild treatment, intensive treatment was associated with increased probability of death at 10 years (p<0.0001) (Figure). Additional results are forthcoming.

Table. Age and sex for overall PD population and by LEDD status in the first year

Characteristic		Low Dose (Mild Treatment) <600 mg LEDD n = 2233	High Dose (Intensive Treatment) >=600 mg LEDD n = 292	*P* value[a]
Age at index date	Mean (SD)	74.4 (10.9)	75.4 (8.8)	.074
	<55 (%)	113 (5.1)	11 (3.8)	.007
	55-65 (%)	286 (12.8)	19 (6.5)	
	65-75 (%)	641 (28.7)	100 (34.2)	
	>=75 (%)	1193 (53.4)	162 (55.5)	
Sex	Male (%)	1222 (54.7)	190 (65.1)	.001

[a]The statistical tests used were *t* test for continuous variables and chi square test for categorical variables.
LEDD, levodopa-equivalent daily dose.

Table. Age and sex for overall PD population and by LEDD status in the first year

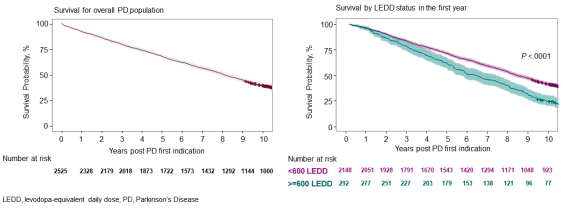

Figure. Survival curves for the overall PD population and for patients stratified by LEDD status in the first year.

Conclusion: PwPD who received intensive treatment early after diagnosis had a worse disease prognosis. The epidemiologic assessment of the early stages of PD in PwPD may help define diverse subgroups who may benefit from more timely and targeted therapeutic interventions.
Disclosure: YB has no disclosures. OS-S, MG-J, LB, and CHY are employees of AbbVie and may hold stock or share options. DA has no disclosures. GC has no disclosures. AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of this abstract. All authors had access to relevant data and participated in the drafting, review, and approval of this abstract and agreed to submit this abstract to the European Academy of Neurology (EAN) 2023 Congress for consideration as an oral presentation or poster. No honoraria or payments were made for authorship. Medical writing support was provided by Morgan Gingerich, PhD, of JB Ashtin, and funded by AbbVie.

EPO-617

Motor resonance in early Parkinson's disease. A Near-Infrared Spectroscopy and EEG study

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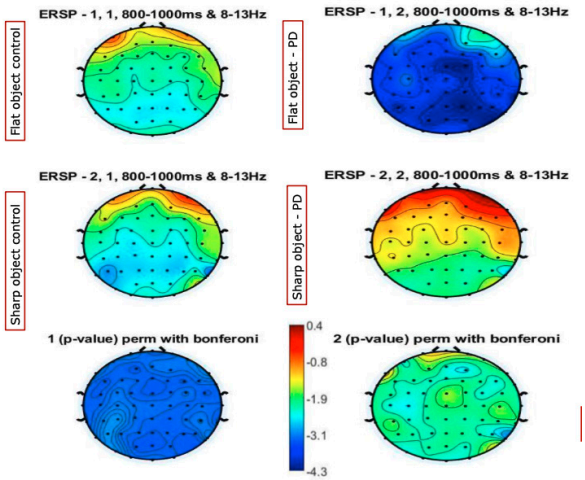
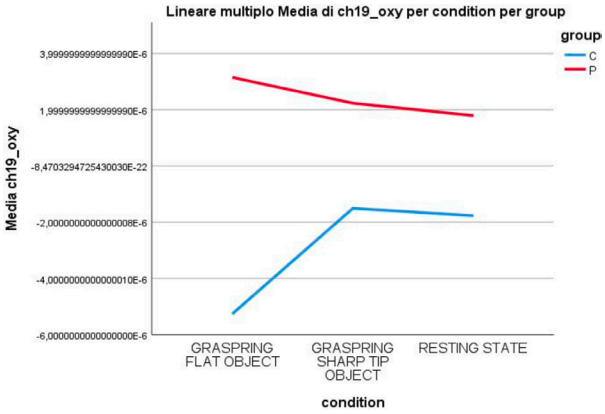
Background and aims: The observation of action seems to involve the generation of the internal representation of that same action in the observer, a process named Motor Resonance (MR).
Methods: The objective of this study was to verify whether an experimental paradigm of action observation in a laboratory context could elicit cortical motor activation. We recruited 21 early Parkinson's disease (PD) patients and 22 controls. Inclusion criteria for PD patients were diagnosis of Idiopathic PD at Hoehn-Yahr stage I-II, age between 40 and 80 years, MMSE>23, and absence of significant visual deficits. Participants were instructed to simply observe (Observation-only session) or to respond (Time-to-contact detection session) at the instant the agent performed a grasping action toward a graspable or ungraspable object. We used functional Near-Infrared Spectroscopy (fNIRS) with 20 channels on the motor and premotor brain areas and event-related desynchronization of alpha-mu rhythm.
Results: In both groups, response times were more accurate in graspable than ungraspable object trials, suggesting that motor resonance is present in PD patients. In the Time-to-contact detection session, the oxyhemoglobin levels and alpha-mu desynchronization prevailed in the graspable vs ungraspable object trials. In the resting state, the alpha mu desynchronization was more evident in PD patients than in controls.



EEG 8–13 Hz frequencies scalp distribution during observation session



f-NIRS, ΔHbO2 in channel 19 (grasping flat, grasping sharp tip, resting state)

Conclusion: This study demonstrates the preservation of MR mechanisms in early PD patients. The action observation finalized to a consequent movement can activate cortical networks in patients with early PD, suggesting early rehabilitation interventions taking into account specific observation paradigms, preceding motor production.
Disclosure: The authors declare no competing interests.

EPO-618

Changes in principal caregiver mood affects the mood of the Parkinson disease patient. The vicious cycle of illness.

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Background and aims: Although many studies have analyzed what factors contribute to caregiver burden in Parkinson´s disease (PD), there is currently no knowledge about how the status of the caregiver could impact the patient. The aim of this study was to analyze how the change in the caregiver´s status influences PD patients.

Methods: PD patients and their caregivers who were recruited from January/2016 to November/2017 from 35 centers in Spain from the COPPADIS cohort were included in the study (V0). They were evaluated again at 2-year follow-up (V2). Caregivers completed the Zarit Caregiver Burden Inventory (ZCBI), Caregiver Strain Index (CSI), Beck Depression Inventory-II (BDI-II), and EUROHIS-QOL 8-item index (EUROHIS-QOL8) at V0 and V2. Multivariate models were used to analyze the impact of the change from V0 to V2 (Δ) on the caregiver´s status over the change in the patient´s status.

Results: ΔBDI-II and ΔEUROHIS-QOL8 in the caregiver predicted ΔBDI-II (β=0.32; p<0.0001; R2=0.71) (Table 1) and ΔEUROHIS-QOL8 (β=0.39; p<0.0001; R2=0.68) in the patient (Table 2), respectively. Variables related to the caregiver were not associated with changes in the patient´s health-related QoL (ΔPDQ-39 [[39-item Parkinson's disease Questionnaire]) or autonomy for activities of daily-living (ΔADLS [Schwab & England Activities of Daily Living Scale]).

Conclusion: The change in the caregiver´s mood and global QoL was associated with the change in the patient´s mood and global QoL, respectively, independently of other variables of the disease influencing both patient´s aspects.

Disclosure: COPPADIS and the present study were developed with the help of Fundación Española de Ayuda a la Investigación en Enfermedades Neurodegenerativas y/o de Origen Genético (https://fundaciondegen.org/) and Alpha Bioresearch (www.alphabioresearch.com). Also, we received grants from the Spanish Ministry of Economy and Competitiveness [PI16/01575] co-founded by ISCIII (Concesión de subvenciones de Proyectos de Investigación en Salud de la convocatoria 2020 de la Acción Estratégica en Salud 2017-2020 por el Proyecto "PROGRESIÓN NO MOTORA E IMPACTO EN LA CALIDAD DE VIDA EN LA ENFERMEDAD DE PARKINSON") to develop a part of the COPPADIS project.

	Univariate analysis			Multivariate analysis		
	β	95% CI	p	β	95% CI	p
Caregiver						
Δ BDI-II	0.42	0.40 – 0.77	<0.0001	0.32	0.27 – 0.67	<0.0001
Δ ZCBI	0.19	0.05 – 0.28	0.006	0.10	-0.02 – 0.22	0.125
Δ CSI	0.14	0.03 – 1.33	0.039	-0.03	-0.89 – 0.50	0.576
Δ EUROHIS-QOL8	-0.21	-7.97 – -1.67	0.003	0.20	1.74 – 8.13	0.003
Patient						
Δ EUROHIS-QOL8	0.22	0.07 – 0.40	0.006	-0.56	-9.34 – -5.95	<0.0001
BDI-II at baseline	0.19	-0.14 – -0.01	0.035	-0.36	-0.64 – -0.32	<0.0001

Dependent variable: change in the PD patient from V0 to V2 (Δ) in the BDI-II total score. β standardized coefficient and 95% IC are shown. [a], univariate analysis; [b], multivariate analysis (Durbin-Watson test=2.11; R^2=0.71). Only significant variables (p<0.01) from the patient in the multivariate analysis are shown. Covariates from the patient included were the change from V0 to V2 (Δ) in LEDD, UPDRS-III-OFF, UPDRS-IV, FOGQ, PD-CRS, NMSS, PDSS, QUIP-RS, NPI, VAS-PAIN, VAFS, ADLS, PDQ-39SI, EUROHIS-QOL8, and the score on the BDI-II at baseline.

ADLS, Schwab & England Activities of Daily Living Scale; BDI-II, Beck Depression Inventory-II; CSI, Caregiver Strain Index; FOGQ, Freezing Of Gait Questionnaire; LEDD, levodopa equivalent daily dose; Non-Motor Symptoms Scale; NPI, Neuropsychiatric Inventory; PD-CRS, Parkinson´s Disease Cognitive Rating Scale; PDQ-39, the 39-item Parkinson's disease Questionnaire Summary Index; PDSS, Parkinson's Disease Sleep Scale; QUIP-RS, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAS, Visual Analogue Scale; ZCBI, Zarit Caregiver Burden Inventory.

Table 1. Effect of changes in the caregiver over the change in mood in PD patients from the COPPADIS cohort after 2-year follow-up (n=192).

	Univariate analysis			Multivariate analysis		
	β	95% CI	p	β	95% CI	p
A) Δ PDQ-39SI						
Caregiver						
Δ BDI-II	0.19	0.10 – 0.62	0.006	0.16	0.01 – 0.54	0.047
Δ ZCBI	0.28	0.16 – 0.46	<0.0001	0.03	-0.13 – 0.20	0.671
Δ CSI	0.20	0.41 – 2.15	0.004	0.04	-0.72 – 1.20	0.818
Δ EUROHIS-QOL8	0.01	-3.89 – 4.64	0.863	0.13	-0.33 – 7.74	0.072
Patient						
Δ UPDRS-III	0.41	0.37 – 0.73	<0.0001	0.20	0.06 – 0.43	0.008
Δ NMSS	0.57	0.16 – 0.25	<0.0001	0.29	0.05 – 0.15	<0.0001
Δ ADLS	-0.48	-0.62 – -0.36	<0.0001	-0.25	-0.39 – -0.10	0.001
PDQ-39 at baseline	-0.20	-0.32 – -0.05	0.005	-0.20	-0.29 – -0.06	0.002
B) EUROSHIS-QOL8						
Caregiver						
Δ BDI-II	-0.14	-0.029 – -0.001	0.039	0.24	0.01 – 0.04	0.001
Δ ZCBI	-0.04	-0.011 – 0.006	0.530	0.02	-0.00 – 0.01	0.679
Δ CSI	-0.09	-0.078- 0.016	0.201	-0.03	-0.06 – 0.03	0.604
Δ EUROHIS-QOL8	0.41	0.454 – 0.878	<0.0001	0.39	0.49 – 0.89	<0.0001
Patient						
Δ BDI-II	-0.63	-0.053 – -0.037	<0.0001	-0.55	-0.03 – -0.66	<0.0001
EUROHIS-QOL8 at baseline	0.39	0.024 – 0.049	<0.0001	-0.37	-0.65 – -0.36	<0.0001

Dependent variable: change in the PD patient from V0 to V2 (Δ) in the PDQ-39 (A) and EROHIS-QOL8 (B). β standardized coefficient and 95% IC are shown. [a], univariate analysis; [b], multivariate analysis: A) Durbin-Watson test=2.07; R^2=0.51; B) Durbin-Watson test=2.02; R^2=0.68. Only significant variables (p<0.01) from the patient in the multivariate analysis are shown. Covariates from the patient included were the change from V0 to V2 (Δ) in LEDD, UPDRS-III-OFF, UPDRS-IV, FOGQ, PD-CRS, NMSS, PDSS, QUIP-RS, NPI, VAS-PAIN, VAFS, ADLS, and the score on the PDQ-39SI (A) and EUROHIS-QOL8 (B) at baseline.

ADLS, Schwab & England Activities of Daily Living Scale; BDI-II, Beck Depression Inventory-II; CSI, Caregiver Strain Index; FOGQ, Freezing Of Gait Questionnaire; LEDD, levodopa equivalent daily dose; Non-Motor Symptoms Scale; NPI, Neuropsychiatric Inventory; PD-CRS, Parkinson's Disease Cognitive Rating Scale; PDQ-39, the 39-item Parkinson's disease Questionnaire Summary Index; PDSS, Parkinson's Disease Sleep Scale; QUIP-RS, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAS, Visual Analogue Scale; ZCBI, Zarit Caregiver Burden Inventory.

Table 2. Effect of changes in the caregiver over the change in health-related and global QoL in PD patients from the COPPADIS cohort after 2-year follow-up (n=192).

EPO-619

Bilateral staged VIM thalamotomy for essential tremor

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Background and aims: Unilateral MRI-guided focused ultrasound (FUS) VIM thalamotomy has established efficacy in tremor relief. However, data regarding the safety and efficacy of bilateral staged treatments is scarce. We report our preliminary results on the safety and efficacy of bilateral staged FUS VIM thalamotomy in essential tremor (ET) patients with severe medication resistant tremor.

Methods: Five patients underwent bilateral staged FUS VIM thalamotomy. Primary outcome was change in tremor score relative to baseline using the Clinical Rating Scale for Tremor (CRST). Secondary outcome was change in quality of life (QOL) in ET (QUEST) score relative to baseline. Adverse event profile was collected.

Results: Tremor significantly improved following bilateral treatments from a median score of 33 at baseline to median score of 8 at 1 month, following second treatment p=0.006. Quest score improved from a median score of 36 before FUS to a median score of 7 at 1 month, p=0.02. All 5 patients experienced mild transient ataxia that resolved (2 days-12 weeks). One patient reported burning tongue sensation that did not resolved at his 1 month visit. One patient reported asthenia and another reported mild facial nerve palsy, both resolved after 3 weeks.

Conclusion: Our preliminary results suggest that staged bilateral MRI-guided focused FUS thalamotomy is safe and effective. It improves tremor and quality of life of ET patients with severe medication resistant tremor. Larger studies and longer-term follow-up are needed to validate these findings.

Disclosure: Nothing to disclose.

EPO-620

Characterization of gait profiles in patients with atypical parkinsonian syndromes

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Background and aims: Impaired gait and postural instability are common symptoms in atypical parkinsonism. Therefore, an early detection of abnormal gait patterns is important for fall prevention. This prospective, multicentric study aims to systematically characterize gait, clinical and cognitive functions of patients with multiple system atrophy (MSA), progressive supranuclear gaze palsy (PSP) and idiopathic Parkinson's disease (IPD).

Methods: Patients were included with stable medication without comorbidities affecting mobility. All participants were assessed using the MDS-UPDRS for motor function and the Montreal Cognitive Assessment (MoCA) for cognition. To characterize mobility, we used sensor based gait analysis with a standardized test battery including a 20-meter-walk-test and a Timed-Up-and-Go (TUG) test.

Results: We assessed 22 MSA, 19 PSP and 39 IPD patients. MSA and PSP had shorter disease duration (p<0.001) and greater motor impairment (MDS-UPDRS III p<0.001) compared to IPD. PSP patients were cognitively most impaired (MoCA p<0.003). Significant differences in 20-meter-walk-test were detected in stride length (mean (m): MSA=0.93, PSP=1.10, IPD=1.27; p<0.001), gait velocity (mean (m/sec): MSA=0.83, PSP=0.88, IPD=1.14; p<0.001) and heel strike angle (mean (°): MSA=-8.0, PSP= -15.5, IPD=-17.9; p<0.001). Parameters directly correlated with fall frequency. The TUG was completed faster by IPDs compared to MSA and PSP patients (p<0.001).

Conclusion: These preliminary data show significantly impaired gait in patients with atypical parkinsonism, correlating with the severity of motor impairment and the frequency of falls. Sensor-based gait analysis is an effective and rater-independent way to objectify gait disturbances and fall-risk. Especially in the context of clinical trials, this can be used as a supportive outcome measure.
Disclosure: Nothing to declare.

EPO-621

Iron deposition in thalamic subregions in early drug-naïve Parkinson's disease patients with mild cognitive impairment

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Background and aims: Iron deposition using Quantitative Susceptibility Mapping (QSM) has been reported in several cortico-subcortical areas within the dopaminergic pathways in patients with Parkinson's disease(PD)and a relationship with cognitive decline has been proposed. Mild cognitive impairment (MCI) is a common non-motor symptom in PD and is considered a risk factor for development of dementia. We aimed at exploring the QSM signature underling MCI in drug-naïve PD patients, focusing on several areas, particularly on the thalamic subregions.
Methods: 3T MRI images of 59 drug-naïve PD patients (20 PD-MCI and 39 PD-noMCI) were analyzed and compared. QSM values were extracted from several subcortical deep gray matter nuclei and 16 thalamic subregions. A partial correlation analyses were run between MRI metrics and clinical data. A ROC curve was performed to test the ability of QSM values in distinguishing PD-MCI from PD-noMCI.
Results: PD-MCI patients showed higher susceptibility values in right subthalamus, in bilateral inferior pulvinar and in bilateral ventral posterolateral thalamus. Moreover, higher susceptibility values in the thalamus correlated with worse motor/cognitive severity and quality of life in patients. ROC curve analysis showed that QSM values extracted from left inferior pulvinar and right ventral posterolateral thalamus could significantly identify the presence of MCI in drug-naïve PD.
Conclusion: This study provides evidence of higher iron deposition within lateral and posterior regions of thalamus in PD patients with MCI patients compared to those without. These findings may reflect the presence of diffuse neuropathological changes occurring at the disease onset, potentially leading to altered cognitive processing and sensorial perception/integration in PD patients.
Disclosure: Nothing to disclose.

EPO-622

Real-World Local Field Potential Dynamics in Patients with Parkinson's Disease

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Background and aims: To determine spectral peak and band power dynamics over time in patients with Parkinson's disease (PwPD) and deep brain stimulation.
Methods: A total of 26 PwPD (age: 67.0[56.8–73.1] years; sex: 8 females; disease duration: 12.0[7.8–15.0] years) with repeated local field potential (LFP)recordings (days between recordings: 33.9[11.0–65.1] were included in this analysis. PwPD with LFPrecordings within 2-weeks of macroelectrode implant were labeled as Acute (n=12). Peak amplitude and frequency, in addition to alpha, low-beta, high-beta, and gamma band power, were calculated for each hemisphere.
Results: Peaks were detected in 41/51(80.4%) nuclei with recordings at the initial session and 43/51(84.3%) nuclei at follow-up. Of the patients with bilateral implants (n=26), 24(92.3%) at visit 1 and 25(96.2%) at visit 2 had at least 1 hemisphere with an identifiable peak. No differences were seen in peak amplitude (left-hemisphere: p=0.695; right-hemisphere: p=0.162) and frequency (left-hemisphere: p=0.320; right-hemisphere: p=0.576) between visits for the cohort. Right-hemisphere low-beta (p=0.018) and bilateral gamma (left-hemisphere: p=0.036; right-hemisphere: p=0.014) band power demonstrated a significant increase at follow-up. No differences were found in the relative change of peak amplitude, frequency, or band power between patients with acute and chronically implanted macroelectrodes (p>0.05).
Conclusion: Our findings provide early, real-world evidence of LFP peak and band power stability in PwPD. Importantly, peak characteristicsdemonstrated no differences between visits or between patients with acute and chronic macroelectrode implants. Moreover, peak detection was stable across timepoints. These findings have implications as LFPsare proposed to be a biomarker for guiding DBSprograming and novel stimulation patterns.
Disclosure: A. Singer, C. Sannelli and N. Morelli are employees of Medtronic, Minneapolis, MN, USA. A. Fasano, H. Mure, G. Oyama and T. Witt are Principal Investigators of the Medtronic Product Surveillance Registry.

Movement disorders 5

EPO-623

Complications of gastrojejunostomy in patients with Parkinson's disease on levodopa/carbidopa intestinal gel treatment

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Background and aims: One of the treatment options of advanced Parkinson's disease is the administration of levodopa/carbidopa intestinal gel (LCIG) through percutaneous endoscopic gastrostomy with jejunal extension (PEG-J), potentially associated with various complications.
Methods: We retrospectively analyzed complications of inserted PEG-J in patients with LCIG in years 2009-2022 at the 2nd Department of Neurology CU in Bratislava (Movement Disorders Centre).
Results: 80 PEG-J were introduced at our centre, two patients died within 30 days of aspiration bronchopneumonia. Of the remaining 78 patients, 47 patients have completed the treatment – 32 patients died, six patients decided to terminate LCIG at their own request, six for non-cooperation, one for skin phlegmon in the PEG-J insertion area, one for buried bumper syndrome and one for gastrointestinal discomfort. Median (min-max) of LCIG treatment duration was 3 (0–11) years and had 2 (0–9) complications per patient. A total of 190 PEG-J revisions were carried out: 42 cases for the inner tube knotting, 37 for the inner tube disconnecting, 31 for the inner tube occlusion, 19 for the inner tube dislocation, 12 for accidentally pull out of the tube, 11 for leakage in the insertion area, eight for malfunction of connectors, two for leakage of the inner tube and 28 patients for PEG-J wear or the cause of the deterioration has not been identified.
Conclusion: Despite frequent complications with need repetitive gastrofibroscopies, less than 10% of patients were finished the treatment for dissatisfaction.
Disclosure: Nothing to disclose.

EPO-624

Managing Parkinson's Disease during pregnancy: A case report

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Background and aims: Since only 5% of cases of Parkinson's disease (PD) present before the age of 40, pregnancy is a rare but feasible occurrence with only a few cases reported.
Methods: A 38-year-old patient with a familiar PARK6 form of PD diagnosed at 25-year-age became pregnant while receiving 800/100 mg/day of L-DOPA/carbidopa (LD/CD) and 6mg of rotigotine. She became aware of her pregnancy at week 23, while associating significant worsening of motor fluctuations with wearing-off and dystonic postures during off period. LD/CD was increased up to 1200/150 mg/day with significant improvement of symptoms, returning to her previous motor situation. Rotigotine was maintained. At 39 gestational weeks she had a cesarean delivery because of podalic presentation. The newborn showed no malformations and is healthy at 6 months follow-up.
Results: There is little information about the effects of pregnancy on PD. Most studies suggest it can worsen its symptoms due to changes in hormonal production and pharmacological metabolism. Knowledge regarding anti-pakinsonian drugs during pregnancy is very limited, with LD being the first-line treatment since it has not been associated with significant adverse effects. Dopamine agonists are thought to be safe, with no reports of rotigotine usage during pregnancy in PD in the literature.
Conclusion: Pregnancy in PD patients is uncommon, with limited information published about its effects and management. We present the case of a pregnant PD patient who received anti-parkinsonian treatment with no complications during pregnancy or the newborn's health.
Disclosure: The authors report no sources of funding and no conflicts of interest related to this presentation.

EPO-625

First description of Episodic kinesigenic dyskinesia 1 with epilepsy in a large Moroccan family with the PRRT2 mutation

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Background and aims: Episodic kinesigenic dyskinesia 1 (EKD1, MIM≠128200), more commonly called paroxysmal kinesigenic dyskinesia (PKD), is a rare movement disorder disease, very heterogeneous clinically and characterized by recurrent and brief attacks of involuntary movement triggered by sudden voluntary movement without alteration of consciousness

Methods: A large family of Moroccan origin (RBT-ELB), with four affected siblings with suspicion of kinesigenic dyskinesia, was recruited in the department of Clinical Neurophysiology of Hôpital des Spécialités of Rabat (Morocco).

Results: We report the first description of PKD in a Moroccan family with the c.649dupC mutation in PRRT2 gene found in 4 patients. Five affected family members were identified (one female and 4 mans) with age of onset around puberty except for one who presented seizures during his first year of life. PKD manifested as brief ballic and/or dystonic attacks, precipitated by sudden movements with variable severity and frequency amongst affected family members. The consciousness was fully preserved during the attacks. Nevertheless, epileptic manifestations were associated with the dyskinetic attacks in 3 cases. The disease course was favorable using carbamazepine and two patients did not seek pharmacological treatment.

Conclusion: Epilepsy and other paroxysmal disorders have already been described in PKD patients with PRRT2 gene mutation. The epileptic phenotypes frequently reported are infantile convulsions with choreoathetosis syndrome ICCA), benign familial infantile seizures. Interestingly, the index patient experienced an adult-onset epilepsy, in addition to the typical attacks of kinesigenic dyskinesia, which is not a common finding in the literature

Disclosure: Nothing to disclose.

EPO-626

Cardiovascular, pelvic and laryngeal functions in multiple system atrophy: a neurophysiological comparative study

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Background and aims: Cardiovascular dysfunction is a prominent manifestation of autonomic failure in multiple system atrophy (MSA). The electromyographic finding of neurogenic damage of the external anal sphincter (EAS) corroborates Onuf's nucleus degeneration in MSA. Electrophysiology is also useful to detect vocal cord correlates of stridor, which contributes to the poor prognosis of these patients. It is unclear whether the neurodegenerative process evenly involves the different areas underlying the variety of symptoms in MSA. In this retrospective study, we explored the links between the clinical and neurophysiological correlates of vagal and sympathetic cardiovascular impairment, pelvic dysfunction, laryngeal abnormalities, parkinsonism, and cerebellar ataxia in MSA patients.

Methods: 61 patients diagnosed as clinically established MSA performed clinical evaluation, cardiovascular reflex tests, and EAS electromyography. Subgroups of 56 and 42 patients also underwent 24-hour blood pressure monitoring and laryngeal electromyography, respectively. In particular, we identified the presence of neurogenic damage and the specific electromyographic pattern of EAS and vocal cord muscles according to previously published electrophysiological classifications.

Results: The multivariate analyses by means of Spearman's rho coefficient did not show any correlation among parameters deriving from cardiovascular reflex tests, nocturnal blood pressure profiles, electrophysiological features of EAS and vocal cord muscles, and severity of motor impairment.

Conclusion: It could be speculated that the neuronal loss within Onuf's nucleus, intermediolateral cell columns, nucleus ambiguus, striatum and cerebellum might not go in parallel in MSA. The multifaceted neurodegeneration may indeed involve several regions to varying degrees or at different disease stages.

Disclosure: Nothing to disclose.

EPO-627

Subjective quality of life (QoL) in patients with Parkinson's disease (PD) - PDQ39 and SEIQol (5-year follow-up)

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Background and aims: PDQ39 (Jenkinson et al., 1995, 1997) is commonly used tool in PD but often doesn't reflect the subjective QoL (e.g. income, partnership...). In a 5-year follow-up study with PD patients, we compared PDQ39 and SEIQoL (McGee et al., 1991) with respect to acceptance, drop-out rates and the most important domains. We aimed to analyse whether there is a correlation between PDQ-39 and SEIQoL sum-scores. Additionally, we examined the overlap between aspects nominated in SEIQoL and domains captured by PDQ-39.
Methods: 31 patients (9 female, mean age at BL 67.23 (±5.95 years) disease duration 3.87 (±3.98 years)) were analysed and assessed at baseline and over a 5-years. PDQ-39 consists of eight domains, from which a sum-score can be calculated (0=best value, 100=worst possible value). SEIQoL invites each patient to nominate 5 aspects and to weight those. Correlations between PDQ-39 and SEIQoL sum-scores were calculated using Spearman's Rank correlations and mixed linear model (GLMM).
Results: The GLMM showed a significant association of p=0.0402 between PDQ-39 and SEIQoL sum-scores. This significance however vanished once LED was added as a control variable. SEIQoL aspects revealed the relevance of social environment and social relationships. PDQ-39 domains showed the worst score in cognition. SEIQoL: Social environment 14%, autonomy 13%, health 11% PDQ39: cognition 35%, stigma 30%, mobility 12%
Conclusion: The disease-related and individual QoL in this analysis did not overlap. Therefore, both instruments can complimentary be used in QoL research of PD patients.
Disclosure: Nothing to disclose.

EPO-628

Social cognition and emotional processing in functional movement disorders

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Background and aims: It is unknown how potentially altered processing of social information may affect the clinical presentation and severity of functional movement disorders (FMD). Our objective was to assess the social cognition (Theory of Mind) and emotional processing (alexithymia) in FMD patients.
Methods: Twenty one patient with clinically established FMD and 19 age, sex and education matched patients with "organic" movement disorders (OMD) underwent a thorough evaluation of psychiatric and cognitive characteristics. Faux Pas situation recognition stories and images for Reading the Mind in the Eye Test (RMET) were used to assess the ToM, while 20-item Toronto Alexithymia Scale (TAS-20) was used for alexithymia analysis.
Results: Compared to OMD, patients with FMD had higher scores for depression, anxiety, and non-motor symptoms, and lower score of the ACE-R subscale for fluency. FMD group in comparison to OMD had lower scores on recognition of Faux Pas (40.8±23.3 and 57.0±19.2, p=0.022) and Ne-Faux Pas situations (57.9±26.0 and 79.2±18.8, p=0.032), while RMET scores did not differ between groups. Also, FMD patients were more alexithymic in comparison to OMD (58.9±9.1 and 48.9±7.5, p=0.001). The lower scores on fluency, language, and attention ACE-R subdomains correlated with ToM deficiency in FMD. The association of different psychiatric symptoms (anxiety, depression, apathy and non-motor symptoms) with the severity of alexithymia in both study groups was shown.
Conclusion: The results of our study show that impairment of social cognition and altered emotional processing are present in FMD, and may represent a significant etiopathogenetic factor.
Disclosure: Nothing to disclose.

EPO-629

Effect of impulse control disorders and related behaviors in quality of life in Parkinson's disease.

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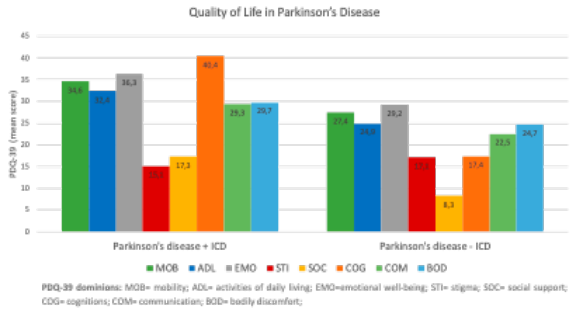
Background and aims: Impulse control disorders (ICD) and related behaviors represent a common psychiatric complication in patients with Parkinson's disease (PD) receiving dopaminergic replacement therapy, particularly dopamine agonists (DA). We aimed to assess the impact of these disabling disorders in quality of life (QoL).
Methods: We performed a cross-sectional study that included 30 patients with PD and ICD (PD+ICD) and 30 patients with PD without ICD (PD-ICD). All 60 patients were previously exposed to DA. Demographic and clinical data were obtained by clinical records and formal interview. The participants underwent a comprehensive neuropsychological evaluation including cognitive assessment, motor and non-motor status, measures of impulsiveness, apathy, ICD, depression, and anxiety. Impact in QoL was assessed by the Parkinson's Disease Questionnaire (PDQ-39).
Results: The mean age of disease onset was 52,8 y.o. in PD+ICD patients and 58,1 y.o. in PD-ICD (p=0,01). Hypersexuality and pathological gambling were the predominant ICD in PD+ICD patients. Scores in QoL were significantly worse in social support and cognition dominions in PD+ICD patients compared with PD-ICD (17,3 vs. 8,3; p=0,02 and 40,4 vs. 17,4; p=0,001 respectively). Non-motor symptoms burden was significantly higher in the PD+ICD group. Prevalence of apathy, impulsiveness, anxiety and depression were also significantly higher in PD+ICD patients. DA dose and subtype did not significantly differed between the 2 groups.
Conclusion: In this study, QoL, non-motor symptoms burden and mood disorders were found to be worse in PD patients with ICD compared to those without ICD. These results highlight the disabling effect of ICD and related behaviors in PD patients wellbeing.
Disclosure: Nothing to disclose.



EPO-630

Alien hand as a transient post-ictal phenomenon – a case series

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Background and aims: Alien limb (AL) refers to involuntary limb activity in which patients report loss of control over the affected limb. Isolated AL is encountered in patients with well-defined lesions, such as stroke or tumour, while in neurodegenerative diseases, AL coexists with other motor and cognitive deficits.
Methods: Clinical evaluation, video recordings and EEG recordings of three patients with post-ictal AL.
Results: 81-yo female was admitted due to epileptic status, caused by an old ischemic lesion in the right temporo-occipital cortex (Figure 1). Postictally, AL was observed in the left arm and leg along with left-sided neglect and Balint syndrome: optic ataxia, oculomotor apraxia and simultagnosia. The symptoms completely subsided after 4 days. 68-yo male was admitted after a series of seizures, caused by an old vascular lesion in the left occipito-parietal cortex (Figure 2). Post-ictal confusion, right arm Todd's paresis and postictal aphasia were followed by right arm AL that continued for 2 days. 81-yo female was admitted due to a convulsive seizure, caused by old ischemic lesions in the left temporo-occipital cortex (Figure 3). Postictal Todd paresis in the right arm was followed by right arm AL which subsided after 2 days. In all cases, prolonged EEG recordings ruled out seizure activity during episodes of AL.

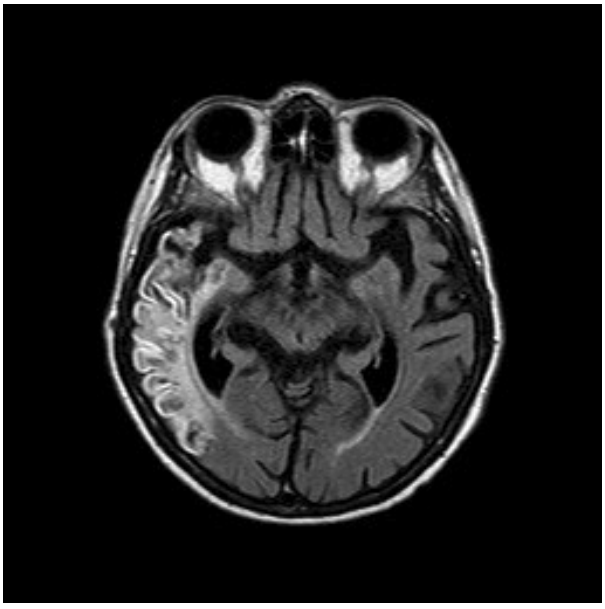

Figure 1: Patient no. 1 - FLAIR sequence showing post-ischemic encephalomalacia in the right occipital and temporo-occipital cortex.

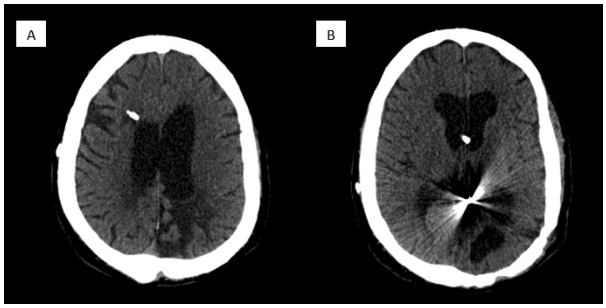

Figure 2: Patient no. 2 - CT scan showing A) encephalomalacia in the left occipito-parietal cortex after aterio-venous malformation (AVM) haemorrhage and B) surgical material near the corpus callosum splenium, left after AVM resection.

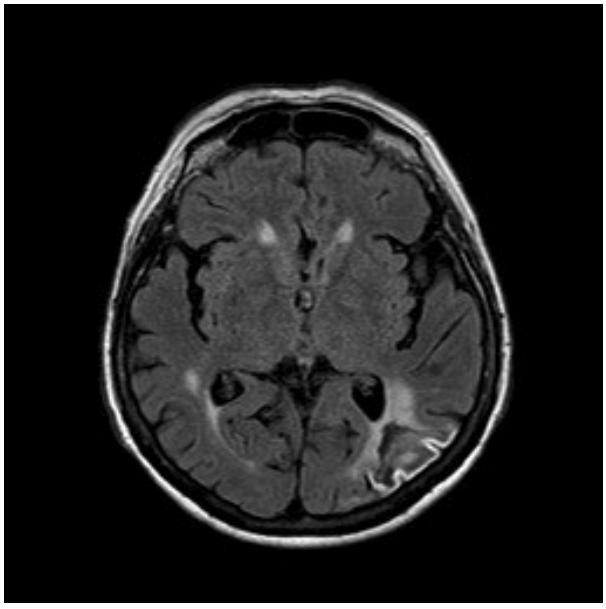

Figure 3: Patient no. 3 - FLAIR sequence showing post-ischemic encephalomalacia in the right temporo-occipital cortex.

Conclusion: Transient post-ictal AL may be observed in patients with posterior cortical lesions. Pathophysiologically, it may arise from postictally suppressed parietal areas, causing disinhibition of the motor areas (transitory disconnection) along with a lack of sense of agency.
Disclosure: Nothing to disclose.

EPO-631

Salivary biomarkers in Parkinson's disease: alpha-synuclein and beyond

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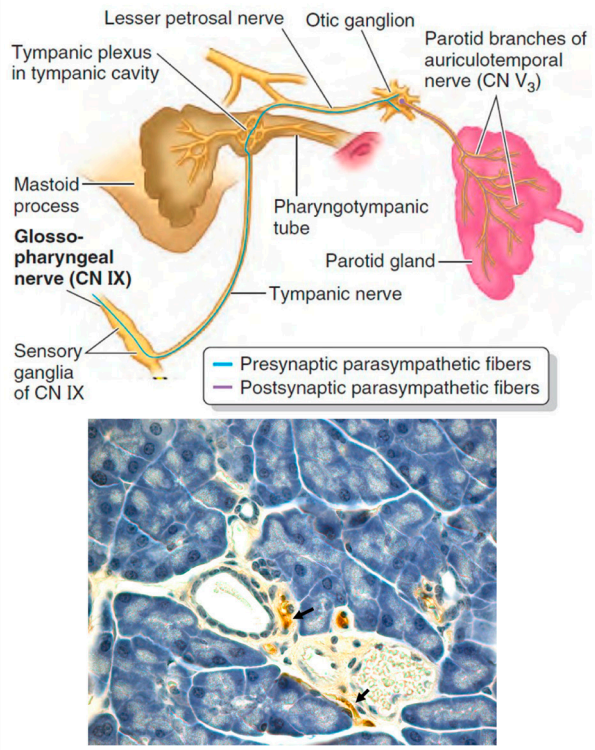
Background and aims: Parkinson's Disease (PD) is characterized by the accumulation of misfolded alpha-synuclein (a-syn) and by the activation of different molecular pathways, converging in neuronal death and synaptic loss. Clinical diagnosis and treatment of PD are hampered by the progressive deterioration of target neuronal circuits and by the mismatch between clinical and neuropathological onset. Molecular biomarkers are of unreplaceable importance to couple neuropathological and clinical features. Saliva is an easily accessible biofluid, whose collection is free of pain and discomfort for the patient and which has recently demonstrated a great potential as source of biomarkers for PD.
Methods: ELISA analysis and Real-Time Quaking Induced Conversion (RT-QuIC) assay have been applied to detect a-syn aggregates, tau aggregation, inflammation and autophagy biomarkers, in the saliva of 80 de novo PD patients and 65 healthy subjects. Molecular data have been correlated with clinical features of PD patients and used for molecular clustering though principal component analysis (PCA).
Results: Reduced levels of total a-syn and increased levels of a-syn aggregates have been demonstrated in the saliva of PD patients by ELISA. Moreover, RT-QuIC assay demonstrated seeding competent a-syn species in the saliva of PD patients and RT-QuIC kinetic parameters correlated with disease severity. Finally, autophagic markers and inflammatory markers were increased in the saliva of PD patients and were responsible of the molecular clustering of PD patients.
Conclusion: Saliva represents a key biofluid candidate for the detection of biomarkers in PD and could be also used for clustering different PD subtypes, improving molecular diagnosis and follow-up.
Disclosure: We have no disclosures.



Schematic representation of the innervation of the parotid gland and alpha-synuclein immunostaining showing the presence of alpha-synuclein positive fibres in the connective storma around the secretory cells of the salivary glands (arrows).

EPO-632

A case report of parkinsonism due to Coxsackie B virus infection

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Background and aims: Since encephalitis lethargica, the pathophysiology of viral parkinsonism has largely remained a mystery. The distinction of directly virus-mediated vs. parainfectious-autoimmune mechanisms is also clinically relevant.
Methods: Case report.
Results: A 73-year-old man without history of neurological symptoms presented with new onset of fatigue, gait disturbance and tremor. Clinical examination showed predominantly axial and only mildly asymmetric parkinsonism with mild cognitive impairment and orthostatic hypotension. Brain MRI showed mild small vessel disease. DaT scan showed decreased tracer uptake in putamen and caudate, predominantly on the right. Cerebrospinal fluid (CSF) analysis revealed pleocytosis (51 cells/µl, 12% neutrophils), elevated protein and absence of intrathecal IgG synthesis. Various neuronal autoantibodies tested negative in serum and CSF. Assuming a parainfectious autoimmune aetiology and while waiting for the viral metagenomics, a steroid pulse with oral tapering was initiated, but showed no benefit apart from improved fatigue. Neither levodopa nor amantadine showed any effect on parkinsonism. Viral metagenomics in CSF was positive for enterovirus, specified by serology as Coxsackie B1 virus. After therapy with intravenous immunoglobulin, however, the patient started to improve. On last follow-up, CSF showed only mildly elevated CSF protein, no pleocytosis and no traces of Coxsackie B virus-RNA.
Conclusion: Differentiating viral parkinsonism from an autoimmune-mediated etiology is challenging but important for treatment strategies. This case highlights the relevance of CSF cytology (the neutrophils were the reason to do viral metagenomics) and the need for better pathophysiological understanding.
Disclosure: There are no financial disclosures or conflicts of interest concerning this research item.

EPO-633

Symptomatic treatment of Huntington's disease (HD) chorea in Polish sites.

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Background and aims: Various drugs are used in management of chorea in HD patients, but there is limited data confirming efficacy. We compared motor symptoms and cognitive competence in HD patients on stable doses of tiapride, olanzapine, tetrabenazine and risperidone for one year.

Methods: We analyzed first-choice drugs for motor symptoms in patients from REGISTRY and Enroll-HD studies of two Polish Sites: Warsaw-IPiN and Poznan. Among 650 subjects (510 from Warsaw-IPiN and 140 from Poznan) we selected 79 patients treated with: tetrabenazine (n=27), tiapride (n=33), olanzapine (n=13) risperidone (n=6) and received stable doses for one year. Total motor score (TMS), chorea and dystonia subscore, cognitive tests at the beginning and after a year were compared.

Results: In all groups except tetrabenazine, changes in total TMS score were insignificant. TMS score significantly increased in a tetrabenazine group △=3.7 pkt, p=0.05 (t-test).Significant reduction in chorea subscore was found in tiapridal group (△=-3.6 pkt, p=0.002 t-test), in other groups was insignificant, buy accompanied with an insignificant increase in dystonia subscore. Patients treated with tetrabenazine characterized with significant decrease of cognitive performance (Stroop interference test △=-3.84, p=0.01, MMSE △=-1.8, p=0.03). In other groups tests results were either insignificantly worser (olanzapine, risperidon) or better (tiapride).

Conclusion: Tiapride, tetrabenazine and olanzapine are the most often first choice drugs in management of chorea in Polish HD Sites: Poznan and Warsaw-IPiN, however their efficacy in one year of observation is insignificant. This could be explained by HD progression and limited neuroprotective effect. Moreover, they may have a negative impact on cognitive abilities.

Disclosure: All authors report no conflict of interests.

EPO-634

Acoustic analysis of speech in Parkinson's disease with motor fluctuations

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Background and aims: Speech disorders of the nature of hypokinetic dysarthria are one of the most common symptoms of PD. The assessment of motor symptoms using non-invasive mobile devices that would enable monitoring of the patient's condition also outside the medical facility may be helpful in precise adjustment of appropriate doses of antiparkinsonian drugs to ensure optimal control of motor symptoms. The aim of the study was to assess the usefulness of speech acoustic analysis in tracking the severity of PD motor symptoms. To achieve the aim of the study, an assessment of the dependence of speech acoustic analysis parameters on the severity of PD motor symptoms was carried out.

Methods: The study involved 27 patients diagnosed with PD based on MDS criteria. Each patient was examined 5 times, at specific times: in the off state and 30-, 60-, 120- and 180-minutes after taking a standard dose of levodopa. At each measurement, speech was recorded, as well as an assessment of the severity of PD motor symptoms in part III of the UPDRS scale.

Results: All patients had a significant decrease in the UPDRS-III score after taking levodopa compared to OFF. In addition, dependencies were obtained that show a decrease in the value of all analyzed acoustic parameters with a decrease in the severity of disease symptoms.

Conclusion: Acoustic analysis of speech parameters is a sensitive marker of the severity of PD motor symptoms and can be used in practice in evaluating the patient's condition, selecting drug dosages and tracking the rate of disease progression.

Disclosure: Nothing to disclose.

EPO-635

Deep-learning-based quantification of the Pull Test for assessment of postural instability in parkinsonian syndromes

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Background and aims: Postural instability and falls are major complications in advanced Parkinson's disease (PD). Clinical evaluation of postural instability in PD and related movement disorders is most commonly based on the Pull Test (PT) that examines the ability to recover from a backward pull on the shoulder, which closely correlates with patients' risk of falling. Clinical application of the PT suffers, however, from several shortcomings such as lack of consensus on the proper execution and a subjective scoring system that both contribute to a low intra- and inter-rater reliability.
Methods: Here, we seek the potential to objectify the execution and patient performance during PT by means of deep-learning-based multi-person pose estimation applied on RGB-D recordings (Microsoft Kinect Azure) of PT examination in a cohort of healthy individuals (n=16) and exemplary patients with idiopathic and atypical PD.
Results: We demonstrate that our approach enables both, an objective monitoring of PT execution (pull strength) and quantitative assessment of patients' postural responses (pull-to-step latency, number of steps, etc.), and allows to reliably discriminate pathological from healthy performance.
Conclusion: Video-based quantitative PT assessment may thus facilitate increased sensitivity and specificity of clinical assessment of postural instability and risk of falling in PD.
Disclosure: No conflicts of interest to disclose.

EPO-636

The utilization of goal attainment scaling in cervical dystonia

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Background and aims: The heterogeneous manifestation of cervical dystonia (CD) makes the identification of the involved muscles and appropriate dose selection of the gold standard botulinum neurotoxin (BoNT) treatment challenging. Accordingly, the aim of the current study was to adapt goal attainment scaling (GAS), a widely used approach to set up treatment goals in the treatment of spasticity, into the individualised management of CD.
Methods: 38 patients with CD, receiving BoNT under ultrasound (US) guidance with standard injection points to the muscles selected according to the collum-caput (COL-CAP) concept, were involved. GAS, adapted with the inclusion of 11 possible domains, was applied to set up individualised goals with the calculation of initial GAS-T scores. Following at least 4 BoNT injections, patients were reassessed whether they reached the pre-set goals, and the GAS-T scores were calculated again.
Results: The initial GAS-T scores (median: 36.9, range: 22.8–40) significantly improved ($p<0.001$) to the end of the study (the median of final GAS-T scores: 50, range: 25.5–63.6). The major determinative factor whether to reach therapeutic aim of GAS-T score of 50 was that at least 50% of BoNT injections were performed according to the COL-CAP concept AND US guidance (odds ratio: 10.5, 95% confidence interval: 1.95–78.7).
Conclusion: In the lack of published studies in that issue the current was the first to demonstrate the applicability of GAS in setting up individualised therapeutic aims in CD in a measurable way. Furthermore, the utility of the COL-CAP concept AND US-guided injections in the management of CD were confirmed as well.
Disclosure: Nothing to disclose.

EPO-637

Inhibitory theta burst rTMS of the left primary and supplementary motor cortex decreases sway path in orthostatic tremor

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Background and aims: A ponto-cerebello-thalamo-cortical network is the pathophysiological correlate of primary orthostatic tremor (POT). Affected patients often do not respond satisfactory to pharmacological treatment. The objective of this study was to examine the effects of inhibitory rTMS of the left primary motor cortex (M1) and supplementary motor area (SMA) on tremor frequency, intensity, sway path and subjective unsteadiness in POT patients.
Methods: In a cross-over design eight POT patients (mean age 70.2±5.4 years, 4 female) received either rTMS of the left M1 leg area or of the left SMA at the first study session, followed by the respective other condition (SMA or M1) at the second study session 30 days later. Tremor frequency and intensity were examined by surface electromyography of lower leg muscles and total sway path by posturography (foam rubber with eyes closed) before and after each rTMS session. Patients subjectively rated postural stability on the posturography platform after each rTMS session.
Results: Tremor frequency and intensity did not change significantly with M1- or SMA-stimulation despite a tendency towards a decrease in tremor intensity after M1-stimulation (p=0.066). The sway path, however, decreased after M1-stimulation (p=0.001) and SMA-stimulation (p=0.046). Accordingly, POT patients indicated a better subjective feeling of postural stability both with M1-rTMS (p=0.014) and SMA-rTMS (p=0.02).
Conclusion: Non-invasive neuromodulation particularly of the M1 area seems a promising add-on therapy in POT.
Disclosure: Nothing to disclose.

MS and related disorders 7

EPO-638

Adding Animation to Case-based MS Education Improves Neurologists' Knowledge of DMT MoA & Competence in Implementation

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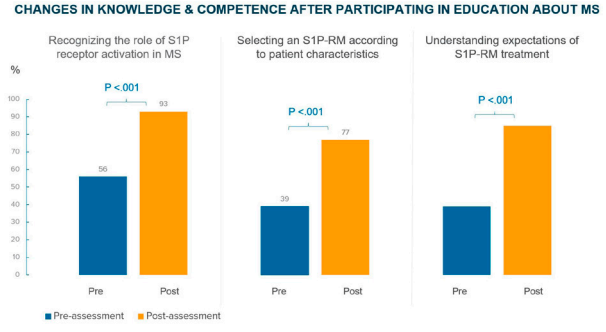
Background and aims: Understanding disease modifying therapy (DMT) mechanism of action in multiple sclerosis (MS) and relating this to implementation is important but challenging for neurologists to understand. To tackle this, we combined animation with MS case-based, text-based education.
Methods: Neurologists participated in a text, case-based activity, viewed animations, and completed pre- and post-questions. Educational effect was assessed using a 3-question repeated-pair design with pre-/post-assessment. A paired samples t-test was conducted for significance testing on overall average number of correct responses and for confidence rating, and a McNemar's test was conducted at the learning objective level (5% significance level, $p<0.05$). Cohen's d with correction for paired samples estimated the effect size of the education on number of correct responses. Data were collected from 3/21/2022–6/1/2022.
Results: Overall significant improvements at the aggregate level were seen after participation for neurologists (45% average correct response rate at pre-assessment vs 85% at post-assessment; $p<0.001$, Cohen's d= 1.25, n=61). Highly significant improvements were achieved with regards to the role of S1P receptor activation in MS, how to choose an S1P receptor modulator (RM) according to patient characteristics, and expectations of S1P-RM treatment (figure). After participating, 43% had measurable improved confidence ($p<0.001$), differentiating and selecting an S1P-RM.



Figure

Conclusion: This study demonstrates the success of this combination of educational elements in improving neurologists' knowledge of S1P-RM mechanism and competence in implementation.
Disclosure: Nothing to disclose.

EPO-639

MRI correlates of manual dexterity asymmetry in people with multiple sclerosis

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Background and aims: Motor, sensory and cerebellar symptoms are often lateralized in people with multiple sclerosis (pwMS). Here we explored associations between manual dexterity asymmetry and structural damage in pwMS and their relation to disability.
Methods: Three hundred thirty-four pwMS and 124 healthy controls (HC) underwent 3T MRI acquisition of 3D-T1-weighted and dual-echo sequences, used to extract left and right normalized brain volumes (cortical and deep gray matter and cerebellum) and lesion loads (cerebral and cerebellar). Hand dexterity was evaluated with the nine-hole peg test (NHPT). Asymmetry indexes (AIs) for these measures were calculated by subtracting left and right z-transformed values, determined based on HC group. Correlations between NHPT AI and AIs of structural measures were performed in HC and in pwMS stratified by disability, measured with the Expanded Disability Status Scale (EDSS) (mild=0–3.5; moderate=4.0–5.5; severe≥6.0).
Results: No side-specific lateralization of dexterity impairment or structural damage emerged in the examination of AIs in pwMS. Greater asymmetries (i.e. larger distributions of AIs) were observed in patients with moderate/severe disability, whereas mildly disabled pwMS had distributions similar to HC (see Figure). No correlations between structural and NHPT AIs were found in HC and mildly disabled pwMS. In moderately disabled pwMS NHPT AI correlated with cortical and deep gray matter volume AIs, while in pwMS with severe disability it was associated with cerebellar lesion load AI.

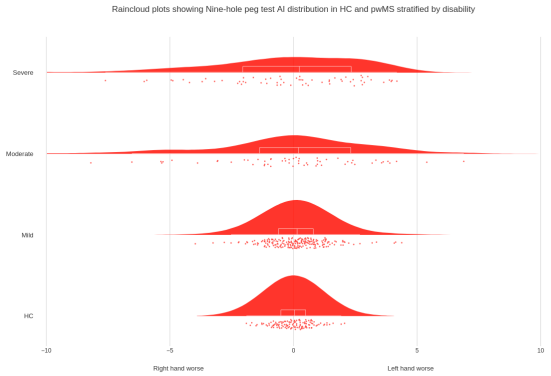

Figure. Raincloud plots showing nine-hole peg test AI distribution in HC and pwMS stratified by disability

Conclusion: Structural asymmetries are associated to asymmetry in NHPT, and both increase with disability in pwMS. Different structural substrates at different levels of disability underlie asymmetry in manual dexterity impairment.

Disclosure: The authors have nothing to disclose.

EPO-640

Structural and functional correlates of disability and gait in multiple sclerosis: focus on the globus pallidus

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Background and aims: The globus pallidus (GP) is divided into an internal (GPi) and an external (GPe) component. Here, we explored in people with multiple sclerosis (pwMS) the added role of studying structural and functional GPi/GPe damage, rather than as a whole, in relationship with clinical measures.

Methods: 60 pwMS and 30 matched healthy controls (HC) underwent 3T MRI including 3D-T1-weighted, dual-echo and resting state (RS) functional MRI. Timed 25-foot walk (T25FW) and Expanded Disability Status Scale (EDSS) were administered. Two operators segmented left and right GP into GPi and GPe starting from FSL FIRST masks (see Figure). Whole-GP, GPi and GPe normalized volumes and T1/T2 ratio were extracted, and seed-based RS functional connectivity (FC) was analyzed.

Results: PwMS had a higher T25FW than HC ($p<0.001$). The GP and its components were not atrophied in pwMS. Compared to HC, pwMS had higher T1/T2 ratio in all GP regions, which correlated with higher EDSS scores. At whole-GP RS FC analysis, pwMS showed decreased connectivity between left GP and right insula and between right GP and frontal cortices. They also showed increased connectivity between right GP and thalamus. When looking at RS FC of pallidal components, pwMS exhibited decreased connectivity between bilateral GPe and frontal cortices, as well as decreased intra-pallidal and increased thalamo-pallidal GPi connectivity. Lower GPe-frontal RS FC correlated with worse T25FW and EDSS scores.

Conclusion: Structural involvement of the GP in pwMS was similar across components. However, GPi and GPe showed specific RS FC alterations, which correlated with walking impairment and global disability.

Disclosure: The authors have nothing to disclose.

EPO-641

Impact of fatigue on spontaneous EEG topographies of patients with Multiple Sclerosis

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Background and aims: Fatigue is a disabling symptom in patients with Multiple Sclerosis (PwMS). Functional Magnetic Resonance Imaging studies demonstrated altered functional brain connectivity in fatigued PwMS (F-PwMS). Our purpose was to evaluate the impact of fatigue on resting-state networks, comparing EEG microstates of F-PwMS, non-fatigued PwMS (noF-PwMS) and healthy controls (HCs).
Methods: We enrolled 44 PwMS and 24 HCs, age and gender-matched. The Modified Fatigue Impact Scale (MFIS) was administered and the high-density EEG was recorded. Patients were divided into F-PwMS (MFIS-score>38, n=32) and noF-PwMS (MFIS-score<38, n=12). Microstates analysis was performed to identify stable scalp potential topographies, which best explained hdEEG variances of all participants. Mean duration (MD), time coverage, occurrence and global explained variance were computed for each map. All parameters of PwMS were standardized with respect to control by calculating the z-score. Differences between F-PwMS vs noF-PwMS were assessed by non-parametric statistical test. A correlation was performed between microstates parameters and fatigue data (alpha=0.05).
Results: We identified six stable scalp potential topographies (A-F). F-PwMS showed a significant decrease in the temporal dynamic of microstate F, and a significant increase in MD of microstate B, compared to noF-PwMS ($p<0.05$). A positive correlation between cognitive fatigue and activation of microstate B was found.
Conclusion: Our findings suggest that F-PwMs have a decreased activity of salience network and an increased activity of visual network, previously associated with microstate F and B respectively. The correlation of microstate B with cognitive fatigue suggests a possible marker for cognitive dysfunctions.
Disclosure: S. Baldini received funding from FISM; A. Sartori received travel grants and/or speaker honoraria from Biogen, Novartis, Merk, Roche, Sanofi, Almirall; L. Rossi, A. Dinoto, A. Favero, A. Bratina, P. Manganotti: nothing to disclose; F. Pasquin received travel grants from Genzyme and Biogen; A. Bosco received travel grants from Biogen and Roche.

EPO-642

Five-Year Safety of Ofatumumab in People Living With Relapsing Multiple Sclerosis

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Background and aims: Previously reported safety data from ALITHIOS open-label extension study for up to 4 years demonstrated that extended treatment with ofatumumab continues to show a favorable safety and tolerability profile in relapsing multiple sclerosis (RMS) participants. Here, we assess the longer-term safety profile of ofatumumab treatment for up to 5 years.
Methods: Participants completing core ASCLEPIOS I/II, APOLITOS and APLIOS clinical trials entered ALITHIOS. We analysed cumulative safety data for up to 5 years (cut-off: 25-Sep-2022) of ofatumumab treatment in the overall (n=1,969), continuous (ofatumumab in core+extension; n=1,292) and newly-switched (teriflunomide in core/ofatumumab in extension; n=677) groups. The analysis included proportion of participants with treatment-emergent adverse events (AEs), serious AEs (SAEs), injection-related reactions (IRRs), serious infections including COVID-19, malignancies, serum immunoglobulin (Ig)G and IgM levels and their association with serious infections.
Results: Overall, 89.9% of patients had ≥1 AEs (exposure-adjusted incidence rate/100 patient-years [EAIR], 124.6) and 14.7% had ≥1 SAEs (EAIR, 4.7) with low incidence of serious infections (5.4%; EAIR, 1.6) and malignancies (1.06%; EAIR, 0.3). Most COVID-19 cases were non-serious (92.3%) and recovered (96.1%) (Table). Overall, 2% of patients had IgG and 30.6% had IgM
Conclusion: Cumulative safety data for up to 5 years indicate that extended treatment with ofatumumab is well-

tolerated, with no new safety risks identified. These data inform physicians on the longer-term safety profile of ofatumumab in people living with RMS.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

Adverse event	Core, ASCLEPIOS OMB (N=946)		Core + extension, Overall OMB, (N=1969)	
	n (%)	EAIR (95% CI)	n (%)	EAIR (95% CI)
Patients with at least one AE	791 (83.61)	188.55 [175.86, 202.16]	1771 (89.9)	124.65 [118.97, 130.59]
Patients with at least one SAE	86 (9.10)	5.39 [4.36, 6.65]	289 (14.7)	4.68 [4.17, 5.26]
AEs leading to discontinuation	54 (5.70)	–	139 (7.1)	–
Infections and infestations	488 (51.58)	51.14 [46.80, 55.88]	1334 (67.75)	40.99 [38.85, 43.25]
Serious infections	24 (2.54)	1.44 [0.97, 2.15]	106 (5.38)	1.63 [1.35, 1.97]
Injection-related systemic reactions	195 (20.61)	15.49 [13.46, 17.83]	508 (25.79)	10.06 [9.22, 10.98]
Injection site reactions	103 (10.88)	7.21 [5.94, 8.74]	243 (12.34)	4.08 [3.60, 4.63]
Malignancies	5 (0.53)	0.32 [0.13, 0.77]	21 (1.06)	0.32 [0.21, 0.48]
Deaths	0	0	9 (0.46)	–

Safety Profile of Ofatumumab for Up to 5 years of Treatment

EPO-643

International Consensus on Smoldering Disease in Multiple Sclerosis using the Delphi Method

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Background and aims: Despite the successful therapeutic suppression of relapses and new MRI lesions, most people with multiple sclerosis (pwMS) experience neurological deterioration. Accumulating data suggest that multiple sclerosis (MS) in addition to being a disease related to acute focal inflammation, involves more widespread, smoldering pathogenic processes that impact the entire central nervous system from early stages of the disease. Understanding and better defining the biology underlying the clinical and radiological manifestations of smoldering pathological processes remain important unmet needs. Greater comprehension of smoldering disease will improve clinical management, promote drug research by identifying new targets, stratifying pwMS for clinical trials and aid pwMS in understanding the causes of disease worsening.

Methods: Fifteen MS experts from eight countries across Europe, US, and Canada convened to develop consensus-driven statements on smoldering disease across multiple domains. They employed the Delphi method to anonymously establish agreement on a 5-point scale with "consensus" defined a priori as >75% who agree or strongly agree.

Results: See Table

Table 1

Statements relating to definition of smoldering disease	Statements relating to disease worsening due to smoldering disease
Smoldering disease is considered an umbrella term characterizing chronic pathobiological processes occurring in the CNS, beyond acute focal inflammation, associated with neurodegeneration leading to clinical worsening in pwMS, that may start early and continues throughout the disease course.	Clinical disease worsening is not just associated with progressive stages of the disease but may be observed at early stages of the disease and throughout the course of MS
Progression independent of relapse activity (PIRA) should be considered primarily a clinical manifestation of smoldering disease and therefore those terms should not be used interchangeably	Disease worsening may be driven by smoldering disease activity, which may be present throughout the disease course (even before clinical features manifest) and may account for physical as well as cognitive dysfunction

Table

Conclusion: This expert panel aims to provide further definitions and recommendations to help raise awareness and educate the neurology community on smoldering disease as well as advise on its implementation into routine clinical practice. Full presentation and publication of all statements with supporting evidence are expected in 2023.

Disclosure: The concepts and contents of this abstract emerged from several meetings facilitated by Sanofi. The experts involved are paid for attending the meetings but not for any writing efforts. Medical writing support was provided by Lionel Thevathasan, MD from LT Associates Ltd who was funded by Sanofi.

EPO-644

Clinical characteristics of late-onset multiple sclerosis: a single centre retrospective cohort study

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Background and aims: Diagnosis of late-onset multiple sclerosis (LOMS), defined as symptom onset at >=50 years of age, is challenging. Despite an aging MS population and evidence of increasing incidence of LOMS, this entity remains scarcely described. We aimed to characterize LOMS patients in a tertiary centre and compare with published data.
Methods: Data was obtained from retrospective review of electronic clinical records. Patients were included if MS diagnosed according to 2017 McDonald criteria and age at symptom onset >=50 years. We retrieved data on demographic, clinical, imaging and laboratory characteristics. We performed a descriptive analysis of the cohort.
Results: We identified 24 LOMS patients, median age at symptom onset of 55.5 years (interquartile range [IQR]=8.75) and at diagnosis of 59 years (IQR=6). Most patients were female (62.5%, female/male ratio=1.7). Relapse-remitting MS (50%) was the most frequent MS subtype, followed by primary progressive MS (41.7%). All patients had registered comorbidities, being hypertension (62.5%) the most frequent. The most common presentation was as isolated medullary syndrome (58.3%). Median EDSS at last follow-up was 4.0 (IQR=2.5). Clinical progression was described in 58.3% and inflammatory activity in 45.8% (median follow-up=3 years, IQR=5). Cervical cord lesions were identified in 62.5% at diagnosis.
Conclusion: In our cohort, LOMS is characterized by high proportion of primary progressive phenotype and frequent medullary involvement, which is in line with previous studies. The high frequency of cardiovascular comorbidities may impact diagnosis and therapeutic decisions. LOMS should be considered in older people with new-onset acute or progressive neurological symptoms.
Disclosure: Nothing to disclose.

EPO-645

piRNA and miRNA in Multiple Sclerosis

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Background and aims: Multiple sclerosis (MS) is a common inflammatory demyelinating disease with a high mortality rate. MS is caused by many candidate genes whose specific involvement has yet to be established.
Methods: In order to establish the possible effect of miRNA and piRNAs on the MS candidate genes, we determined the interaction characteristics using the MirTarget program. Program defines the following features of miRNA and piRNA binding to mRNA: the initiation of the miRNA and piRNA binding to the mRNAs from the first nucleotide of the mRNAs, the localization of the piRNA and miRNA BSs in the 5′UTR, CDS and 3′UTR of the mRNAs, the schemes of nucleotide interactions between piRNAs, miRNAs, and mRNAs, the free energy of the interaction between piRNA and the mRNA.
Results: The piRNA BSs were predominantly located in the 3'UTR and only two genes were located in the 5'UTR and the TNFRSF1A gene in the CDS. The mRNAs of the IL2RA, MGAT5, and ZBTB46 genes each had one piRNA BS, and the mRNA of the MLANA gene had three piRNA BSs. ADAM17, AHI1, EVI5, and TNFRSF1A genes was the target of several piRNAs whose BSs were located with overlapping nucleotides, which we called clusters of BSs.
Conclusion: The piRNA and miRNA target genes were EOMES, ADAM17, AHI1, EVI5, IL2RA, and MGAT5. These genes were most dependent on piRNA and miRNA, and therefore, their associations with the corresponding piRNA and miRNA are the most suitable for use in MS diagnosis.
Disclosure: The EOMES, ADAM17, AHI1, EVI5, IL2RA, and MGAT5 genes were targets for piRNA and miRNA.

EPO-646

Pregnancy effect on disease activity in women treated with cladribrine

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Background and aims: Cladribrine is an oral pulsed therapy for relapsing multiple sclerosis (RMS).Hormonal and immune changes are responsible for the decline of disease activity in the third trimester of pregnancy and disease reactivation in the early post-partum period.To date there are no available studies on the pregnancy effect on disease activity in women with MS who conceived after cladribrine treatment.
Methods: We recruited women of childbearing age with RMS who became pregnant or not after being treated with cladribrine.For both groups, demographic,clinical and radiological data were collected one year before and after treatment to compare the disease activity.
Results: 47 childbearing women mean age 35.05 ys were included. 24 women had a pregnancy after a mean of 1.75 years from the first treatment cycle,5 pregnancies occurred between the first and second cycle.Women with or without pregnancy did not differ for demographics or disease activity pre cladribrine. No significant differences in disease activity post cladribrine were found between women with or without pregnancy (0.12 vs 0.04 for ARR p=0.36; 1.9 vs 1.1 p=0.65 for new T2 lesions and 0.29 vs 0.3 p= 0.60 for new gd+ lesions). No significant differences were found between women with pregnancy occurred between the first and second cycle or after the second cycle.
Conclusion: Pregnancy does not appear to influence disease activity in women previously treated with cladribrine; further studies with larger numbers are needed to confirm this finding and to identify the best timeframe to conceive after cladribine treatment that guarantees to be still protected from reactivation in the post-partum period.
Disclosure: Nothing to disclose.

EPO-647

NEDA-3 achievement in early highly active RR-MS patients treated with Ocrelizumab or Natalizumab

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Background and aims: the use of high-efficacy disease-modifying therapy(HE DMT)at the beginning of the Multiple Sclerosis(MS)may be the best strategy to delay or minimizing neurological damage and progression of the disease in the long term especially for highly active MS patients (HAMS).Natalizumab(NTZ) and Ocrelizumab (OCR) are considered HE DMT with a significant anti-inflammatory effect. Here we investigate the NEDA-3 achievement in naïve patients with HAMS treated with NTZ or OCR after two years of follow-up.
Methods: we retrospectively recruited naïve HAMS patients treated with NTZ or OCR and we collected demographic,clinical and instrumental characteristics before and after starting any treatment in order to compare disease activity, disability progression and NEDA-3 achievement.
Results: we recruited 141 naïve patients (pts) with RR-MS with(mean age 33.2±11.17) treated with NTZ (90 pts) or OCR(51 pts). Comparing disease activity pre and post therapies after six months of re-baseline,we registered a significant reduction of ARR from 1.47 to 0.015 for NTZ and from 1.24 to 0.030 for OCR without significant differences between treatments (p=0.36). Also for gd+ lesions we registered a significant reduction(1.31 vs 0.067 in NTZ and 1.29 vs 0.030 in OCR) without significant differences between treatments (p=0.46). Globally 81.6% of pts were NEDA-3 after two ys of follow-up, 87.3% (95% CI: 77.7–93.0) of NTZ pts and 72.6%(95% CI: 55.4–84.1) of OCR pts (p=0.026).
Conclusion: starting HE DMT with monoclonal antibodies for HAMS could achieve NEDA-3 in a high percentage of patients, however the drivers of response to therapy in this category of patients needs to be further investigated.
Disclosure: Nothing to disclose.

EPO-648

Prospective outcome analysis of multiple sclerosis cases reveals candidate prognostic markers

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Background and aims: Predicting long-term disability outcomes of multiple sclerosis (MS) cases is challenging. We prospectively analysed our previous MS cohort with initial cerebrospinal fluid (CSF) proteomics data to reveal disability markers after 8.2±2.2 years of follow-up.
Methods: Patients with regular follow-up visits were assigned into two groups: those with an age-related MS severity (ARMSS) score ≥5 (unfavourable course group, n=27) and ARMSS score <5 (favourable course group, n=67). A machine learning-based algorithm was applied to reveal candidate poor prognosis-associated initial CSF proteins, which were then measured in an independent MS cohort (verification group, n=40) by ELISA. Additionally, the correlation of initial clinical and radiological parameters with long-term disability was analysed.
Results: CSF alpha-2-macroglobulin (p=0.0015), apo-A1 (p=0.0016), and haptoglobin (p=0.0003) protein levels were significantly higher in the unfavourable course group than in the favourable course group. Among the clinical and radiological parameters, cerebral lesion load (>9 lesions) on magnetic resonance imaging, gait disturbance (p=0.04), and bladder/bowel symptoms (p=0.01) at disease onset were higher in the unfavourable course group, while optic nerve involvement evident on initial magnetic resonance imaging (P=0.002) and optic neuritis (p=0.01) were more frequent in the favourable course group. Correlation analyses between other clinical parameters and protein levels did not disclose reliable findings due to the small number of cases in the subgroups.
Conclusion: Higher levels of CSF alpha-2-macroglobulin, apo-A1, and haptoglobin proteins at disease onset are associated with a poor disease outcome and may have predictive value of long-term disability of MS cases.
Disclosure: Nothing to disclose.

EPO-649

Different initial treatment strategies and their impact on disability progression in Multiple Sclerosis

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Background and aims: Treatment approach in Multiple Sclerosis (MS) is changing. The classic escalation strategy is giving way to an early high-efficacy treatment. This renowned "inversion of the pyramid" is exhibiting promising results in different cohorts. This study aimed to identify how initial treatment strategy could be associated with the progression of disability, specifically the need for walking aid.
Methods: An observational, single-center, retrospective cohort study was conducted, including all patients in an MS center with relapse-remitting MS (RRMS) starting treatment between 2012–2022. Baseline characteristics (gender, age, diagnosis' delay) were assessed, and patients' classification according to treatment strategy for the first 2 years: escalation (ESC); early intensive (EIT); first treatment's efficacy (modest, moderate, high). A multivariate Cox regression was performed to compare the risk of reaching an Expanded Disability Scale Score (EDSS) 6.0.
Results: 303 patients were included: 67.7% were women, mean age at diagnosis was 36.3±11.2 years, mean diagnosis' delay was 2.17±4.474 years. Most patients began treatment with a low-efficacy drug (78.0%) and followed ESC strategy (70.6%). 18 patients reached EDSS 6.0 (5.9%), in a mean interval of 3.83±2.83 years. There was a lower risk in reaching EDSS 6.0 in EIT patients when the first treatment was a moderate or high efficacy drug (HR 0.150, CI 0.039–0.580, p=0.006).
Conclusion: In this cohort, MS patients selected for EIT strategy have a lower risk of disability progression when the first treatment is one of moderate or high-efficacy.
Disclosure: Nothing to disclose.

EPO-650

Does the target NEDA comply with functional measure changes after 2 years in early phase of Multiple Sclerosis?

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Background and aims: Few studies investigated the longitudinal changes of functional measures in people with MS (PwMS) with low disability. The aim of the study is to evaluate after two years of follow-up (2FU) the evolution of clinical and functional measures stratified for NEDA (no-evident-disease-activity).
Methods: We assessed PwMS at baseline and after 2FU: Six Minute Walking Test (6MWT), Timed up and Go test (TUG), Timed-25 Foot Walking (T-25FW), Fatigue Severity Scale (FSS), Twelve-Multiple Sclerosis Walking Scale (MSWS_12), Fullerton Advanced Balance-short (FAB-s), 9-Hole Peg Test (9-HPT), Manual Ability Mesure-36 (MAM-36), Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS).
Results: 57 PwMS were enrolled [baseline: 35F, mean age 38.97 (SD=10.76) years, mean disease duration 2.14 (SD=1.84) years, mean EDSS 1.41), 57 relapsing-remitting MS course; 2FU: mean EDSS 1.83]. At 2FU, 30 PwMS were NEDA (NEDAgroup) while 27 not (noNEDAgroup) In the NEDAgroup the number of PwMS worsened: 14 at 6MWT, 9 at TUG, 13 at FSS, 14 at T-25FW, 9 at MSWS-12, 10 at FAB, 21 at 9-HPT, 5 at MAM-36, 12 at SDMT, 11 at CVLT-II, 8 at BVMT-R. In the noNEDAgroup the number of improved: 9 at 6MWT, 12 at TUG, 14 at FSS, 11 at T-25FW, 10 MSWS-12, 8 at FAB, 12 at 9-HPT, 8 at MAM-36, 10 at SDMT, 14 at CVLT-II, 9 at BVMT-R.
Conclusion: In conclusion, MS subjects classified as NEDA showed a decrease of function in at least one domain at 2FU. Several subjects showed an improvement underline the importance of an extensive clinical evaluation beyond the EDSS.
Disclosure: All authors have no conflict of interest.

EPO-651

Is brain atrophy a good surrogate for cognitive outcomes in Multiple Sclerosis? A meta-regression of randomized trials

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Background and aims: Magnetic Resonance Imaging lesions have been successfully used as primary outcomes for Phase-2 studies in relapsing-remitting Multiple Sclerosis (MS), while it is still challenging to select an optimal outcome to design Phase-2 studies in progressive MS. Up to now brain atrophy was proposed as a "ready-to-use" outcome for progressive MS trials, even if it its role as a surrogate for inflammation and/or neurodegeneration is still not fully clarified. We aim here to evaluate the surrogacy of brain atrophy for cognitive outcomes in MS clinical trials.
Methods: We collected all the 2-year randomized clinical trials in relapsing-remitting and progressive MS reporting data on the treatment effect on brain atrophy and cognition (PASAT-3). We run a meta-regression (weighted on trial size) of the effect of treatment on PASAT-3 and on brain atrophy. The standardized mean difference (Hedges' g) between baseline and follow-up PASAT-3 assessment was used as the main effect size measure on cognition and the log-percentage brain volume change (PBVC) was used as the main effect size measure on brain atrophy.
Results: 10 trials (16 contrasts, 12 vs placebo, 4 vs active treatment) were included. The weighted correlation between the effects on PBCV and cognition was r=0.57. The R2 was 0.32 (p=0.017), indicating that the 32% of variability of treatment effects on PASAT-3 can be explained by the effects on brain atrophy (Figure).

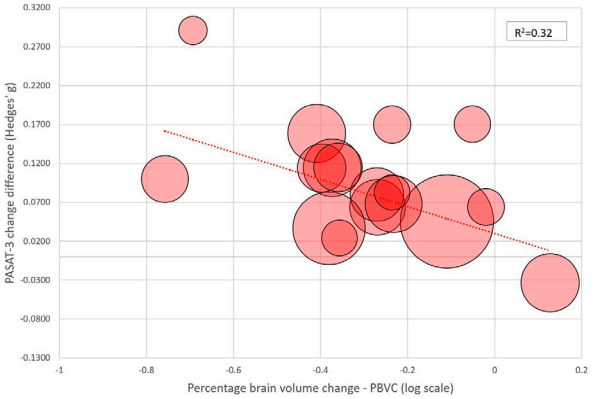

Figure: Association between cognition (PASAT-3) and brain atrophy (PBVC)

Conclusion: Brain atrophy is a good surrogate outcome for treatment effect on cognitive outcomes, despite the limitations related to lack of homogeneity in assessing cognition in MS studies.

Disclosure: Irene Schiavetti has nothing to disclose Marta Ponzano has nothing to disclose Sormani MP received consulting fees from Roche, Biogen, Merck, Novartis, Sanofi, Celgene, Immunic, Geneuro, GSK, Medday; received payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Roche, Biogen Merck, Novartis, Sanofi, Celgene; participated on a Data Safety Monitoring Board or Advisory Board for Roche, Sanofi, Novartis, Merck.

EPO-652

Low serum vitamin D levels are associated with cognitive impairment in multiple sclerosis

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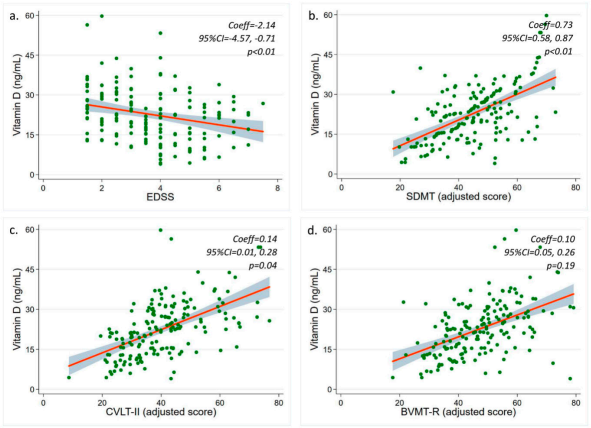
Background and aims: Cognitive impairment (CI) frequently affects people with multiple sclerosis (MS) possibly due to neurodegenerative mechanisms. Low vitamin D levels have been associated with cognitive dysfunction in Alzheimer's and Parkinson's disease, and, in MS, with motor disability and disease activity. We aim to investigate associations between vitamin D and cognitive status in MS.

Methods: In this cross-sectional study, we included 181 MS patients with serum 25-hydroxy-vitamin D measurements using Chemiluminescence ImmunoAssay, and cognitive assessment using Symbol Digit Modalities Test (SDMT), California Verbal Learning Test II (CVLT-II) and Brief Visuospatial Memory Test-Revised (BVMT-R). We collected demographic (age, sex), and clinical variables (disease duration, disease subtype, expanded disability status scale (EDSS), disease modifying treatment (DMT), relapses in previous 12 months, steroid treatment in previous 12 months, concomitant vitamin D supplementation, comorbidities).

Results: At univariate linear regression models, higher levels of vitamin D were associated with higher scores on SDMT (Coeff=0.93; 95%CI=0.81, 1.04; p<0.01), CVLT-II (Coeff=0.68; 95%CI=0.53, 0.83; p<0.01), and BVMT-R (Coeff=0.58; 95%CI=0.43, 0.73; p<0.01), and with lower EDSS (Coeff=-2.16; 95%CI=-3.57, -0.75; p<0.01). At multivariate linear regression models including all demographic, clinical and cognitive variables, we confirmed associations for EDSS (Coeff=-2.14; 95%CI=-4.57, -0.71; p<0.01), SDMT (Coeff=0.73; 95%CI=0.58, 0.87; p<0.01), and CVLT-II (Coeff=0.14; 95%CI=0.01, 0.28; p=0.04), but no association was found for BVMT-R (Coeff=0.10; 95%CI=-0.05, 0.26; p=0.19).



Scatter plots show associations between vitamin D and EDSS (a), SDMT (b), CVLT-II (c), and BVMT-R (d). Coefficients (Coeff), 95% confidence intervals (95%CI, represented as grey shadow), and p-values are reported from multivariate linear regression models

Conclusion: Higher vitamin D levels were associated with better performance in MS on multiple cognitive domains, including attention, information processing speed and verbal memory. Vitamin D possibly affects neurodegenerative aspects of MS.

Disclosure: The authors declare no conflict of interest.

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EPO-653

Czech MS registry ReMuS: Trends in patients initiating their first disease-modifying therapies from 2013 to 2021

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Background and aims: We aimed to describe the trend in the characteristics of patients with multiple sclerosis (MS) initiating their first disease-modifying therapies (DMTs) in the Czech Republic. The secondary objective was to present the Czech national MS registry (ReMuS) with its history, data collection, and scientific potential.

Methods: First, using descriptive statistics, we analysed the characteristics of patients initiating their first DMTs, either platform (including dimethyl fumarate) or high efficacy DMTs (HE-DMTs), each year. Second, a detailed description of the history, data collection, completeness, quality optimising procedures, and legal issues of ReMuS was provided.

Results: Based on the dataset from December 31, 2021, the total number of monitored patients with MS in ReMuS increased from 9,019 in 2013 (referred from 7 of 15 MS centres) to 12,940 in 2016 (already referred from all 15 Czech MS centres) to 17,478 in 2021. In these years, the percentage of patients treated with DMTs in the registry ranged between 76 and 83%, but the proportion of patients treated with HE DMTs changed (from 16.2% in 2013 to 37.1% in 2021). During the follow-up period, a total of 8,491 treatment-naive patients initiated DMTs. The proportion of patients (all MS phenotypes) starting with HE DMTs increased from 2.1% in 2013 to 18.5% in 2021.

Conclusion: An increasing proportion of patients initiating HE-DMTs can bring considerable efficacy to therapy. However, it also carries greater potential risks. Consistent long-term follow-up of patients in real-world clinical practice, which only registries allow, is therefore crucial.

Disclosure: This work was supported by Roche. D.S., M.P., M.V. and D.H. received also financial support for conference travel and/or speaker honoraria and/or consultant fees from Biogen and/or Novartis and/or Merck and/or Bayer and/or Sanofi and/or Teva and/or Lundbeck.

EPO-654

Pseudotumoral demyelinating lesions of the central nervous system

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Background and aims: Pseudotumoral demyelinating lesions (PDL) of the central nervous system (CNS) are large lesions visualized on magnetic resonance imaging (MRI). We investigated the etiology of PDL of the CNS, clinical and neuroradiological characteristics of inflammatory PDL and tumefactive MS lesions.

Methods: The patients with PDL of the CNS treated at the Neurology Clinic, University of Belgrade between 2018 and 2022. Demographic, clinical and neuroradiological data were collected prospectively and retrospectively using the hospital's digital clinical records and analyzed using descriptive statistics. We have classified PDL according to MAGNIMS criteria

Results: 53 patients with PDL of the CNS were analyzed. Concordance of initial and final diagnoses was 64.2%. Out of these, 29 patients (m:f ratio 1:1.25) had inflammatory demyelinating etiologies, among which 10 (34.5%) had previously established MS, 11 (37.9%) got diagnosed with MS in the later course of disease and 8 (27.6%) met criteria for related demyelinating entities. Solitary lesions were seen in 16 (55.2%) patients while 13 (44.8%) had multiple ones. Out of the 11 patients, who went on to develop MS after initial tumefactive lesion 72.7% demonstrated oligoclonal bands. Out of a.m. 29 patients 58.6% had ring-like lesions, 44.8% parietal lobe as predilection site, and 41.4% sensory disturbance as the presenting symptom of the disease.

Conclusion: MS was the most common cause of parietal and ring-like PDL, but not the exclusive cause. This highlights the importance of a thorough and targeted diagnostic workup that utilizes routine analyses, the whole spectrum of neuroimaging modalities, including repeated MRI scans and advanced methods.

Disclosure: Nothing to disclose.

EPO-655

Abstract withdrawn

EPO-656

Prospective trial of personalized extended dosing of natalizumab by therapeutic drug monitoring in multiple sclerosis

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Background and aims: Extended interval dosing (EID) of natalizumab is a promising strategy for reducing the risk of progressive multifocal leukoencephalopathy (PML) in multiple sclerosis (MS). Personalized EID, in which treatment intervals are extended based on natalizumab concentrations, could be superior in comparison to fixed EID in terms of PML risk and healthcare costs.

Methods: The NEXT-MS trial is an ongoing investigator-initiated prospective non-randomized study containing three groups: personalized EID with an aim natalizumab drug trough concentration of 10 µg/mL (EID10), standard interval dosing (SID) of 4 weeks, and an exploratory group of personalized EID with an aim of 5 µg/mL (EID5). The primary outcome is radiological disease activity on MRI (new/enlarged T2 lesions) comparing the EID10 group to a historical cohort of SID.

Results: In December 2022, median treatment interval was 5 weeks (IQR 5 to 6 weeks) in the EID10 group (n=251). Two participants (1.8 participants/year, n=171) showed radiological disease activity during follow-up, which was comparable to the historical SID cohort (2.3 participants/year, n=88). One participant had a relapse (0.65 participants/year vs 4.1 participants/year in the historical cohort). In the EID5 group (n=66), median treatment interval was 6 weeks (IQR 5 to 7 weeks, 32% extended >6 weeks). One participant (0.51 participants/year) showed radiological disease activity and there were no relapses.

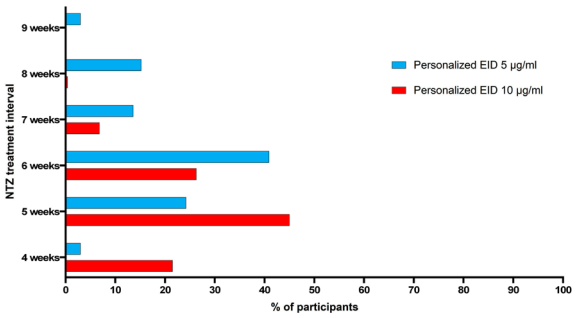

Figure 1: Natalizumab treatment intervals in the personalized EID groups. Percentage of participants in each study group (EID10 in red; EID5 in blue) is displayed on the x-axis. The y-axis indicates the natalizumab treatment interval at last available FU.

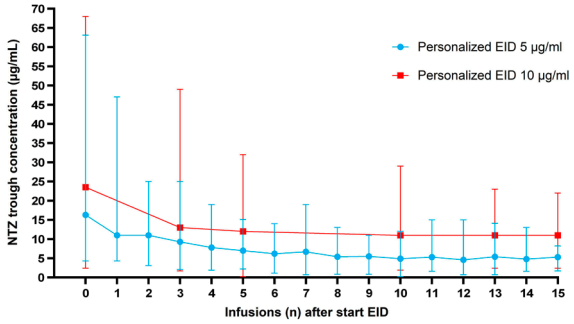

Figure 2: Natalizumab drug concentrations in the personalized EID groups. Values are presented as medians with ranges (min-max). Number of infusions after start of EID are displayed on the x-axis. The y-axis indicates natalizumab trough concentrations.

Conclusion: MS disease activity is adequately controlled with personalized EID of natalizumab. The study will continue in 2023 with an amended study protocol with personalized EID starting from 6 weeks.

Disclosure: This study was kindly funded by the Dutch MS Research Foundation (18-1030), the Brain Foundation Netherlands, and Innovation Fund Healthcare insurers. The funding sources had no further involvement in the study. On behalf of the NEXT-MS study group; A.A. Toorop: nothing to disclose; T. Rispens received funding for research from Genmab; received consulting fees from Novartis; B.M.J. Uitdehaag received research support and/or consultancy fees from Biogen Idec, Genzyme, Merck Serono, Novartis, Roche, Teva and Immunic Therapeutics; J. Killestein received research grants for multicentre investigator initiated trials DOT-MS trial, ClinicalTrials.gov Identifier: NCT04260711 (ZonMW) and BLOOMS trial (ZonMW and Treatmeds), ClinicalTrials.gov Identifier: NCT05296161); received consulting fees for F. Hoffmann-La Roche Ltd, Biogen, Teva, Merck, Novartis and Sanofi/Genzyme (all payments to institution); reports speaker relationships with F. Hoffmann-La Roche Ltd, Biogen, Immunic, Teva, Merck, Novartis and Sanofi/Genzyme (all payments to institution); adjudication committee of MS clinical trial of Immunic (payments to institution only); Z.L.E. van Kempen: nothing to disclose.

EPO-657

Humoral vaccine response and COVID-19 hospitalizations in vaccinated multiple sclerosis patients treated with rituximab

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Background and aims: People with multiple sclerosis (MS) treated with anti-CD20 therapies like rituximab have increased risk of severe COVID-19 disease. Vaccination protects patients from severe COVID-19 disease, but humoral vaccine responses are usually diminished in rituximab treated patients, indicating a need for more clinical data.

Methods: Rituximab-treated patients registered in the National MS Registry, living in Bergen and neighboring municipalities were invited to participate by giving a consent and providing a blood sample 3–12 weeks after ordinary vaccination, i.e. 2 doses, against SARS-CoV-2. Blood samples were analyzed with Enzyme-Linked Immunosorbent assay (ELISA) to detect SARS-CoV-2 specific antibodies with screening test against receptor-binding domain (RBD) and confirmatory Spike IgG-specific ELISA. Patient serum concentration of rituximab were quantified using LC-MS/MS. Registry data from the Norwegian MS registry, and information on hospitalization from patient records were collected and linked to laboratory results.

Results: 140 patients met the criteria and were included in the study. 67% of the included patients had a low or undetectable humoral vaccine response. A total of 10 (7.1%) were admitted for observation and/or treatment for COVID-19 during the observation period. None of the patients were admitted to ICU and there were no deaths.

Conclusion: The majority of rituximab-treated patients with MS had a reduced vaccine response after 2 doses of SARS-cov-2 vaccine. Despite this, only few patients were admitted to hospital and none required ICU treatment. The results indicate that vaccinated patients with MS treated with rituximab have a protective effect despite a low humoral antibody response.

Disclosure: H.Torgauten has nothing to disclose. Ø. Torkildsen has received speaker honoraria from and/or served on scientific advisory boards for Biogen, Roche, Teva, Sanofi-Aventis, Merck and Novartis. R.J. Cox has nothing to disclose. N. Langeland has nothing to disclose. S. Skrede has nothing to disclose. T. Serkland has nothing to disclose. E. Hallin has nothing to disclose. KM. Myhr has received speaker honoraria from Biogen, Roche, Sanofi-Aventis, and Novartis, and participated in clinical trials sponsored by Biogen, Roche, Sanofi-Aventis, and Novartis.

EPO-658

TYSABRI® Observational Program: Long-term Safety and Effectiveness in Relapsing-Remitting Multiple Sclerosis over 15 years

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Background and aims: The Tysabri Observational Program (TOP) is the largest ongoing real-world observational study to inform on long-term safety and effectiveness of natalizumab (NTZ) in relapsing remitting multiple sclerosis (RRMS) in clinical practice.

Methods: Annualized relapse rates (ARRs) for the year prior to NTZ and the period on NTZ (and ≤84 days after the last dose) were compared using a repeated Poisson model. Confirmed Expanded Disability Status Scale (EDSS) worsening and improvement were estimated by Kaplan-Meier analysis. Serious adverse events (SAEs) were assessed at clinical visits.

Results: As of November 2022, TOP included 6,321 patients. At baseline (BL), mean EDSS score was 3.5; 92.6% had prior disease-modifying therapy (DMT) use. A total of 3,993 patients (63.2%) discontinued NTZ; 2,721 (43.0%) withdrew from TOP. Median exposure was 46 (range, 1–191) doses; median follow-up time was 116 (range, 1–200) months. ARR was 2.00 pre-NTZ and 0.18 on NTZ (91.0% reduction, $p<0.001$). For those with BL EDSS scores <3.0 or ≥3.0, ARR decreased by 93.0% ($p<0.001$) and 90.0% ($p<0.001$), respectively. For those with 0, 1, or ≥2 prior DMTs, ARRs were reduced by 93.7% ($p<0.001$), 92.6% ($p<0.001$), and 89.3% ($p<0.001$), respectively. At 15 years, cumulative probabilities of 24-week–confirmed EDSS worsening and improvement were 42.9% and 39.6%, respectively. Overall, 1,122 of 6,321 patients (17.8%) experienced ≥1 SAE (most commonly reported by system organ class: infections and infestations, 320 patients [5.1%]).

Conclusion: This interim analysis of TOP reinforces the consistent effectiveness and established safety profile of NTZ, now assessed over 15 years.

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EPO-659

Predicting cognitive outcomes using deep learning derived brain age in people with multiple sclerosis

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Background and aims: Cognitive decline affects up to 70% of people with multiple sclerosis (MS). The MRI surrogate marker brain age has been shown to be associated with cognitive performance. We investigated the applicability of a deep learning-based algorithm estimating brain age using T1-weighted images to predict cognitive outcomes in people with MS.

Methods: In total, 67 people with MS from a local prospective longitudinal cohort were included in this study (mean age: 35.6 years, 70% females, mean disease duration 2.9 years, mean follow-up time 4.4 years). T1-weighted MRI data was acquired at two time points. The deep learning model, which was trained on 53,542 structural scans from healthy individuals (age range 3–95), was applied to estimate brain age . Annualized brain ageing and brain age gap (BAG), which is the difference between biological and estimated brain age, was then calculated. The patients underwent extensive cognitive testing, and a sum score for global cognitive function was calculated. Linear regression models were used to investigate the correlations between brain age, annualized brain ageing and cognitive performance.

Results: Annualized brain ageing and the BAG were not associated with the overall cognitive outcomes (t=-1.49, p=0.14 and t=0.50, p=0.61, respectively). However, accelerated annualized brain ageing was associated with reduced processing speed at follow-up (t=-2.17, p=0.03) and with increased verbal fluency score at follow-up (t=-2.06, p=0.04).

Conclusion: BAG did not predict global cognitive performance in our MS cohort. Accelerated annualized brain ageing was associated with reduced processing speed and lower verbal fluency.

Disclosure: Einar Høgestøl received honoraria for lecturing and advisory board activity from Biogen, Merck and Sanofi-Genzyme and unrestricted research grant from Merck. Gro Owren Nygaard, Esten H. Leonardsen reports no diclosures. Synne Brune has received honoraria for lecturing from Biogen and Novartis Elisabeth G Celius has received honoraria for advisory boards and/or speaker honoraria from Almirall, Biogen, Merck KGaA, Roche, Novartis, Genzyme and Teva, and unrestricted research grants from Novartis and Genzyme, and reports personal fees from Biogen, Sanofi, and Novartis, and personal fees from Roche and Merck KGaA.

EPO-660

Clinical utility of serum neurofilament light chains in multiple sclerosis measured by Ella™ versus Simoa™ assays.

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Background and aims: Neurofilament light chains (NfL) are cytoskeletal biomarkers of axonal damage, about 200 times lower in serum (s) compared to cerebrospinal fluid. Ultrasensitive techniques are employed to determine s levels, mostly a single molecule array (Simoa™). We aimed to compare sNfL levels determined with Simoa™ versus another platform, the Ella™, in multiple sclerosis (MS) patients at diagnosis.

Methods: 66 newly-diagnosed relapsing-remitting MS patients (42 females; mean age: 36.7 years, standard deviation or SD=10.4) were enrolled before steroid or disease-modifying treatments. sNfL were determined both with the commercial Ella™ microfluidic platform (Bio-Techne) and Simoa™ on SR-X instrument using NF-light assays (Quanterix).

Results: Mean sNfL levels were 37.6 pg/ml (SD=36.8, range 12–262) with Ella™ and 24.8 pg/ml (SD 34.1, range 3.8–208.4 pg/mL) with Simoa™. We observed a positive correlation between the two measures (Spearman's rank test: R=0.9, p<0.0001), and the Bland-Altman method showed a mean bias of 12.7% with Ella™ overestimating. sNfL did not correlate with gender and age at diagnosis.

Conclusion: sNFL serum levels measured with Ella™ resulted higher compared to Simoa™ in naïve patients. Despite this difference in absolute values, a good correlation between the two assays was demonstrated, showing that Ella™ is reliable to measure sNfL in MS. However, Ella™ and Simoa™ can not be interchanged in longitudinal studies.

Disclosure: The study was partially supported by Roche.

EPO-661

Characterization of ms patients at diagnosis through serum and cerebrospinal fluid biomarkers: preliminary data

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Background and aims: Multiple Sclerosis (MS) is highly heterogeneous. Moreover, multiple disease-modifying treatments (DMTs) are available. Therefore, there is a need for robust fluid biomarkers from diagnosis, for characterization, and to monitor follow-up from early disease stages. Several biomarkers are consolidated, particularly neurofilaments light chains (NFL), but the value of others is less explored.

Methods: We aimed to evaluate the usefulness of different axonal damage and inflammatory biomarkers in cerebrospinal fluid (CSF) and serum in a cohort of 60 newly-diagnosed MS. Samples were obtained at diagnosis. CSF, serum NFL and osteopontin (OPN) were obtained using Ella microfluid platform, CSF total-tau and phosphorylated-tau using CLEIA Luminpulse.

Results: We observed a strong correlation between total-tau and p-tau (rs=0.76, p<0.0001) and between CSF and serum NFL (rs=0.80, p<0.0001) whereas, CSF and serum OPN did not. CSF and serum NFL correlated with total-tau (rs=0.45, p=0.0004 and rs=0.29, p=0.02), and not with p-tau. Patients with higher CSF NFL (rs=0.39 p=0.0019), total-tau (rs=0.27, p=0.03), and OPN (rs0.37 p:0.003) displayed higher EDSS at diagnosis. CSF (p=0.01) and serum NFL (p=0.04) were higher in patients with gadolinium-enhancing lesions and only CSF in patients treated after diagnosis with highly-efficacy DMTs (p=0.049), whereas high CSF OPN was observed in male patients (p=0.02).

Conclusion: Our preliminary data confirm the usefulness of CSF axonal damage biomarkers performed at MS diagnosis. Follow-up data such as disability scores over time and repeat serum dosages are needed. We suggest that a combination of several fluid biomarkers might be useful for a better characterization at diagnosis.

Disclosure: No disclosures related to the present study.

EPO-662

Patient centered outcomes of the ageing population in Multiple Sclerosis compared with the Danish background population

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Background and aims: The fraction of elderly patients with multiple sclerosis (MS) is growing and knowledge about patient-centered outcomes in this population remain sparse. The aim of the study was to compare socioeconomic and comorbidity metrics in aging patients with MS compared to the background population.

Methods: A matched cross-sectional study based on the nationwide population-based Danish Multiple Sclerosis Registry and nationwide public registries. Matching was done 1:10 on sex, age, and region to individuals from a 25% random sample of the background population.

Results: The study population was 8,336 patients with MS and 83,360 matches. The average age was 63.3 years (SD= 8.9) and 68.2% were females. There was no difference between the MS and matches on number of comorbidities (p=0.17), but the MS population had significantly more acute hospitalizations (p<0.0001). The MS population received more social care with a median of 20.5 (Q1–Q3: 5.0–60.5) monthly hours of practical help and 2.0 (Q1–Q3: 1.3–4.1) of personal care (p<0.0001). In the age-group 50–65 years, the proportion of MS patients receiving disability pensions was higher 46.1% versus 13.3 % (p<0.0001), and for those having a job, the annual salary was lower 45,000 € versus 50,000 € (p<0.0001). Progeny of both populations had similar marital status (p=0.26) and level of education (p=0.79).

Conclusion: The ageing population in MS are hospitalized more frequently, receive more social care, and perform worse on socioeconomic metrics compared to the background population. However, the prevalence of comorbidities is equal and progeny of patients with MS perform like those of the background population.

Disclosure: Malthe Wandall-Holm has received speaker honoraria from Novartis and Sanofi. Olivia Sarah Strandbech has nothing to disclose. Melinda Magyari has served in scientific advisory board for Sanofi, Novartis, Merck, and has received honoraria for lecturing from Biogen, Merck, Novartis, Roche, Genzyme, Bristol Myers Squibb.

EPO-663

Patients with benign multiple sclerosis have a much higher risk of disability pension than the background population

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Background and aims: Patients with multiple sclerosis (MS) experience vastly heterogenous disease courses. A subpopulation presents with benign MS (BMS), characterized by limited disability accumulation on the expanded disability status scale (EDSS), however their socioeconomic performance is poorly described. The aim of the study was to investigate the risk of disability pension of BMS patients compared to the background population.
Methods: A cohort study of MS patients of the working age (30–64) from the Danish Multiple Sclerosis Registry. The study period was 1998 to 2021, and matching was done 1:10 on age, sex, educational level, municipality, and calendar year to individuals from a 25% random sample of the Danish background population. We followed individuals to disability pension, censoring or a competing risk, and estimated absolute risk and cause specific hazard ratio (HR) of receiving disability pension.
Results: We identified 1,868 BMS patients with a mean age of 43.1 (SD=8.0) years and 69% were females. Most received a disease modifying treatment (87%) and the mean EDSS was 1.4 (SD=0.9). The absolute risk of receiving disability pension 20 years after disease onset was 13.7% (95% CI: 11.6–16.1) for the BMS-patients, significantly higher than the matches: 3.9% (95% CI: 3.5–4.3), $p<0.001$. Correspondingly, the BMS-patients displayed a fourfold increase in the hazard of receiving disability pension compared with controls, HR: 4.1 (95% CI: 3.4–4.8).
Conclusion: Despite a benign disease course defined by the standard clinical disability metric, EDSS, patients with BMS exhibit a much higher risk of disability pension compared to matches from the Danish background population.
Disclosure: Malthe Wandall-Holm has received speaker honoraria from Novartis and Sanofi. Mathias Due Buron has received speaker honoraria from Novartis. Rolf Pringler Holm has nothing to disclose. Finn Sellebjerg has served on scientific advisory boards for, served as consultant for, received support for congress participation or received speaker honoraria from Alexion, Biogen, Bristol Myers Squibb, H. Lundbeck A/S, Merck, Novartis, Roche and Sanofi Genzyme. His laboratory has received research support from Biogen, Merck, Novartis, Roche and Sanofi Genzyme. Melinda Magyari has served in scientific advisory board for Sanofi, Novartis, Merck, and has received honoraria for lecturing from Biogen, Merck, Novartis, Roche, Genzyme, Bristol Myers Squibb.

EPO-664

Baseline Characteristics in the Tolebrutinib Phase 3 Relapsing Multiple Sclerosis GEMINI 1 and 2 Trials

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Background and aims: GEMINI 1 (NCT04410978) and GEMINI 2 (NCT04410991) are two Phase 3 trials with identical designs, evaluating the efficacy and safety of tolebrutinib, an oral, brain-penetrant, Bruton's tyrosine kinase inhibitor, compared with teriflunomide in participants with relapsing multiple sclerosis (RMS). Our objective is to present baseline characteristics of GEMINI 1 and 2 trial participants.
Methods: GEMINI 1 and 2 are randomised, double-blind, double-dummy, parallel-group, event-driven (6-month confirmed disability worsening) trials in RMS participants aged 18–55 years, with an Expanded Disability Status Scale (EDSS) score $\leq$5.5 at screening and either $\geq$1 documented relapse within the previous year, $\geq$2 documented relapses within the previous 2 years, or $\geq$1 documented gadolinium-enhancing brain lesion on magnetic resonance imaging (MRI) within the previous year. Participants were randomised 1:1 to receive 60 mg oral tolebrutinib or 14 mg oral teriflunomide, once daily.
Results: 1,873 participants were enrolled (974 in GEMINI 1 and 899 in GEMINI 2), with a mean age of 36.7 and 36.4 years, and a mean time since diagnosis of 4.7 and 3.8 years, respectively. The majority were female (67% combined), more than half were treatment-naïve (66%), and the mean number of relapses in the year prior to enrolment was 1.2. At baseline in both trials, the mean EDSS score was 2.4, and 35% of participants had gadolinium-enhancing lesions.
Conclusion: GEMINI 1 and 2 trial cohorts have similar baseline characteristics, consistent with the tolebrutinib Phase 2b RMS trial (NCT03889639). These trials will provide a comprehensive assessment of tolebrutinib efficacy and safety in RMS.
Disclosure: STUDY FUNDING: Sanofi. HW: honoraria (Abbvie, Alexion, Argenx, Biogen, BMS, F Hoffmann-La Roche, Janssen, Merck, Neurodiem, Novartis, Roche, Sanofi, Teva, WebMD); consulting (Abbvie, Actelion, Argenx, Biogen, BMS, EMD Serono, Fondazione Cariplo, Gossamer Bio, Idorsia, Immunic, Immunovant, Janssen, Lundbeck, Merck, NexGen, Novartis, PSI, Roche, Sanofi,

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EPO-665

What is the best titration protocol for dimethyl fumarate? Preliminary results of a multicenter real-world study

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Background and aims: Dimethyl fumarate (DMF), an oral medication commonly used to treat relapsing forms of multiple sclerosis (MS), is generally well tolerated, with common side effects including flushing, and gastrointestinal symptoms, particularly in the first month of the treatment. Slower titrations of DMF and dietary recommendations may reduce side effects. However, to date, there are no studies comparing titration protocols. The aim of this study is to exhibit a real-world safety profile and to compare the titration protocols.

Methods: Individuals with MS who were started on DMF treatment in thirteen tertiary MS centers were included in the study. In addition to the demographic and disease characteristics of the participants, DMF side effects and other safety data, titration protocols were recorded to an online database.

Results: A total of 825 individuals were included in the study. Mean age at the initiation of DMF treatment was 32.5±9.7 and the mean EDSS was 1.2 (0.8). In 505(61.2%) individuals, DMF was started as first-line therapy. 405(49.08%) individuals experienced flushing, 89 (11.38%) abdominal pain and 51 (6.53%) diarrheas. 694 individuals (84.12%) continued DMF treatment. The protocol increasing 120 mg weekly to 240 mg BID in the fourth week was associated with less flushing and GI side effects compared to the protocol increasing to 240 mg BID in the second week.

Conclusion: In this study, it has been shown that slower titration is associated with less flushing and fewer GI symptoms, and it has been demonstrated that appropriate patient management and supportive treatment can increase treatment adherence.

Disclosure: Nothing to disclose.

EPO-666

Acute hemorrhagic leucoencephalitis with subacute onset: a case report.

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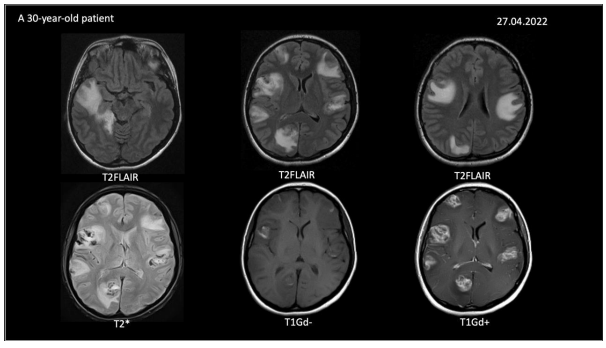
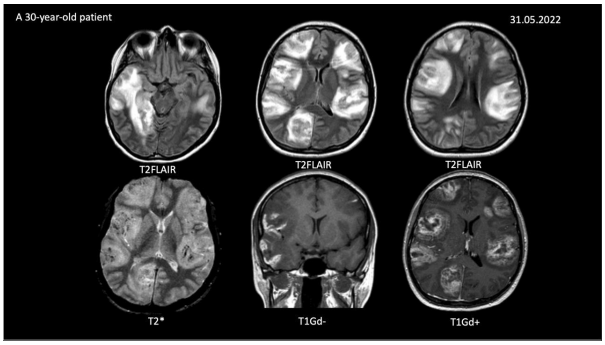
Background and aims: Acute hemorrhagic leukoencephalitis (AHLE), rare and severe form of acute disseminated encephalomyelitis, is an inflammatory fulminant CNS disorder.

Methods: We report a case of a 30-year-old patient with a rare AHLE presentation characterized by subacute onset and slow progression, her clinical, radiological, laboratorial and post-mortem histological findings.

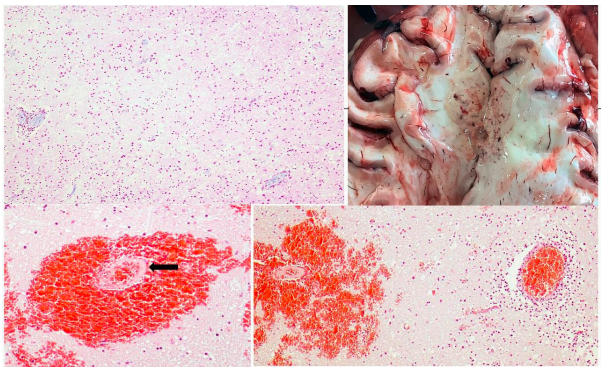
Results: AHLE is usually characterized by an acute onset and fulminant disease course. In our case first symptoms appeared in April 2022 as a nonspecific headache. MRI demonstrated large multifocal T2 and T2-FLAIR-hyperintense brain lesions, surrounded by T2*-hypointense areas (signs of blood). Lesions heterogeneously accumulated contrast. Diagnostic search included CNS paraneoplastic processes and infectious diseases. During the following month, relatives noted only slight personality changes, like irritation and hypersomnolence. In the end of May she was admitted to our department where negativism, aggression, psychomotor agitation, sensorimotor aphasia. CSF analysis showed an increased protein (0.551 g/l) and slight pleocytosis (8 cells/mm^3). Preliminary diagnosis of AHEM was established. High-volume plasmapheresis couldn't be performed due to the patient's menarche and large hemorrhagic component in the brain foci. Therefore, methylprednisolone pulse therapy was initiated, however patient's state gradually deteriorated resulting in coma and subsequent death on the 10th day of hospitalization. Post-mortem histological analysis revealed the classic triad - white matter demyelination in cerebral hemispheres, multiple perivascular hemorrhages and inflammatory infiltrate.



MRI demonstrated large multifocal T2 and T2-FLAIR-hyperintense brain lesions, surrounded by T2*-hypointense areas (signs of blood). Lesions heterogeneously accumulated contrast



The negative dynamics in MRI of the brain



Post-mortem histological analysis revealed the classic triad - white matter demyelination in cerebral hemispheres, multiple perivascular hemorrhages and inflammatory infiltrate

Conclusion: Approximately in 30% of AHLE cases, patients survive due to early disease recognition and following aggressive immunosuppression. Unusual subacute onset and progression impede AHLE recognition and life-threatening delay in treatment, as in our case.

Disclosure: No conflict of interest.

EPO-667

Abstract withdrawn