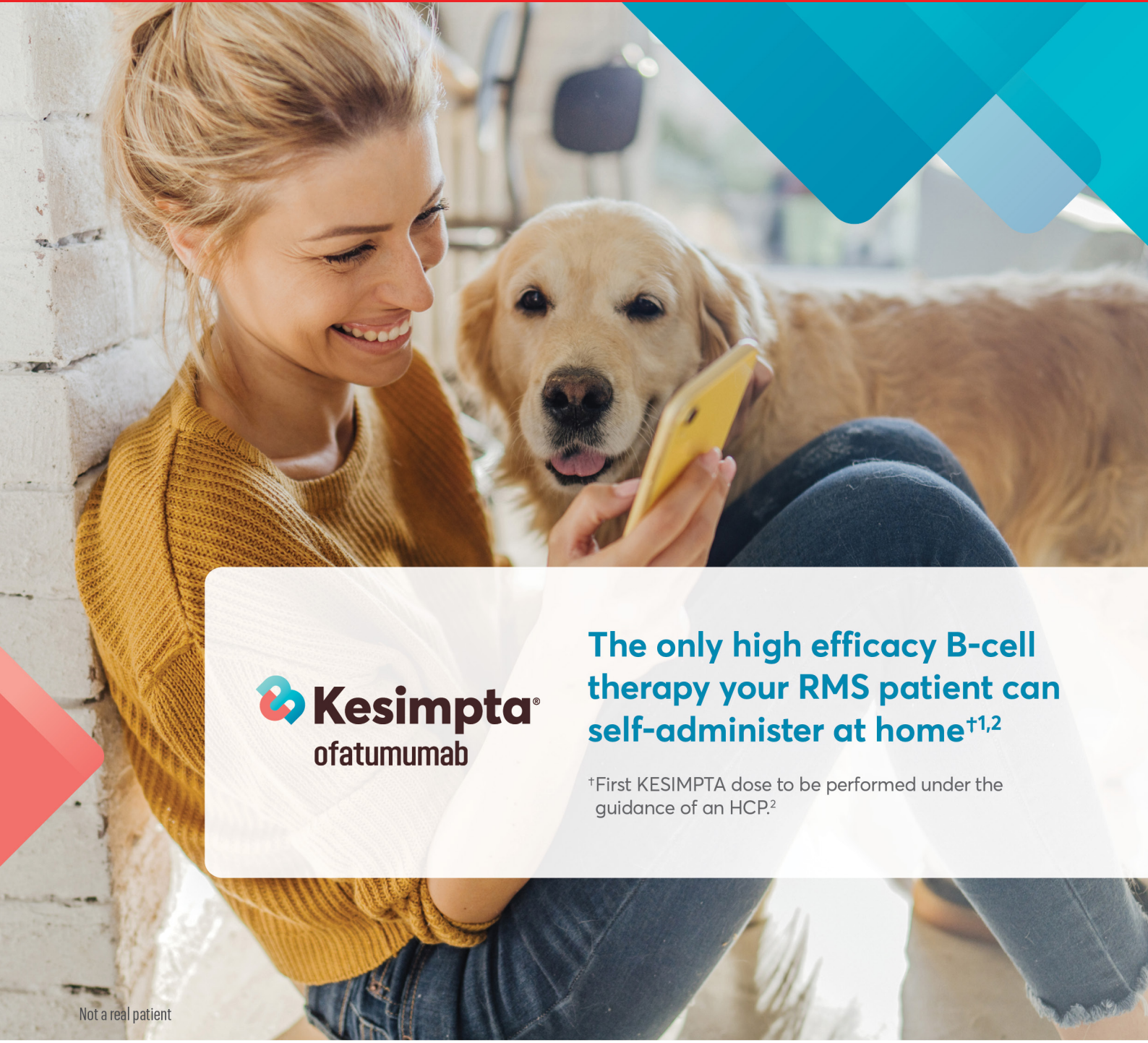
pactrims
Pan-Asian Committee
for Treatment and Research in Multiple Sclerosis

THE 15th PAN-ASIAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS CONGRESS

23 to 25 November 2023, Perth, Australia



PBS Information: Authority Required (STREAMLINED). For use in patients with relapsing-remitting multiple sclerosis who meet certain criteria. Refer to PBS Schedule for full Authority Required information.

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

KESIMPTA is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) to delay the progression of physical disability and reduce the frequency of relapse.

PKES1011

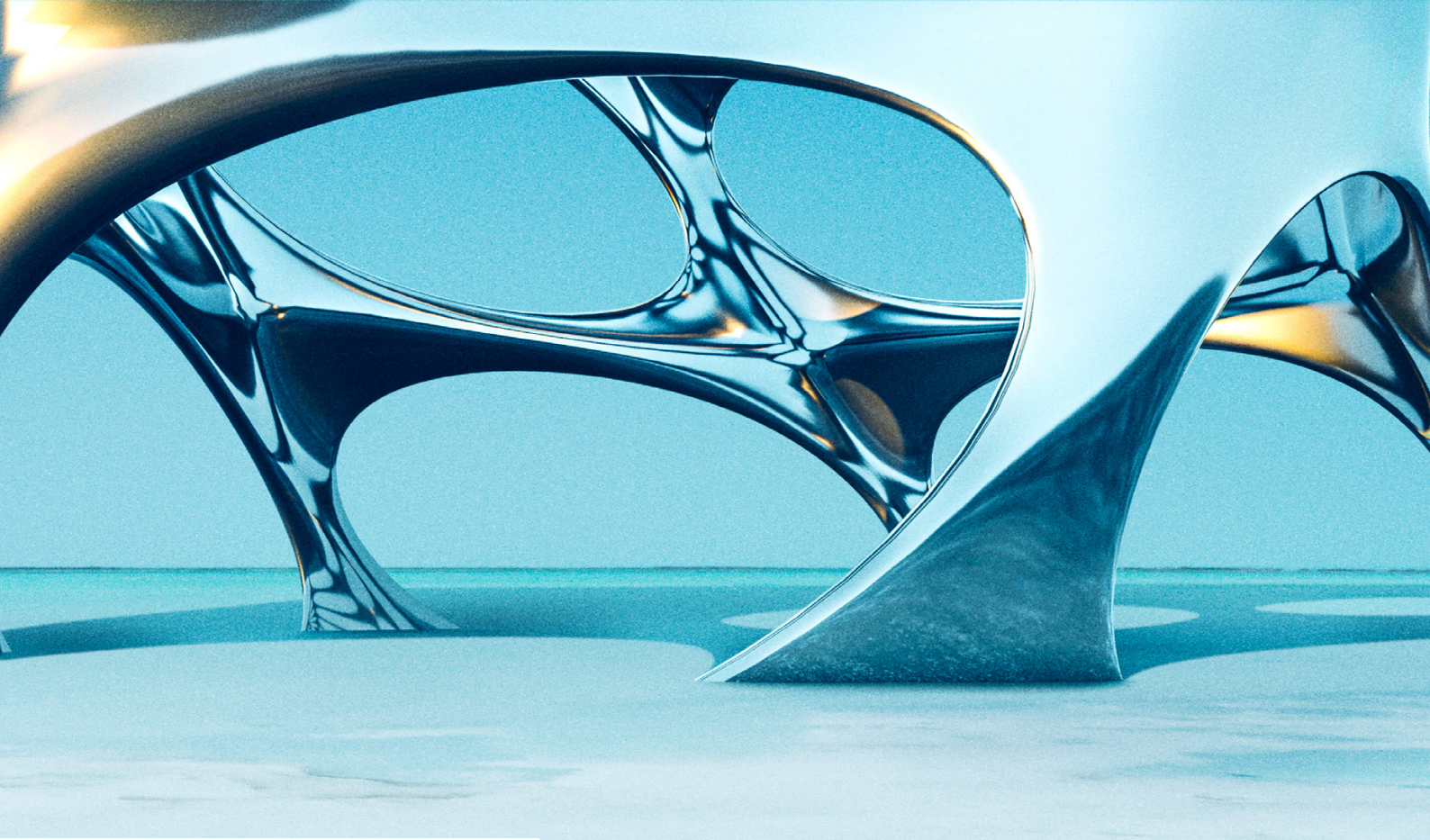
For healthcare professionals only. Please review full Product Information before prescribing. Very common adverse effects (≥10%) include injection related reaction, nasopharyngitis, injection site reaction and urinary tract infection. For more detailed safety information, scan QR code for full KESIMPTA Product Information. Alternatively, please contact med info at 1 800 671 203 or visit www.novartis.com.au/products/healthcareprofessionals/products to access the full Product Information.

Abbreviations: HCP=healthcare professional; RMS=relapsing multiple sclerosis. **References 1.** MS Treatments. MS Australia www.msaustralia.org.au/treatments/ (Accessed 20 March 2023). **2.** KESIMPTA approved Product Information.

Novartis Pharmaceuticals Australia Pty Limited. ABN 18 004 244 160. 54 Waterloo Road, Macquarie Park, NSW 2113.

NOVARTIS

CONTENTS



We don't only fight disease.

We also take on drug discovery paradigms.

Our unprecedented medicines are

a step ahead of illness.

And when the world says there's no cure,

we don't give up until we find one.

INNOVATION BEYOND IMAGINATION

CHUGAI PHARMACEUTICAL CO., LTD.

Roche Group

Dear Friends and Colleagues,

We wish to acknowledge the Nyoongar Whadjuk (Perth region) people - traditional custodians of the land we are meeting on. We wish to acknowledge the strength of their continuing culture and offer our respects to Elders past and present.

We would like to welcome you to the 15th Congress of the Pan-Asian Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS) that will take place in Perth, Western Australia from 23 to 25 November 2023.

PACTRIMS is an annual event that aims to provide clinical and scientific updates in the care of patients with multiple sclerosis (MS), neuromyelitis optica and related conditions in the Asia-Pacific region. Patients in this region face different challenges where clinical care could vary depending on different healthcare reimbursement, perceptions of disease and accessibility to diagnostic assays and medications. PACTRIMS 2023 strives to provide opportunities for participants representing their MS communities to exchange knowledge, acquire skills, share experiences, foster collaborations and work towards our shared vision of improving the care and lives of patients with MS and other CNS inflammatory demyelinating diseases.

Perth is privileged to host PACTRIMS this year. We are excited that we are chosen to organise an in-person meeting for our community to meet, build networks and share knowledge and ideas. It gives me great pleasure to welcome our delegates to enjoy not just the conference, but also the many sights and attractions that Western Australia has to offer.

On behalf of the organising committee, we welcome you and wish you a productive congress in Perth.

Yours sincerely,

Dr Marzena Fabis-Pedrini
Chair, Local Organising Committee
PACTRIMS 2023

WELCOME NOTE

PACTRIMS
Committee Members 2023

EXECUTIVE COMMITTEE

President
Kazuo Fujihara

Vice President
Ho Jin Kim

Treasurer
Allan Kermode

Secretary
Lekha Pandit

Emeritus
Takahiko Saida

Patron
William Carroll

CENTRAL ORGANISING COMMITTEE

Australia
Allan Kermode

China
Fu-Dong Shi
Yaou Liu

Hong Kong
Patrick Li

India
Lekha Pandit

Japan
Kazuo Fujihara
Jin Nakahara

Republic of Korea
Byoung-Joon Kim
Ho Jin Kim

Malaysia
Joyce Joseph

New Zealand
Ernest Willoughby

Singapore
Kevin Tan

Taiwan
Jen-Jen Su

Thailand
Sasitorn Siritho

SCIENTIFIC PROGRAM COMMITTEE

Chairperson
Noriko Isobe, Japan

Vice-Chairpersons
Alexander Lau,
Hong Kong

Advisor
Michael Barnett,
Australia

Regional Members

Deborah Mason, New Zealand
Helmut Butzkueven, Australia
Ichiro Nakashima, Japan
Jen-Jen Su, Taiwan
Jennifer Massey, Australia
Lekha Pandit, India
Riwanti Estiasari, Indonesia
Simon Broadley, Australia
Su-Hyun Kim, Korea
Sung-Min Kim, Korea
Thomas Matthew, India
Tianrong Yeo, Singapore
Wei Qiu, China
Yaou Liu, China

EDUCATION COMMITTEE

Chairpersons
Joyce Joseph, Malaysia
Kevin Tan, Singapore

Regional Members

Chang Kuo Hsuan, Taiwan
Ichiro Nakashima, Japan
Kim Su-Hyun, Korea
Lekha Pandit, India
Ma Yuetao, China
Noriko Isobe, Japan
Sasitorn Siritho, Thailand
Simon Broadley, Australia
Simon Ling, Singapore

15TH PACTRIMS LOCAL ORGANIZING COMMITTEE

Chairperson
Marzena Fabis-Pedrini

PROGRAM OVERVIEW

Thursday, 23 November 2023		
PRE-CONGRESS PACTRIMS TEACHING COURSE		
Chairpersons: Joyce Joseph (Malaysia) & Kevin Tan (Singapore)		
09:00-09:05	Welcome Address	Joyce Joseph (Malaysia) & Kevin Tan (Singapore)
09:05-09:35	PL1: Application of current MOGAD diagnostic criteria	Lekha Pandit (India)
09:35-10:05	PL2: Selection of Disease Modifying Treatment	Sasitorn Siritho (Thailand)
10:05-10:20	Coffee Break	
10:20-10:50	PL3: MS nurse role, family planning and the postpartum period - a collaborative approach	Meaghan Osborne (Australia)
10:50-11:30	Interactive Case Discussions	Giancarlo Comi (Italy), Lekha Pandit (India), Sasitorn Siritho (Thailand), Meaghan Osborne (Australia)
EUROPEAN CHARCOT FOUNDATION - UNDERSTANDING AND TREATING PROGRESSION		
Chairpersons: Kazuo Fujihara (Japan) & Giancarlo Comi (Italy)		
13:00-13:25	ECF1: Immunopathology of progressive MS	Hans-Peter Hartung (Germany)
13:25-13:50	ECF2: Detection and monitoring of progressive MS	Giancarlo Comi (Italy)
13:50-14:15	ECF3: Treatment of progressive MS	Kazuo Fujihara (Japan)
14:15-14:40	ECF4: Neuromodulation	Letizia Leocani (Italy)
14:40-14:50	Q&A	
PACTRIMS CONGRESS OPENING		
15:15-15:20	Welcome Address by the Local Organizing Chairperson	Marzena Pedrini (Australia)
15:20-15:25	Opening Address by the President	Kazuo Fujihara (Japan)
15:25-15:30	Special Address by the Guest of Honour	William Carroll (Australia)
PLENARY 1: EPSTEIN-BARR VIRUS IN MS: UPDATE		
Chairpersons: Ho Jin Kim (Korea) & Jennifer Massey (Australia)		
15:30-15:55	L1. EBV specific TCR in MS	Heinz Wiendl (Germany)
15:55-16:20	L2. Pathomechanisms of EBV association in MS	Jennifer Massey (Australia)
16:20-16:45	L3. EBV in MS and other diseases including malignancy	Mainthan Palendira (Australia)
16:45-17:00	Q&A	
17:00-17:30	Coffee Break and Poster Viewing Session 1	
17:30-19:00	Mitsubishi Tanabe Pharma Symposium	
19:30-21:30	Welcome Reception at Songbird Lounge (Poolside)	
Friday, 24 November 2023		
PLENARY 2: MAKING EARLY DIAGNOSIS WHILE PREVENTING MISDIAGNOSIS		
08:00-09:30	Novartis Pharmaceuticals Symposium	
09:30-10:00	Coffee Break and Poster Viewing Session 2	
Chairpersons: Ichiro Nakashima (Japan) & Yeo Tianrong (Singapore)		
10:00-10:25	L4. Making early diagnosis while preventing misdiagnosis	Todd Hardy (Australia)
10:25-10:50	L5. MS mimics: what to be distinguished from MS in Asian countries (especially infectious diseases)	Riwanti Estiasari (Indonesia)
10:50-11:15	L6. Strategy to make early diagnosis	Hans-Peter Hartung (Germany)
11:15-11:30	Q&A	
11:30-12:30	ORAL PRESENTATION PART ONE- 5 presentations	Chairpersons: Deborah Mason (New Zealand) & Jen-Jen Su (Taiwan)
12:30-13:30	Lunch	

PROGRAM OVERVIEW

PLENARY 3: ADVANCED STUDY TOOLS TO UNTANGLE DISEASE PATHOMECHANISMS		
Chairpersons: Lekha Pandit (India) & Yaou Liu (China)		
13:30-13:55	L7. Transcriptome signatures of NMOSD	Makoto Kinoshita (Japan)
13:55-14:20	L8. NfL and other candidate biomarkers in MS & NMOSD	Mitsuru Watanabe (Japan)
14:20-14:45	L9. Single cell techniques to reveal pathogenic TCR and autoantigens	Belinda Kaskow (Australia)
14:45-15:00	Q&A	
15:00-15:30	Coffee Break and Poster Viewing Session 3	
15:30-16:30	ORAL PRESENTATION PART TWO- 5 presentations	Chairpersons: Riwanti Estiasari (Indonesia) & Simon Broadley (Australia)
16:30-18:00	Chugai Pharmaceutical Co., Ltd. Symposium	
18:45-22:00	Gala Dinner: Dining with the Blue Whale (Please gather at the lobby at 6.45pm to board the bus).	
Saturday, 25 November 2023		
PLENARY 4: NEW MS TREATMENT STRATEGIES AND EVALUATION		
Chairpersons: Allan Kermode (Australia) & Alexander Lau (Hong Kong)		
10:00-10:25	L10. The WHO Essential Medicines List expands to include DMTs for MS	Tomas Kalincik (Australia)
10:25-10:50	L11. Future MS treatment strategies	Su-Hyun Kim (Korea)
10:50-11:15	L12. Neuromodulation as a novel MS treatment	Letizia Leocani (Italy)
11:15-11:30	Q&A	
CLOSING AND AWARD CEREMONY		
11:30-11:40	Poster Award ceremony	Noriko Isobe (Japan)
11:40-11:45	Closing Remarks by the Vice-President	Ho Jin Kim (Korea)

PACTRIMS TEACHING COURSE

PL-1

Application of current MOGAD diagnostic criteria

Lekha Pandit, MD, DM, PhD
Professor of Neurology
Director of Centre for Advanced Neurological Research, Nitte University, Karnataka, India

The International MOGAD panel proposed diagnostic criteria was published earlier this year. In the first instance, clinical phenotypes known to be associated with MOGAD were listed - optic neuritis, myelitis, ADEM, brainstem/cerebellar dysfunction, symptomatic brain disease or a combination. There are clinical and MRI supportive features that may be used to support clinical diagnosis. At the core of this criteria is the testing and interpretation of MOG-IgG assays. Despite the fulfilment of these criteria, alternate causes need to be excluded. This talk will focus on all aspects of this criteria using illustrative cases.

PL-2

Application of current MOGAD diagnostic criteria

Sasitorn Siritho
Senior Consultant Neurologist at Bumrungrad International Hospital, Bangkok, Thailand

Multiple sclerosis (MS) is a multifaceted central nervous system disease characterized by inflammation, autoimmunity, and demyelination. The disease's intricate pathogenesis involves an initial phase of neuroinflammation followed by secondary neurodegeneration.

Extensive research emphasizes the importance of early intervention in the "window of opportunity" to mitigate irreversible damage. High-efficacy disease-modifying drugs (DMDs) have garnered substantial evidence supporting their use for long-term positive outcomes. The landscape of MS treatment is swiftly evolving, with numerous DMDs available. However, there exists a need for more head-to-head comparative data among these drugs, along with a lack of clearly defined biomarkers to guide treatment effectiveness and disease progression.

Selecting the most suitable DMD demands careful consideration of factors such as the type of MS, disease activity, progression patterns, and potential side effects. During the decision-making process, it's vital to weigh the underlying aspects of the patient's condition alongside the anticipated impacts of the chosen DMD. We will illustrate some cases during the discussion.

PL-3

MS nurse role, family planning and the postpartum period - a collaborative approach

Meaghan Osborne
Nurse Practitioner Neurology and Stroke

The Multiple Sclerosis Nursing role is integral to the care of the person with MS. The MS Nurse practitioner is an advanced practice provider that provides comprehensive care to MS patients across the continuum. It includes assessment and management using nursing knowledge and skills. The role may include, but is not limited to, the direct referral of patients to other healthcare professionals, prescribing medications, ordering, and interpreting diagnostic investigations. It is grounded in the nursing profession's values, knowledge, theories, and practice, and provides innovative and flexible health care delivery that complements other health care providers.

The Nurse Practitioner practice is embedded in the nursing profession and provides holistic care to MS patients and their families. This session will highlight the strengths of the MS nurse practitioner and MS, whilst providing practical examples of its implementation during family planning and caring for the woman with MS post-partum.

INVITED LECTURES

L-1

EBV specific TCR in MS

Heinz Wiendl, MD
Professor and Chair, Department of Neurology with Institute of Translational Neurology, University Hospital Münster, Germany

EBV has been accused to be involved in the tissue mechanisms to unravel clinical multiple sclerosis and pathogenic concepts consider EBV persistence a mechanism potentially propagating MS disease progression. Our work intended to define unsupervised immunological signatures associated to the disease, looking at different compartments, hence discovered that there is a broader T cell receptor repertoire against EBV in MS patients. Our work investigates a large number of MS patients, controls, and monozygotic twin pairs discordant for multiple sclerosis and includes the assessment of different compartments (peripheral blood, cerebrospinal fluid). Following the notion that CSF also contains EBV-specific central neural CD8 cells, suggesting recent finding, MS is not only preceded by EBV infection, but also associated with a broader EBV repertoire and this is consistent with an ongoing EBV immune alteration in MS. Further data show the response of EBV-specific T cell receptor repertoire by therapeutic modification, particularly treatment with CD20-depleting antibodies.

L-2

Pathomechanisms of EBV association in MS

Jennifer Massey, MBBS (Hon), FRACP, PhD
Staff Specialist Neurologist, St Vincent's Hospital, Sydney

Interest in the role of Epstein Barr Virus (EBV) in multiple sclerosis has intensified based on strong epidemiological evidence of an association between EBV seroprevalence and MS. Hypotheses proposed to explain the biological relationship between EBV and MS include molecular mimicry, EBV immortalised autoreactive B cells and infection of glial cells by EBV.

Examining the interaction between EBV and immunotherapies that have demonstrated efficacy in MS offers clues to the validity of these hypotheses. The efficacy of B cell depleting therapies could be consistent with a hypothesis that EBV-infected B cells drive MS; however, loss of T cell control of B cells does not exacerbate MS. A number of MS therapies invoke change in EBV-specific T cell populations, but public/shared pathogenic EBV-specific T cells with cross-reactivity to CNS antigen remain elusive. Immune reconstitution therapies induce EBV viraemia and expansion of EBV-specific T cell clones, but this does not correlate with relapse. Much remains unknown regarding the role of EBV in MS pathogenesis. This talk will review the current field and explore important knowledge gaps.

L-3

EBV in MS and other diseases including malignancy

Mainthan Palendira
A/Prof, Human Immunology Laboratory, The University of Sydney

Epstein-Barr virus (EBV) is perhaps one of the most successful pathogens to infect humans. With over 90% of the population sero-positive for this virus and lifelong persistence in the infected host, EBV defines one of the most successful host-pathogen interactions known to mankind. However, EBV is also the first human oncogenic virus to be identified and thus far has been implicated in at least 7 different types of malignancies in human. There is mounting evidence implicating EBV in the development of MS. Risk of developing MS is extremely low in uninfected individuals, however, a history of symptomatic primary infection and elevated antibody responses to EBV significantly increase the risk of MS. There are, however, many questions that remain unanswered, and the underlying mechanism is far from clear. In this talk I will provide a summary of all the evidence we have on the role of EBV in MS, show where there are still gaps in our understanding and discuss the future directions.

L-4

Making early diagnosis while preventing misdiagnosis

Todd Hardy
Senior Staff Specialist Neurologist, Concord Hospital

There are now substantial data from DMT clinical trials, extension studies, and real-world MS registries that early treatment, especially with high efficacy disease modifying therapies, improves outcomes in MS. This has been reflected in successive iterations of the McDonald criteria for the diagnosis of MS which have enabled earlier recognition facilitating earlier treatment.

Despite the high sensitivity of the McDonald criteria, specificity is low, and misdiagnosis of MS is common - mainly due to a failure to apply the criteria correctly. Numerous conditions have the potential to mimic MS and the McDonald criteria were not designed to distinguish MS from other conditions. A new revision of the McDonald criteria is currently underway and an important topic for consideration will be if an even earlier diagnosis is possible. The downside of trying to diagnose and treat MS earlier is a risk of overdiagnosis and misdiagnosis.

This talk will address the need for early MS diagnosis and the potential for MS misdiagnosis with examples of red flags that cast doubt upon the diagnosis of MS. It will also cover new advances with the potential to improve the specificity of MS diagnosis.

L-5

Making early diagnosis while preventing misdiagnosis

Riwanti Estiasari
Associate Professor, Neurology Department, Faculty of Medicine Universitas Indonesia

Multiple sclerosis is a demyelinating disease that has the potential to cause disability and affects many young people. MS is mainly found in Western countries. Although the number is not as high as in Western countries, the prevalence continues to increase in Asia Pacific. In diagnosing MS, one thing that needs to be considered is to differentiate the clinical findings from infectious diseases, especially those endemics in Asian countries.

The clinical symptoms of central nervous system infection can resemble MS and the imaging features. Since the management will differ, distinguishing between the two is very important.

Screening before starting treatment is also essential to ensure no latent infection in the patient.

Some common infections, such as tuberculosis neurocysticercosis, can appear similar to MS. Other diseases that also need attention include hepatitis C, Progressive Multifocal Encephalopathy, syphilis, and HTLV-1.

It is essential to exclude the possibility of an infectious disease early in diagnosing MS. The findings of infectious diseases can affect the diagnosis that is made and the treatment that will be given.

L-6

Strategy to make early diagnosis

Hans-Peter Hartung, M.D., Ph.D
Professor of Neurology, Heinrich Heine University Düsseldorf, Germany

MS clinically manifests with symptoms and signs that can mimic a host of other diseases. A key principle adhered to in the multiple revisions the diagnostic criteria (Schumacher, Poser, MdDonald) is the careful exclusion of differential diagnoses. These can be autoimmune, infectious, vascular, neoplastic in etiology. More recently, delineation of NMOSD and MOGAD as separate entities emerged as major disorders presenting with MS similar phenotypes.

For this diagnostic workup standardized MR imaging is paramount as may in certain contexts spinal fluid analysis. To rule out NMOSD and MOGAD cell-based testing for aquaporin 4 and MOG IgG is required.
Fundamental in the diagnosis is the establishment of dissemination in space and time. Appropriate imaging of the brain and spinal cord can provide this information if not conspicuous from history and clinical examination. Evoked potentials can provide evidence of spatial dissemination of clinically silent lesions, and VEPs as well as OCT should be carried out to demonstrate involvement of the visual pathways.

Establishing the correct diagnosis as early as possible is mandatory since effective therapies are available that work best when embarked on early in the course of the disease.

L-7

Transcriptome signatures of NMOSD

Makoto Kinoshita, M.D., Ph.D
Special Lecturer, Department of Neurology, Osaka University

Dysregulation of immune responses is the hallmark of peripheral immunity in the pathogenesis of neuromyelitis optica spectrum disorder (NMOSD). In this regard, the comprehensive understanding of immune signature is crucial to have deeper and previously unrecognized insight of the NMOSD pathogenesis. Transcriptome analysis conducted by RNA-seq methods is a powerful tool to detect both comprehensive and interactive responses of various types of immune subsets. In the lecture, the recent advance of our understanding related to NMOSD patients is presented from our findings of novel role of peripheral neutrophils and disease activity marker.

L-8

NfL and other candidate biomarkers in MS & NMOSD

Mitsuru Watanabe, MD, PhD
Assistant Professor, Department of Neurology, Kyushu University Hospital

Multiple sclerosis (MS) is a chronic inflammatory demyelinating and neurodegenerative disease of the central nervous system. In clinical practice, disease activity is mainly assessed by clinical evaluation and neuroimaging. However, more sensitive biomarkers reflecting disease activity are needed to improve the prognosis. The levels of neurofilament light chain (NfL), one of three types of neuronal intermediate filament, elevate upon neuroaxonal damage not only in cerebrospinal fluid but also in blood. In MS, many studies showed that blood NfL can be a good biomarker representing disease activity, treatment response and prognosis. Therefore, blood NfL is expected to be used in daily clinical practice in the future to monitor disease activity and predict prognosis in each individual. Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune astrocytopathy mediated by anti-aquaporin 4 antibody that typically presents with severe and recurrent attacks in the optic nerve and spinal cord. Glial fibrillary acidic protein (GFAP), an intermediate filament of astrocytes, in blood is reported to be associated with disease activity and disability in NMOSD. This lecture provides updates on biofluid biomarkers including NfL and GFAP in MS and NMOSD and discuss whether they can be applied to clinical practice.

L-9

Single cell techniques to reveal pathogenic TCR and autoantigens

Belinda Kaskow, PhD
Lecturer, School of Biomedical Sciences, University of Western Australia

Single-cell techniques enable the detailed analysis of individual cells with high resolution across the epigenome, transcriptome, and/or proteome. Unlike multicellular studies, single-cell methodologies facilitate the recognition of matched alpha and beta chains of T cell receptors (TCRs) which can be harnessed to generate a functional TCR, allowing thorough exploration in assays to identify its cognate antigen. Recent advances in epitope discovery assays have revolutionized the unbiased screening of both the virome and human proteome providing powerful tools to uncover disease-related exogenous and endogenous antigens. Additionally, tissue-specific techniques including single-nucleus technologies provide new avenues for investigating CNS infiltrating immune cells behind the blood-brain barrier shedding light on the pathogenic mechanisms occurring within MS lesions.

L-10

The WHO Essential Medicines List expands to include DMTs for MS

Tomas Kalincik
Dame Kate Campbell Professorial Fellow

Earlier this year the World Health Organisation has reached a landmark decision to include, for the first time, disease modifying therapies for multiple sclerosis on the Essential Medicines List. This is a culmination of a large effort led by the MS International Federation and the Cochrane MS and Rare Diseases of the CNS Review Group, with support from two expert and consumer panels over the last two years. Tomas, who took part in this work, will talk about the synthesis of the evidence, the rationale for the proposal and the therapies that constitute the first entry for MS on the WHO Essential Medicines List.

L-11

Future MS treatment strategies

Su-Hyun Kim, MD, MS
Neurologist, Department of Neurology, National Cancer Center, Goyang, South Korea

Over the years, significant progress in understanding the underlying mehanisms of multiple sclerosis (MS) pathogenesis had led to introduction of an arsenal of disease-modifying therapies (DMT) that has provided neurologists more options for treating MS, improving neurological outcomes. Recent clinical studies have demonstrated the benefits of initiating highly effective DMT at an earlier stage of MS. Even with accurate early diagnosis, aggressive treatment, and vigilant clinical and paraclinical monitoring for breakthrough disease activity, a proportion of MS patients inevitably accumulate neurological disability and transition into a progressive disease course. The need for treatments that can stop or slow progression or improve disability in progressive forms of MS is even higher. Safety, tolerability, adherence, and possibly severe side effects are still unmet needs. Given this, more targeted and effective immunotherapies that restore self-tolerance, thereby reinstating the immune balance without causing general immune suppression, may hold promise for the treatment of MS. Furthermore, advancements in neuroprotective and remyelination therapies can offer new horizons for preventing long-term disability in MS patients. The future of MS treatment strategies lies in the convergence of personalized immunomodulation, neuroprotection, remyelination therapies, and combination therapies.

L-12

Neuromodulation as a novel MS treatment

Letizia Leocani, MD, PhD
Associate Professor of Neurology, University Vita-Salute San Raffaele, Milan

Preclinical evidence points to the potential beneficial effects of neuronal activity on (re-)myelination during development and in demyelinating diseases. Repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) are non-invasive brain stimulation (NIBS) techniques widely explored as a potential treatment in several neuropsychiatric disorders. Repetitive TMS is routinely used for the treatment of major depression and obsessive-compulsive disorder not responsive to a first pharmacologic treatment. More recent studies proposed to profit of the benefits of combining rehabilitation – physical, cognitive – with non-invasive brain stimulation in movement disorders, stroke, multiple sclerosis, and neurodegenerative dementing diseases. In most neurological diseases, neurons are the main target of NIBS for promoting their survival and plasticity of synaptic connections. In Multiple Sclerosis, two additional targets for NIBS are represented by the immune and myelination mechanisms, which may be modulated directly, or indirectly by changes in neuronal activity and polarization.

ORDINARY SUBMISSION

PLENARY ORAL PRESENTATION - 1

Advances in Technology in Diagnosis and Care

O-1

Longitudinal analyses of serum NfL, GFAP, and tau in patients with MOGAD

Hee-Jae Jung[1], Wangyong Shin[1], Da-Young Seo[2], Inhye Jang[2], Lynkyung Choi[2], Ji-yon Kim[1], Jungmin So[1], Hyunjin Kim[1], Young-Min Lim[1], Eun-Jae Lee[1]

[1]Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

[2]AMIST, University of Ulsan College of Medicine, Seoul, 05505, South Korea

Background: Prior studies have suggested that serum biomarkers such as neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP), and tau protein are potential useful biomarkers in patients with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). However, it remains unclear which one most accurately reflects disease course.

Objective: In a prospective longitudinal cohort of MOGAD, we aimed to identify the most appropriate biomarker (NfL, GFAP, or tau) for the disease by evaluating its correlations with disease disability and activity.

Methods: We prospectively enrolled consecutive MOGAD patients and obtained serum samples at enrollment, after 6–12 months of follow-up, and at relapses. Using ultrasensitive single-molecule array assays, we measured the levels of NfL, GFAP, and tau in the sera of MOGAD patients. We evaluated their associations with disease disability (Expanded Disability Status Scale, EDSS) score, and examined their longitudinal changes based on relapse status to assess the ability to reflect disease activity. We also explored their capability to distinguish relapses from remissions. Statistical analyses involved log-transformed serum biomarker levels.

Results: We enrolled 67 patients (including 40 women), with a mean age of 49.8 years and a disease duration of 4.6 years, collecting 134 samples. All biomarkers exhibited positive correlations with both EDSS score (NfL: $r = 0.36$, $p < 0.001$; GFAP: $r = 0.21$, $p = 0.020$; tau: $r = 0.20$, $p = 0.030$) and age (NfL: $r = 0.272$, $p = 0.026$; GFAP: $r = 0.434$, $p < 0.001$; tau: $r = 0.281$, $p = 0.021$). After adjusting for age, only NfL remained significantly correlated with EDSS scores ($r = 0.31$, $p < 0.001$), while GFAP ($r = 0.12$, $p = 0.140$) and tau ($r = 0.15$, $p = 0.100$) did not. Longitudinally, NfL and GFAP levels tended to increase during relapses but decrease during remission, whereas tau levels did not exhibit such trends. Between relapses and remission, only NfL levels showed significant differences (19.4 ± 22.8 vs. 66.0 ± 88.7 pg/mL, $p = 0.002$), with the highest area under the receiver operating characteristic curve (0.729, 95% confidence interval: 0.626–0.832).

Conclusion: Among NfL, GFAP, and tau, serum NfL may serve the most appropriate biomarker for longitudinal MOGAD monitoring, warranting confirmation in future studies.

O-2

Digital symbol-digit modalities test with modified protocols in patients with CNS demyelinating diseases: feasibility and patient preference

Da-Young Seo[1], Inhye Jang[1], Wangyong Shin[2], Lynkung Choi[1], Ji-yon Kim[2], Hyunjin Kim[2], Lee Eun-Jae[2], Young-Min Lim[2], Jungmin So[2], Jasoon Choi[3]

[1]AMIST, University of Ulsan College of Medicine, Seoul, 05505, South Korea

[2]Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

[3]Biomedical Engineering, University of Ulsan College of Medicine, Seoul, 05505, South Korea

Background: Cognitive impairment (CI) is prevalent in patients with multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD), and its monitoring is important. We developed a novel tablet-based modified digital SDMT (MD-SDMT), of which symbol-digit combination changes with every trial and devised two protocols according to test time.

Objective: We hypothesized that modifying the SDMT protocol to prevent learning effects may reliably evaluate CI with a shorter test time and improve patient satisfaction.

Methods: Patients with CNS demyelinating disease were prospectively enrolled in the outpatient clinic at the Department of Neurology, Asan Medical Center (Seoul, South Korea) between July 2021 and January 2022. All participants provided informed consent, and the study had approval from the hospital's institutional review board (IRB No. 2020-1038). Under the supervision of a study investigator, participants underwent MD-SDMT. Detailed instructions were provided to ensure correct performance. Participants were evaluated sequentially with paper-based SDMT, MD-SDMT_2 min, and MD-SDMT_1 min. During the MD-SDMT trials, participants were given a randomly changed key of nine symbol-digit pairs with each test trial. Participants who agreed to undergo additional questionnaires provided feedback on their user experience with the assessment tools. The survey items focused on patients' preferences, reliability, and convenience. Pearson correlations (r) between MD-SDMT and paper-based SDMT scores were evaluated. Also, we compared the MD-SDMT_1 min, MD-SDMT_2 min, and paper-based SDMT according to the degree of cognitive dysfunction, patients' age, and their preference by conditions using one-way ANOVA.

Results: We evaluated correlations between paper-based SDMT and MD-SDMT scores. Both MD-SDMT scores significantly correlated with paper-based SDMT (2 min, $r = 0.88$; 1 min, $r = 0.85$, all $p<0.001$) in all participants.

Conclusion: MD-SDMT protocols reliably evaluated CI even in patients with MS and NMOSD. Most (>90%) patients preferred MD-SDMT over paper-based SDMT, while the preferred test time may vary depending on patient characteristics.

Basic Science

O-3

Microglia Extracellular Traps Enriched in mtDNA Exacerbate Inflammatory Demyelination in Multiple Sclerosis

Shishi Shen[1], Shilin Wu[1], Wei Cai[1], Zhengqi Lu[1], Wei Qiu[1]
[1]*The Third Affiliated Hospital of Sun Yat-sen University*

Background: Multiple sclerosis (MS) is a chronic autoimmune, demyelinating, and neurodegenerative disease that leads to neurological dysfunction in early adulthood. It is reported that microglia release DNA- and proteinase-containing extracellular traps (MiETs) under bacterial stimuli. Whether MiETs are implicated in MS pathophysiology remains elusive.
Objective: To study the roles of MiETs on inflammatory demyelination in MS and the potential of MiETs as a therapeutic target.
Methods: Single cell RNA sequencing (scRNA-seq) analysis and immunofluorescent staining were performed to detect MiETs in experimental autoimmune encephalomyelitis (EAE). Stereotaxic injection and cerebellum organic slice culture (OSC) were performed to study the impact of MiETs on inflammatory demyelination. DNA immunoprecipitation was performed to measure enrichment of mtDNA in MiETs. Flow cytometry was performed to detect mitochondrial ROS. Transmission electrical microscopy (TEM) and JC-1 staining were used to display mitochondrial damage.
Results: MiETs was evident in the demyelinating lesions of EAE mice (N=8, P<0.05). In vitro experiments revealed that myelin debris efficiently induced MiETs formation (N=3, P<0.05), which caused pronounced inflammatory demyelination when injected to healthy spinal cord (N=8, P<0.05). Unexpectedly, we found that the DNA in MiETs was mainly derived from mitochondria (N=3, P<0.05). Mechanistically, myelin debris induced increment of mitochondrial ROS (N=3, P<0.05), which resulted in mitophagy and release of mitochondrial DNA (N=3, P<0.05). Clearing mitochondrial ROS inhibited MiETs formation (N=3, P<0.05).
Conclusion: Microglia in EAE lesions release MiETs enriched in mtDNA after myelin phagocytosis. Mechanistically, overload of myelin debris leads to oxidative mitochondrial injury and subsequent mitophagy. As a result, MiETs was released to cause demyelination.

O-4

Complement biomarkers reflect the pathological status of neuromyelitis optica spectrum disorders (NMOSD)

Katsuichi Miyamoto[1], Hidefumi Ito[1], Norimitsu Inoue[2]
[1]*Neurology, Wakayama Medical University*
[2]*Molecular Genetics, Wakayama Medical University*

Background: NMOSD is a disease in which astrocytes are damaged, resulting in injury to the optic nerve and spinal cord. Complement activation is involved in the pathogenesis of the disease, and antibody preparations against complement C5 have been approved for prevention of relapse, but the detailed mechanism of action is unknown.
Objective: In this report, we focused on the activating and regulating factors of complement and examined their relationship to the pathogenesis of NMOSD. Furthermore, we aimed to find effective biomarkers that reflect complement activation in NMOSD.

Methods: Twenty-one NMOSD cases (19 women and 2 men) with paired sera from the acute and stable phases were selected retrospectively, and complement-related items (sC5b-9, Ba, CFH, CFI) were measured. Medical information was collected from the medical charts, which were obtained in the usual medical practice. For healthy controls, the reference values for healthy subjects indicated by the Japanese Society for Complement Research were used. This study was approved by the ethics committee of the institution.
Results: The mean age was 48.0 years, the mean duration of illness was 5.1 years, and the mean physical disability level (EDSS) was 4.9. Ba, an activation marker of the alternative complement pathway, and sC5b-9, an activation marker of activation of the terminal complement pathway, were both elevated in the acute phase and significantly higher than in the remission phase. Complement factor H (CFH), a complement regulatory factor, was decreased in the acute phase as well as the remission phase of NMOSD.
Conclusion: Complement biomarkers, such as Ba, sC5b-9 and CFH in peripheral blood, have potential utility in understanding the pathological status of NMOSD.
Disclosures: KM received speaker honoraria from Alexion Pharmaceuticals, Inc., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Corporation, and Teijin Pharma Ltd.; NI received speaker honoraria from Alexion Pharma Corporation, Chugai Pharmaceutical Co. Ltd. and research support from Alexion Pharmaceuticals, Inc.

Comprehensive Clinical Care

O-5

Relaxing Rituximab infusion intervals may be a cost effective and safe recommendation for management of Multiple Sclerosis in resource poor settings.

Suhan Alva[1], Lekha Pandit[1], Akshatha Sudhir[1], Anitha D'Cunha[1]
[1]*Justice K. S. Hegde Charitable Hospital*

Background: Rituximab (RTX) bio-similar is available at subsidised rates in our demyelinating disease registry in southern India, and is prescribed for active MS. However, not all patients are able to meet the conventional 6 monthly dosing due to financial constraints.
Objective: Our objective was to assess the clinical course and MRI features in patients receiving RTX for MS (Multiple Sclerosis) at 6 -7 months and those ≥ 8month intervals to develop recommendations for our registry.
Methods: In this retrospective observational study (July 2019- June 2023), we included patients diagnosed with RRMS or SPMS with relapses who received a minimum of 2 additional infusions after the initial induction. Annualised relapse rate (ARR), EDSS (expanded disability status scale) and MRI contrast enhancing lesions (MRI-CEL) before initiating and after last infusion, were noted. CD19 counts were calculated (percentage of all PBMC), prior to every infusion, in a subset of patients.
Results: A total of 73 patients were included, 48 patients in Group 1(mean infusion interval 6.4 +/-1.91 years) and 25 patients in group 2 (mean infusion interval 9.5+/-1.51). There was no significant difference between the baseline characteristics, disease duration, ARR, EDSS & MRI-CEL between the 2 groups. After last infusion, there was a significant reduction in ARR (Group1- p 0.005; Group 2- $p < 0.0001$), EDSS (Group1&2- p 0.04), and reduction in MRI-CEL (Group1- $p < 0.0001$, Group 2- p 0.0004). Median CD19 count for Group 1 was 1.9% (0.5-11.8) and group 2- 2% (0.53%-15.4%) prior to infusions.
Conclusion: The results of our small study suggest that RTX infusion may be administered at intervals longer than the conventional 6 months, without clinical or radiological aggravation, despite B cell re-population as a cost-effective strategy in poor setting.

PLENARY ORAL PRESENTATION - 2
Disease modifying therapies

O-6
Immunosuppressive therapy in elderly patients with neuromyelitis optica spectrum disorder
Ki Hoon Kim[1], Su-Hyun Kim[1], Jae-Won Hyun[1], Ho Jin Kim[1], Yeon Hak Chung[2], Ju-Hong Min[2], Hee Jo Han[3], Seung Woo Kim[3], Shin Ha Young[3], Yong Nam Kwon[3], Sung-Min Kim[4], Hyunjin Kim[5], Eun-Jae Kim[5]
[1]*National Cancer Center of Korea, Department of Neurology*
[2]*Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine*
[3]*Department of Neurology, Yonsei University College of Medicine*
[4]*Department of Neurology, Seoul National University College of Medicine*
[5]*Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine*
Background: The immunosuppressive treatment (IST) of elderly individuals is challenging due to pre-existing comorbidities, frailty, changes in pharmacokinetics, and immunosenescence. This could frequently result in suboptimal treatment for these individuals, despite reports that late-onset NMOSD is associated with more severe disability.
Objective: Therefore, we aimed to investigate a detailed clinical analysis of elderly patients (≥ 65 years old) with AQP4-positive NMOSD who received IST, focusing on safety and efficacy of IST.
Methods: This retrospective study included 101 patients with AQP4-positive NMOSD over the age of 65 who have received IST for at least 6 months from the five referral centers in Korea. All patients fulfilled the 2015 diagnostic criteria for NMOSD and were positive for anti-AQP4 antibodies using cell-based assays.
Results: The median age at disease onset was 62.5 and the female to male ratio was 4:1. The median interval between onset and the initiation of IST was 15 months, and the EDSS score at the initiation of IST was 4.0. The administrative ISTs were azathioprine (n=61, 60%), MMF (n=48, 48%), and rituximab (n=41, 41%). Over a median of 5.7 years of IST, 58% of patients were relapse-free and the ARR (total number of attacks per patients-year) decreased from 0.62 to 0.12 (80.6% reduction). Patients treated with rituximab had a greater relapse-free rate (83%) than those treated with azathioprine (66%) or MMF (46%) (p=0.022). During median 3.6 years under IST after the age of 65, 47% had 89 infections and 21% of them experienced 25 severe infection events (SIE). Three patients expired due to pneumonia at ages 79, 67, and 68, respectively (two under rituximab, one under MMF). In addition, 45 adverse events (AE) were reported in 37 (37%) patients.
Conclusion: In elderly patients with NMOSD, the benefit of IST to prevent relapse appears to outweigh the risk of adverse effects. Rituximab showed a better benefit profile than MMF or azathioprine in elderly patients.

O-7
Efficacy and Safety of Rituximab in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder
Tatchaporn Ongphichetmetha[1], Jiraporn Jitprapaikulsan[1]
[1]*Siriraj Neuroimmunology Center, Division of Neurology*
Background: Most patients with multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) in Thailand receive immunosuppressive drugs due to low socioeconomic status. Previous studies demonstrated the efficacy of rituximab among such patients.
Objective: This study aimed to evaluate the efficacy and safety of RTX in Thai MS and NMOSD patients with the CD19-based treatment regimen.

Methods: We performed a retrospective review of MS and NMOSD patients at the Faculty of Medicine Siriraj Hospital from January 1994 to April 2023. The primary outcomes were changes in annualized relapse rate (ARR), the Expanded Disability Status Scale (EDSS) score, and the time to first relapse after RTX initiation for those who received RTX for more than one year. The secondary outcome was the safety of RTX.
Results: Seventy-five MS and NMOSD patients were included; 36 (48%) were MS and 39 (52%) were NMOSD. Thirty-three (91.7%) of MS patients and 31 (79.5%) of patients with NMOSD did not relapse after starting RTX, with a median follow-up period of 30 months (IQR 20-46) and 31 months (IQR 23-41), respectively. Among those who had previously received other medications (68%), the median ARR was significantly reduced from 0.87 (IQR 0.44-1.26) to 0 (IQR 0-0) after switching to RTX, $p < 0.001$. The median ARR between patients who received a fixed 6-month time point, and a CD19-based reinfusion regimen was not different (0.94 [IQR 0.58-2.83] and 1.00 [IQR 0.52-2.20], $p = 0.789$). A significant reduction in ARR was also demonstrated in patients who received an extended RTX dosing interval (every 10-12 months), adjusted treatment intervals using a CD19-based reinfusion regimen. Thirty-three patients (44%) experienced minor adverse events related to RTX.
Conclusion: RTX is effective for the prevention of relapse in Thai patients with MS and NMOSD with a moderate risk of adverse events. An extended dosing interval regimen of RTX under B lymphocyte monitoring is warranted.

Epidemiology, Genetics, and Epigenetics

O-8
Racial differences in Multiple Sclerosis disease characteristics amongst Chinese, Malay and South Asian patients in Singapore
Min Jie Koh[1], Tianrong Yeo[2], Seyed Ehsan Saffari[1], Kevin Tan[2], Janis Tye[2], Jeanne Tan[2], Amelia Aw[2], Rachel Siew[2]
[1]*Duke-NUS Medical School*
[2]*National Neuroscience Institute (NNI)*
Background: In Western populations, racial differences in Multiple Sclerosis (MS) disease characteristics have been observed. To date, no comparative studies have been performed amongst different Asian racial groups located within the same geographical region, thus it is uncertain whether differences in MS disease course exist amongst them.
Objective: In this study, we sought to compare Chinese, Malay, and South Asian (SA) MS patients in Singapore with regards to their disease phenotype and clinical course.
Methods: This study was performed at the National Neuroscience Institute (Tan Tock Seng Hospital campus). One hundred and eighty-eight patients were identified: 90 Chinese, 32 Malay, and 66 SA. Data collected included: socio-demographics (age, gender, smoking status), co-existing autoimmune conditions, initial presentation of MS (severity, sentinel imaging and biochemical investigations, clinical phenotype, MS type), disease-modifying therapy (DMT) usage (choice of DMT, time on DMT, number of DMT changes) and long-term disease characteristics (number of relapses, total disease duration, disability severity). The EDMUS Grading Scale (EGS), Expanded Disability Status Scale (EDSS), and Multiple Sclerosis Severity Score (MSSS) were used to quantify disability. Univariate analyses were done on continuous data using Kruskal-Wallis one-way analysis of variance followed by Dunn's test for post-hoc analysis, while Fisher exact test was utilised for categorical data. Univariate Cox proportional-hazards regression was performed to investigate the time to reach EDSS 6.0. P-values were 2-tailed, and significance set at <0.05.

Results: MS prevalence, corrected for population racial demographics, was the highest in SA followed by Malays and Chinese (pair-wise prevalence ratios: Chinese/Malay 0.52, Chinese/Indian 0.17, Malay/Indian 0.32). While socio-demographics and health-seeking behaviour/healthcare access parameters were similar across the races, a difference was observed at the initial presentation: the severity of the first MS attack was milder in SA compared to Chinese (median EGS, 2.0 vs 3.0; p = 0.010) and Malays (2.0 vs 3.0; p = 0.006). No differences in DMT usage were demonstrated, and importantly, long-term disease course as measured by time to reach EDSS 6.0 (p = 0.660) and MSSS (p = 0.667) were identical across the 3 races.
Conclusion: While there were obvious differences in MS prevalence amongst the 3 races, MS disease characteristics including long-term disability were similar, highlighting that MS is a singular disease across these genetically diverse groups.

O-9

Early-onset versus Late-onset MOGAD in a single center study: real-world data

Hyunjin Ju[1], Yeon Hak Chung[1], Ju-Hong Min[1]
[1]*Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Background: Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) is an inflammatory disorder of the CNS involving the brain, optic nerve, and spinal cord. MOG-antibody-associated disease is known to be more common in children; however, it also occasionally presents in the elderly group.
Objective: We aim to describe the clinical characteristics and treatment outcomes in patients with late-onset (≥50 years) MOGAD (LO-MOGAD) compared to patients with early-onset (<50 years) MOGAD (EO-MOGAD).
Methods: We prospectively enrolled 75 patients who had positive MOG-IgG using cell-based assay in the CNS Inflammatory and Demyelinating Disease Registry from 2015 to July 2023 at the Samsung Medical Center. After excluding 8 patients who did not satisfied the newly proposed criteria for MOGAD, 67 patients were analysed. Clinical data from medical record were collected retrospectively.
Results: 23 (34.3%) LO-MOGAD patients and 44 EO-MOGAD (65.7%) patients were analysed. LO-MOGAD had significantly higher frequency of ON at onset and higher prevalence of comorbidities of hypertension, diabetes and solid tumor compared to EO-MOGAD. Follow up studies for MOG-IgG revealed no significant difference for the rate of seroconversion (4/16 (25.0%) vs. 4/29 (13.8%), p=0.347). In LO-MOGAD, while IST usage was less common compared with EO-MOGAD (14/21 (66.7%) vs. 36/42 (85.7%), p=0.078), it tended to start earlier stage before second relapse (10/13 (76.9%) vs. 20/36 (55.6%), p=0.175). During the follow-up period, there were no significant differences in the annual relapse rates (0.72±1.04 vs. 0.88±1.36, p=0.313) or overall frequency of relapses (13/22 (59.1%) vs. 33/44 (75.0%), p=0.185) between LO-MOGAD and EO-MOGAD.
Conclusion: LO-MOGAD had higher frequency of ON at onset and higher prevalence of comorbidities compared to EO-MOGAD. There was no significant difference in treatment or follow up data. further study with larger sample size is needed.

Neuroimaging and Neurophysiology

O-10

Different activation pattern of late complement pathway in the CSF between MOGAD and AQP4+N-MOSD.

Kimihiko Kaneko[1], Hiroshi Kuroda[2], Hirohiko Ono[1], Yuki Matsumoto[3], Naoya Yamazaki[1], Naoki Yamamoto[1], Shu Umezawa[1], Chihiro Namatame[1], Yoshiki Takai[1], Toshiyuki Takahashi[4], Juichi Fujimori[5], Ichiro Fujimori[5], Yasuo Harigaya[6], Kazuo Fujihara[7], Tatsuro Misu[1], Masashi Aoki[1]

[1]Tohoku University

[2]Southern Tohoku Research Institute for Neuroscience Southern Tohoku General Hospital

[3]NHO Miyagi National Hospital

[4]NHO Yonezawa National Hospital

[5]Tohoku Medical and Pharmaceutical University

[6]Japanese Redcross Maebashi Hospital

[7]Fukushima Medical University

Background: Complement system serves an important role in the pathogenesis of aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+NMOSD). Although myelin oligodendrocyte glycoprotein-associated disease (MOGAD) clinically resembles AQP4+NMOSD, the significance of complement system in MOGAD has not been fully clarified.

Objective: To elucidate pattern of complement activation in the cerebrospinal fluid (CSF) during the acute phase of MOGAD, especially compared to AQP4+NMOSD.

Methods: We collected CSF samples from 13 patients with MOGAD, 12 with AQP4+NMOSD, 5 with MS, and 2 with non-inflammatory neurological diseases (NIND) from the participating facilities. All samples were collected and stored at -80□ until analysis. We measured levels of C3a, C4a, C5a by beads-based assay (Human Anaphylatoxin Kit, BD, San Jose, CA) and C5b-9 level by enzyme-linked immunosorbent assay (Human C5b-9 ELISA Set, BD, San Jose, CA) according to the manufacture's protocol. We also collected clinical data, such as age, gender, clinical phenotype, duration from onset to sample collection, antibody titter, onset/relapse, IgG index, oligoclonal bands (OCB), expanded disability status scale (EDSS), and CSF myelin basic protein (MBP) level. Antibody status was measured by in-house cell-based assay. We compared clinical and laboratory data; compared complement levels in MOGAD, AQP4+NMOSD, MS and NIND.

Results: On patient background, age of NMOSD [median 32 (range 19-47), years old] was significantly higher than that in MOGAD [32(17-48)] or MS [32 (19-47)]. CSF cell count (/mm3) was [6.5 (0-256)], [10 (0-93)], [1 (1-4)] in MOGAD, NMOSD, and MS. The levels of complement [MOGAD; NMOSD; MS] (pg/ml) were C3a [median 148.8 (interquartile range 97.6–184.5); 241.6 (1.12–269.3); 43.68 (19.1–75.0)], C4a [0.714 (0–4.141); 0.883 (0.318–1.47); 0 (0–0.707)], C5a [3068 (2545–3216); 2935(6.98–54.51); 335.7 (193.8–731.7)], and C5b-9 [4.355 (1.86–20.18); 41.86 (17.05–111.2); 22.14 (18.9–22.84)]. The C5b-9 levels were significantly higher in AQP4+NMOSD compared to those in MOGAD, but C3a, C4a, and C5a levels did not reach significant differences. The results were essentially same when corrected by protein level. Since C5 is cleaved into C5a and C5b-9 equally, we calculated C5b-9/C5a ratio to assess the late pathway progression; the C5b-9/C5a was significantly higher in AQP4+NMOSD than that in MOGAD.

Conclusion: In the CSF, complement system is activated both in MOGAD and AQP4+NMOSD, but the progression of late complement pathway differs between the two disease entities.

Disclosures: No COI to disclose

POSTER SESSION - 1
Advances in Technology in Diagnosis and Care

P-1
Novel findings of distinctive peripapillary retinal venous changes in multiple sclerosis: "central vein sign" in retina
Soo-Hyun Park[1], Nam-Hee Kim[2]
[1]*Hallym University Kangdong Sacred Heart Hospital/Department of Neurology*
[2]*Dongguk University Ilsan Hospital/Department of Neurology*
Background: The "central vein sign" has recently been proposed as a highly sensitive and specific biomarker for MS, indicating venous abnormalities related to the pathogenesis of MS. Histopathologic studies of MS reported that local disrupted venous flow leads to remodelling of the medullary veins and a breakdown of the endothelium.
Objective: Our study aims to investigate how the characteristics of the retinal vascular diameter differ between arteries and veins in MS compared to healthy individuals for the possibility of venous involvement in the retina of MS.
Methods: Visual function testing, including optical coherence tomography (OCT) and fundus photography, was performed in 33 MS (33 non-ON eyes vs. 33 ON eyes) patients and 34 healthy controls. To evaluate retinal vascular change, the diameters of the vein on the optic disc margin were measured by the KOWA-VK-2 software on the fundus photography image.
Results: Retinal vein diameter was dilated in MS non-ON eyes (113.7±6.6 µm) compared to control eyes (109.3±6.8 µm). This trend is also similarly found in MS ON eyes (112.4±6.9 µm) compared to control eyes. Retinal artery thinning was seen in MS non-ON eyes (83.6±7.1 µm) relative to control eyes (85.6±6.7 µm). This difference was found after adjusting the number of ON episodes (p=0.001). Intriguingly, a more severe thinner retinal nerve fibre layer correlated with a thicker retinal vein diameter (r=-0.388, p=0.041) in MS ON eyes.
Conclusion: Our study results are a novel finding that the vein changes early exhibited in fundoscopy. It suggests that MS is associated with more severe retinal vein injury than control, which suggests the different pathogenesis of vein involvement in MS.
Disclosures: No conflict of interest

P-2
PET in Autoantibody-negative but probable Autoimmune Encephalitis (ANPRA) - A sensitive and early biomarker
Parthvi Ravat[1], Sangeeta Hasmukh Ravat[1], Shwetal Pawar[1]
[1]*Seth GS Medical College and King Edward Memorial Hospital, Mumbai*
Background: AE is no longer a rare entity and newer antibodies are being found everyday. Hence, in the absence of an all-comprehensive antibody testing, characterizing ANPRA becomes important and PET scan seems to be an important biomarker on that horizon. Our study aims to explore the importance of PET scan in the diagnostic armamentarium for AE/ANPRA.
Objective: To study PET scan as an investigational tool in the diagnosis of Autoimmune encephalitis and its sensitivity.

Methods: A prospective study of 57 Autoimmune encephalitis patients over the last 5 years (2018 to 2022) at a tertiary care center in western India successively visiting and diagnosed in the Neurology department of a major public hospital in Mumbai. Ethics approval and informed consent were taken.
Inclusion criteria: Adults (> 18 years), patients who fulfilled the autoimmune encephalitis criteria used by Dalmau et al 2016 and/or had a high index of clinical suspicion.
PET protocol included 18F-FDG - iv 2.5 mbq/kg bolus, 60 min waiting followed by reconstruction of images reconstructed using an iterative reconstructive algorithm. It was interpreted visual semiquantitative assessment with normalization to the Occipital cortex and Z scores on cortex ID (age-matched normative data) by a nuclear medicine Associate Professor, assisted by Senior Resident in Nuclear medicine.
Results: Out of a total of 57 [antibody positive (n =20), ANPRA (n=37)] AE patients, 85.7% (N=48) showing PET positivity (active encephalitis) and 14.2%(n=8) were PET negative (i.e., age-appropriate normal metabolism). Out of the 37 ANPRA patients, 30 had PET positivity. Amongst the patients with Normal MRI (n=34), 26 were PET positive, which highlights the importance of PET. ANPRA, with normal MRI, but PET scan positive had a similar response to standardized treatment for AE (in terms of seizure reduction, symptom remission, and behavioural symptom remission) compared to those who had MRI, AB, and PET-positive. This adds more weight to our ANPRA diagnosis. PET Sensitivity was 84.62% (65.13% to 95.64%) which corroborates with global studies. The results also showed that the patients whose PET scan was done earlier in their natural history of disease (<30 days of symptom onset) had lesser days of hospital stay (<10 days) as compared to patients who underwent a PET scan at >30 days of symptom onset.
Conclusion: Our results suggest PET scan as a more sensitive and more time-sensitive biomarker for AIE. There were some limitations of the study that follow-up PET scans were done only in 5 patients which showed a reduction of hypermetabolism.

P-3

Profiling Serum Small Extracellular Vesicle miRNAs in patients with Multiple Sclerosis, Neuromyelitis Optica Spectrum Disorder, and Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease

Hyunjin Ju[1], Yeon Hak Chung[1], Ju-Hong Min[1]
[1]*Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Background: CNS demyelinating diseases encompass conditions such as MS, NMOSD, and MOGAD, which are now recognized as separate entities with distinct pathogenesis. MicroRNAs are single-stranded small non-coding RNAs functioning in gene expression and protein synthesis and are emerging as novel diagnostic and prognostic biological markers.
Objective: We identified differentially expressed miRNAs (DE miRNAs) in patient with MS, NMOSD, MOGAD, and healthy controls.
Methods: Serum samples were obtained from 12 patients with MS, 12 patients with seropositive NMOSD, 11 patients with MOGAD, and 12 healthy controls (HC). We performed a comprehensive analysis of differentially expressed miRNAs (DE miRNAs) in serum extracellular vesicles (EVs) and identified miRNAs that exhibited significant differential expression between the groups using Nanostring analysis. We evaluated the diagnostic potential of miRNAs and miRNA panels using receiver operating characteristic (ROC) analysis for distinguishing demyelinating diseases.

Results: In MS, we identified the three miRNAs upregulated and 13 miRNAs down-regulated relative to HC. We also found 10 miRNAs up-regulated and 22 miRNAs down-regulated in patients with NMOSD, and 22 miRNAs up-regulated and 55 miRNAs down-regulated in patients with MOGAD. We identified several highly correlated miRNAs with EDSS scores in each disease group. In ROC analysis, we found several miRNAs showing high AUC values for distinguishing MS vs NMOSD, NMOSD vs MOGAD, and MOGAD vs MS, which showed significantly increasing AUC values when combined as a panel.
Conclusion: We successfully identified DE miRNAs in serum EVs specific to MS, NMOSD, and MOGAD, suggesting that miRNA-based biomarkers can potentially improve the diagnostic accuracy of CNS demyelinating diseases.
Disclosures: This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (2021R1F1A1049347).
JH Min is funded by and has received research support from the National Research Foundation of Korea and SMC Research and Development Grant. She has lectured, consulted, and received honoraria from Bayer Schering Pharma, Merk, Biogen Idec, Sanofi, UCB, Samsung Bioepis, Mitsubishi Tanabe, Celltrion, Roche, Janssen and Astrazeneca.

P-4

Longitudinal analyses of serum NfL, GFAP, and tau in patients with MOGAD

Hee-Jae Jung[1], Wangyong Shin[1], Da-Young Seo[2], Inhye Jang[2], Lynkyung Choi[2], Ji-yon Kim[1], Jungmin So[1], Hyunjin Kim[1], Young-Min Lim[1], Eun-Jae Lee[1]
[1]Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea
[2]AMIST, University of Ulsan College of Medicine, Seoul, 05505, South Korea

Refer to O-1 in Plenary Oral Presentation - 1

P-5

Digital symbol-digit modalities test with modified protocols in patients with CNS demyelinating diseases: feasibility and patient preference

Da-Young Seo[1], Inhye Jang[1], Wangyong Shin[2], Lynkung Choi[1], Ji-yon Kim[2], Hyunjin Kim[2], Lee Eun-Jae[2], Young-Min Lim[2], Jungmin So[2], Jasoon Choi[3]
[1]AMIST, University of Ulsan College of Medicine, Seoul, 05505, South Korea
[2]Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea
[3]Biomedical Engineering, University of Ulsan College of Medicine, Seoul, 05505, South Korea

Refer to O-2 in Plenary Oral Presentation - 1

POSTER SESSION - 2
Basic Science

P-6
The Influencing Factors Of Retinal Nerve Fiber Layer Thickness In Patients With Multiple Sclerosis: A Logistic Analysis From A Chinese Cohort
Chao Quan[1], Hongmei Tan[1], Yuxin Li[2], Fanru He[2], Jingzi ZhangBao[1], Lei Zhou[1], Liqin Yang[2], Chongbo Zhao[1], Chuanzhen Lu[1], Qiang Dong[1], Haiqing Li[2]
[1]Department of Neurology, Huashan Hospital, Shanghai Medical College, Fudan University, Shanghai, China
[2]Department of Radiology, Huashan Hospital, Fudan University
Background: Multiple sclerosis (MS) is a chronic inflammatory and immune mediated demyelinating disease of the central nervous system (CNS). Its global prevalence are still increasing. Optic neuritis is a common initial manifestation of MS. Monitoring and delaying optic neuropathy is crucial for predicting the prognosis of MS, especially in Asian countries.
Objective: This study investigated the clinical factors that correlated to retinal nerve fiber layer (RNFL) thickness in Chinese patients with MS.
Methods: 207 patients with MS were diagnosed using McDonald criteria 2017. RNFL thickness was examined using optical coherence tomography. Visual functions were evaluated using optical coherence tomography, neurological functions were evaluated using Expanded Disability Status Scale (EDSS), Nine-Hole Peg Test (9HPT), Timed 25 Foot Walk (T25FW), Symbol Digit Modalities Test (SDMT), Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE). Spearman correlation analysis was used to analyze the relevant factors influencing RNFL thickness.
Results: The results showed that RNFL thickness was positively correlated with age of onset ($\rho = 0.220$, $p = 0.001$), ganglion cell-inner plexiform layer (GCIPL, $\rho = 0.330$, $p < 0.001$), and negatively correlated with EDSS ($\rho = -0.243$, $p < 0.001$), disease course ($\rho = -0.346$, $p < 0.001$), the number of infratentorial T2 lesions ($\rho = -0.259$, $p < 0.001$). The RNFL thickness was not associated with gender ($\rho = -0.012$, $p = 0.866$), 9HPT ($\rho = 0.045$, $p = 0.559$), MMSE ($\rho = 0.028$, $p = 0.712$), MoCA ($\rho = 0.048$, $p = 0.513$), the positivity of oligoclonal bands ($\rho = -0.013$, $p = 0.860$), SDMT ($\rho = 0.066$, $p = 0.411$) and T25FW ($\rho = -0.136$, $p < 0.001$).
Conclusion: RNFL thickness was significantly corelated to the age of onset, EDSS, GCIPL, course of disease, and the number of infratentorial T2 lesions in patients with multiple sclerosis.

P-7
Study of AQP4 Antibody-Mediated Platelet Inflammation in the Involvement of Organ-Specific Immunity in Optic Neuromyelitis Spectrum Disorders
Jin Bi[1], Ying Fu[1]
[1]The First Affiliated Hospital of Fujian Medical University
Background: Neuromyelitis Optica Spectrum Disorder (NMOSD) is a neuroimmune disease characterized by localized damage limited to the optic nerve and central nervous system (CNS) organs. AQP4 antibody is the pathogenic antibodies in this disease, primarily produced periphery. How they penetrate the blood-brain barrier to cause pathology is a subject of study.
Objective: Many researchers have observed that platelet-related inflammation can lead to endothelial cell damage. To determine whether AQP4 antibodies in NMOSD induce platelet inflammation leading to blood-brain barrier damage.

Methods: With a deeper understanding of immunity, the role of platelet inflammation is gradually being recognized, and among them, FcγRIIA is an activated FcγR expressed on human platelets, capable of recognizing the constant region of immunoglobulin IgG expressed by most cells in the immune system and immune complexes. Based on the Central Inflammatory Demyelinating Disorders Cohort at the First Affiliated Hospital of Fujian Medical University (ClinicalTrials.gov NCT 04388072), AQP4 antibody-positive NMOSD patients were enrolled. The relationship between antibodies and platelets was analyzed from three perspectives: (1) Peripheral blood platelet activation and platelet-derived microparticle release in patients; (2) Co-incubation of serum from AQP4 antibody-positive NMOSD patients with healthy human platelets; (3) Co-incubation of purified AQP4 antibodies with healthy human platelets.
Results: We conducted flow cytometry to measure the peripheral blood platelet activation marker CD62P in 20 AQP4 antibody-positive NMOSD patients and 10 healthy individuals. Flow cytometry analysis revealed that peripheral blood platelet CD62P levels in acute-phase NMOSD patients (20.1% ±10.8%) were higher than those in the stable phase (4.4% ± 1.4%) and healthy control (2.9% ± 0.2%). The proportion of CD62P activation increased ($P < 0.05$) when serum from AQP4 antibody-positive NMOSD patients was co-incubated with healthy individuals' platelets. Following purification of AQP4 antibodies using a Protein G column and co-incubation with healthy individuals' platelets, there was a significant increase in platelet CD62P levels ($P < 0.05$).
Conclusion: In acute phases of NMOSD patients, AQP4 antibodies could potentially mediate platelet inflammation.

P-8
Microglia Extracellular Traps Enriched in mtDNA Exacerbate Inflammatory Demyelination in Multiple Sclerosis
Shishi Shen[1], Shilin Wu[1], Wei Cai[1], Zhengqi Lu[1], Wei Qiu[1]
[1]*The third affiliated hospital of Sun Yat-sen University*
Refer to O-3 in Plenary Oral Presentation - 1

P-9
Screening and pathogenicity study of human anti-myelin oligodendrocyte glycoprotein monoclonal antibody
Lijie Zhang[1], Ying Fu[1]
[1]*Department of Neurology and Institute of Neurology of The First Affiliated Hospital, Institute of Neuroscience, Fuzhou, China*
Background: Myelin oligodendrocyte glycoprotein associated disease (MOGAD) is a newly defined central nervous system demyelinating disease. However, the pathogenicity of MOG-IgG and its relationship to the disease phenotype remain unclear. Currently, there is a lack of human disease-specific antibodies to study the pathophysiological mechanisms.
Objective: The aim of this study is to screen and generate patient-derived MOG monoclonal antibodies (mAbs) and to test their pathogenicity in vitro and in vivo.

Methods: The immunoglobulin (Ig) sequences of memory B cells and MOG-specific B cells in the cerebrospinal fluid or peripheral blood of patients with acute MOGAD were identified by single-cell flow cytometry and single-cell PCR. The paired heavy and light chain sequences were constructed into antibody expression vectors to generate recombinant antibodies (rAbs), and antibody reactivity to MOG was verified by CBA and immunohistochemistry. Stable MOG monoclonal cell lines were established by lentivirus infection to verify the specificity and binding capacity of the MOG-rAbs. The pathogenicity of the antibodies was preliminarily verified in vivo and in vitro.
Results: We have reconstituted two MOG monoclonal antibodies (ZM-2F-rAb and TXW14-rAb) from the cerebrospinal fluid of MOGAD patients that are reactive with full-length MOG conformational proteins. TXW14-rAb bound human MOG more strongly than ZM-2F-rAb, whereas the reverse was true for murine MOG. Two MOG monoclonal antibodies killed MOG-expressing cells in vitro with complement-dependent cytotoxicity. In vivo, only ZM-2F-rAb increased the clinical score of half-dose EAE and led to increased demyelination of the spinal cord.
Conclusion: Two pathogenic natural MOG-rAbs from two MOGAD patient donors were screened. It is beneficial for the establishment of a MOG disease model and helps to understand the binding epitopes of autoantibodies to CNS self-antigens.

P-10
Complement biomarkers reflect the pathological status of neuromyelitis optica spectrum disorders (NMOSD)
Katsuichi Miyamoto[1], Hidefumi Ito[1], Norimitsu Inoue[2]
[1]*Neurology, Wakayama Medical University*
[2]*Molecular Genetics, Wakayama Medical University*
Refer to O-4 in Plenary Oral Presentation - 1

POSTER SESSION-3
Comprehensive Clinical Care

P-11
Peculiar Gyratory Movement In Autoimmune Encephalitis
Parthvi Ravat[1], Sangeeta Ravat[1], Shwetal Pawar[1]
[1]*Seth GS Medical College and King Edward Memorial Hospital, Mumbai*
Background: Autoimmune encephalitis (AE) was first described in the last 2 decades, but its varied presentations and varied antibodies are discovered everyday. We discuss here a case of a peculiar presentation of AE.
Objective: To address and bring to light one of the rare presentations of AE, so that it isn't missed in the clinics, considering it is a treatable condition to quite a large extent.
Methods: A 42-year-old, female started with behavioral symptoms, significant cognitive decline, and self-destructive behavior like hair pulling along with stereotypical gyratory movements, without any constitutional symptoms and rapid deterioration of ADL over a span of 3 months. These gyratory movements were random in direction (either left to right or right to left) and she did not have any ictal activity on Scalp EEG during these episodes. She was able to talk and respond during these episodes, which made the possibility of a seizure less likely (Video available). An array of neurologists, psychiatrists, neuropsychologists, and hypnotherapists were consulted. Her investigations were normal including an extensive list of blood tests, CSF tests, and 3T MRI brain imaging. CSF Biofire (viral, bacterial m fungal panel), Autoimmune, and paraneoplastic antibody panels, in serum and CSF were also negative. This is when a PET scan was advised.
Results: PET showed significant evidence of encephalitis with hypermetabolism in dorsolateral frontal regions, bilateral mesial temporal regions (left > right), and midbrain. (image available) After this, decided to pursue her as ANPRA (Antibody negative probable autoimmune encephalitis). The peculiar gyratory movements were attributed to be a manifestation of disinhibition due to frontal lobe involvement. She was treated with intravenous steroids and immunoglobulin after which there was near complete resolution of her symptoms including memory complaints, with a minor relapse at 6 months, which was addressed with Rituximab. Now, at 3 year follow-up, she remains symptom free.
Conclusion: This patient would have continued morbidly if one had not thought of a PET scan early on. The gyratory movements are rare and atypical but should be kept in mind especially in the setting of other features of AE.

P-12
Clinical Features of MOGAD In A Tertiary Academic Centre In Singapore
Yihui Goh[1], Derek Soon[1], Amy Quek[2]
[1]*National University Health System*
[2]*National University Hospital*
Background: The clinical spectrum of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) continues to unfold. Limited data are available on the clinical characteristics of multiethnic Southeast Asian patients and their predilection to relapsing disease.

Objective: We describe the clinical characteristics of MOGAD patients seen at the National University Hospital, Singapore, and examine their clinical course for relapses.
Methods: Since 2015, we tested for MOG-IgG to diagnose MOGAD in our patients with suspected inflammatory demyelinating disorders. A retrospective review of patients older than age 16 years with MOGAD seen from 2015 to 2023 was conducted. Analysis of disease relapses was done among those with at least 3 months of follow-up.
Results: Twenty-seven patients with MOGAD (Chinese,17; Malay,4; Indian,2; others,4) were included. Seventeen (63%) were female, and median age at diagnosis was 34 years. Of 47 attacks, the majority were optic neuritis (30,64%), followed by brainstem/meningoencephalitis (7,15%), transverse myelitis (3,6%) and others (7,15%). Twenty patients were followed up for at least 3 months, with median duration of 30 months (range 4-93).
Twenty relapses occurred in 9 (45%) patients. The first relapse occurred at a median of 11 months (range 1-117) after an initial presentation. Most relapses were of similar presentation as the initial attack, except for one patient who had myelitis following an optic neuritis presentation. In 6 (66.7%) patients, relapses occurred whilst on immunotherapy.
Persistent MOG-IgG was observed in 7 (54%) patients out of 13 who were retested; 6 patients seroconverted. Four of 7 (57%) patients with persistent seropositivity relapsed, and 3 patients (50%) who seroconverted had relapses.
Conclusion: Optic neuritis is the commonest neurologic manifestation observed in this cohort of multiethnic Asian patients with MOGAD. Half of the patients had a relapsing course, which often occurred despite immunotherapy or seroconversion.
Disclosures: NA

P-13
Clinically Isolated Syndrome Presenting with Writer's Cramp: A Rarity at Neuroimmunology-Movement Disorder Interface
Kadam Nagpal[1], Swayam Prakash[2]
[1]*Pushpawati Singhania Research Institute, Saket, New Delhi, India*
[2]*Kins Institute of Neurosciences, Siliguri, West Bengal, India*
Background: Clinically isolated syndrome (CIS) refers to a first clinical episode suggestive of multiple sclerosis (MS). CIS presentations can be monofocal or multifocal and typically involve the optic nerve, brainstem, cerebellum, spinal cord, or cerebral hemispheres. However, writer's cramp presenting as CIS is quite rare.
Objective: Through this case report, we aim at creating awareness regarding rare presentation of CIS as writer's cramp as well as to incite discussions and debate regarding such rare presentation amongst the neuroimmunology and movement disorder community.

Methods: Phenomenology of the abnormal movements of the patient was observed and video recorded and matched with the described phenomenology of writers' cramps. Symptoms defined as CIS was as per Revised McDonald's criteria.
17-year-old male presented with acute onset writer's cramp on the right side. There was no weakness or numbness in any limbs and no abnormal movements at rest. No history of speech difficulty, headache, trauma to head/neck, fever, recent vaccination, or any significant past history. On examination, cognition and cranial nerves were intact. He had twisting movements of right hand which were more pronounced upon writing such that his writing became illegible, and he had to stop writing thereafter due to a painful cramp. His Routine blood investigations, slit lamp microscopy was normal. Vasculitis panel was negative. MRI brain showed Gd-enhancing signal in left pericallosal region and right periventricular region. MRI cervical spine with screening showed hyperintense signal on T2W images with expansion on cervical spinal cord suggestive of demyelinating plaques. VEP, BAER and SSEP were also normal. CSF for oligoclonal bands was positive, however routine and other tests were normal. Patient was administered Intravenous methylprednisolone for 5 days and then subsequently started upon Dimethylfumarate 240 mg Twice daily.
Results: Patient had near complete recovery in dystonic posturing of right hand and was able to resume all his clinical activities. Follow up neuroimaging did not show any expansion in preexisting lesions or any occurrence of new lesion.
Conclusion: Early diagnosis and prompt treatment lie at the core of effective management. CIS presenting as writer's cramp is very rare but maintaining high index of suspicion is the key to right diagnosis and appropriate treatment.
Disclosures: There are no sources of funding or any conflicts of interest.

P-14
NMDAR Encephalitis In A Young Girl With Ovarian Teratoma
Simon Ling[1], Jocelyn Lim[1]
[1]*KK Women's & Children's Hospital Singapore*
Background: N-methyl-D-aspartate receptor (NMDAR) autoimmune encephalitis (AIE) occurs in children and adults. Notably it can be associated as a paraneoplastic disorder in young adult females with ovarian teratomas.
Objective: We describe the case of a young girl with seropositive NMDAR encephalitis who had ovarian lesion excised with final histopathology that of mature teratoma.
Methods: Case description including clinical features and investigation findings.
Results: A 14-year-old Chinese girl presented with urinary incontinence, seizures and periods of dysphasia. Initial treatment was with anticonvulsant medications and antimicrobials. MRI brain and EEG were unremarkable. CSF white cell count was mildly elevated. She developed neuropsychiatric features with stupor, agitation, anxiety, and sleep disturbance requiring psychiatric and sedative medications. She also had movement disorder with abnormal posturing. NMDA antibody was positive in serum and CSF. She received intravenous methylprednisolone and immunoglobulin. Ultrasound showed a 4cm hyperechoic right ovarian lesion suggesting dermoid cyst. This was excised via laparoscopic cystectomy. Histopathology showed a cyst containing tooth, hair and calcified nodule. Cyst wall contained ectodermal, mesodermal, and endodermal elements. There were scattered histiocytes but no other inflammatory infiltrate. The final diagnosis was mature teratoma.

Conclusion: The patient improved markedly after pulse steroids, IVIg and cystectomy. No biologics or other immune therapy have been given as yet. Prompt discovery and removal of ovarian teratomas in females with NMDAR encephalitis confers improved prognosis.
Disclosures: NA

P-15
The disease burden among Neuromyelitis Optica patients in Taiwan
Chia-Yi Tian[1], Chen-Shu Chang[1], Kai-Chen Wang[1]
[1]*Changhua Christian Hospital*
Background: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory disease of the central nervous system. The Real-World data of NMOSD in Taiwan is limited.
Objective: To delineate the demographic, clinical, and risk factors predictors of disease burden such as infection or relapse for hospitalization in NMOSD in Taiwan.
Methods: We retrospectively identified NMOSD patients by diagnostic codes or being positive for AQP4 autoantibody, and then confirmed through physician chart reviews based on the 2015 NMOSD criteria with a diagnosis of NMOSD between 2014 and 2021. The patients were divided into three groups based on their history of emergency room visits or hospitalizations in the observation period: Group A, patients who had no hospitalizations or emergency room visits; Group B, patients who had only one hospitalization or emergency room visit; and Group C, patients who had two or more hospitalizations or emergency room visits. Statistical analyses were performed to find out the risks such as hospitalization, infection, or relapsing among these patients in the follow-up period.
Results: During a median follow-up period of 3.5 years, 59 NMOSD patients were identified and analyzed. Our findings indicated that higher doses of Azathioprine (54.6mg, P=0.04) and a higher trend of oral steroids (P=0.048, mean 14.1mg) were associated with higher frequent hospitalizations or emergency room visits. The disease severity of the first two years can't determine the later frequency of hospitalization(P=0.10) and emergency visits(P=0.58). Furthermore, the adjusted Cox regression analysis revealed that NMOSD patients who were older or had comorbid Sjogren's syndrome were more likely to experience infections (Hazard ratios of 1.1 [95% CI 1.0-1.2] and 31.7 [95% CI 1.5-693.5], respectively). Male gender was associated with a higher risk of relapse, with a hazard ratio of 3.8 [95% CI 1.0-18].
Conclusion: Our study reports the demographic, clinical, and risk factors predictors of disease burden such as infection or relapse for hospitalization in Taiwan NMOSD.

P-16
Validation of the International MOGAD Panel proposed criteria
Ki Hoon Kim[1], Su-Hyun Kim[1], Jae-Won Hyun[1], Ho Jin Kim[1]
[1]*National Cancer Center of Korea, Department of Neurology*
Background: The criteria proposed by the international MOGAD panel were recently released, and these criteria are expected to have a major impact on the diagnosis and management of MOGAD as well as the design of clinical trials evaluating new therapies.
Objective: This study aimed to assess their diagnostic performance in a MOGAD cohort from the National Cancer Center (NCC) at disease onset and throughout the follow-up period.

Methods: All 100 patients, diagnosed with MOGAD from the NCC registry for CNS inflammatory demyelinating disease (CNS-IDD) between 2007 and March 2023, were enrolled in this study. To evaluate MOG-IgG seropositivity, a live cell-based assay was performed with serum using a full-length MOG-transfected stable cell line. When the immunofluorescence intensity score (IF-score) of MOG-IgG was 2+ or greater (range 1 to 4), MOG-IgG results were classified as clear-positive based on the International MOGAD Panel's proposal.
The MOGAD criteria were retrospectively applied to our cohort during the first attack and during the follow-up period to evaluate the diagnostic performance.
Results: Among enrolled 100 patients, 93 fulfilled the criteria throughout the median 24 months of follow-up. All 36 patients with a clear-positive MOG-immunoglobulin G (IgG) satisfied the supporting features, except one who did not undergo MRI scan at disease onset. The criteria also contributed significantly to the confirmation of MOGAD in 57 of 64 patients without clear-positive MOG-IgG. When limited to the first attack, 51 of 61 patients (84%) satisfied the criteria, four of whom were initially negative for MOG-IgG.
Conclusion: The results demonstrated that the MOGAD criteria captured most patients previously labeled with MOGAD, despite the diagnosis of MOGAD has become more stringent due to the required supporting features for patients without a clear-positive MOG-IgG.
Disclosures: KH Kim received speaker fees from Merck Serono. S-H Kim has lectured, consulted, and received honoraria from Bayer Schering Pharma, Biogen, Genzyme, Merck Serono, and UCB and received a grant from the National Research Foundation of Korea. J-W Hyun has received a grant from the National Research Foundation of Korea. HJ Kim received a grant from the National Research Foundation of Korea and research support from Aprilbio and Eisai; received consultancy/speaker fees from Alexion, Aprilbio, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll BioPharma, Horizon Therapeutics (formerly Viela Bio), Kaigene, Kolon Life Science, MDimune, Merck Serono, Mitsubishi Tanabe Pharma, Novartis, Roche, Sanofi Genzyme, Teva-Handok, and UCB; is a co-editor for the Multiple Sclerosis Journal and an associate editor for the Journal of Clinical Neurology.

P-17
A case of Anti-Hu associated Paraneoplastic Neuropathy with Multifocal Brain Lesions
Joong-Yang Cho[1], Ki Chang Oh[2]
[1]*Department of Neurology, Ilsan Paik Hospital, Inje University College of Medicine*
[2]*Department of Neurology, Inje University College of Medicine, Ilsan Paik Hospital, Goyang, Korea*
Background: An overlapping peripheral nervous system (PNS) and central nervous system (CNS) syndrome is a rare condition, and it is related to immune-mediated disorders of the nervous system including paraneoplastic neurological syndromes, vasculitis, and autoimmune demyelinating disease.
Objective: Anti-Hu antibodies can cause paraneoplastic neurological syndromes, including sensory neuropathy, cerebellar ataxia and encephalitis. Herein, we present a case of a patient with anti-Hu antibody showing peripheral neuropathy and encephalopathy.

Methods: A 77-year-old man was admitted to our hospital with a progressive both leg paresthesia, gait disturbance, and mild dyspnea 2 weeks ago. On neurologic examination, he had impaired position and vibration sensation of both legs. Additionally, he had decreased reflex in knee and ankle, and decreased ankle dorsiflexion and plantarflexion. There was no definite lesion which could explain the patients' symptoms on spine magnetic resonance imaging (MRI). Brain MRI revealed focal tiny acute infarction at right frontal area, but the lesion seemed to be not related to his symptoms. Cerebrospinal fluid (CSF) examination showed elevated protein (179 mg/dl) without pleocytosis (5/ul). Nerve conduction study showed mild sensorimotor polyneuropathy. Chest computed tomography (CT) and PET-CT revealed inflammatory change, and no evidence of malignancy despite a positive anti-Hu antibody.
Results: A few days later, he showed stuporous mental status with left side motor weakness. Brain MRI presented multiple focal demyelinating lesions at both frontoparietal area with elevated CSF protein (> 499 mg/dl) without pleocytosis. He showed some response to high dose methylprednisolone and intravenous immunoglobulin G, but eventually his condition worsened, and he expired.
Conclusion: Given clinical presentation including peripheral neuropathy, multifocal brain lesions and positive anti-Hu antibody, we considered this case might be the paraneoplastic neurological syndrome associated anti-Hu antibody.

P-18
A case of Primary Spinal Arachnoiditis
Joong-Yang Cho[1], Ki Chang Oh[1]
[1]*Department of Neurology, Ilsan Paik Hospital, Inje University College of Medicine*
Background: Spinal arachnoiditis describes inflammation of the meninges, subarachnoid space and, in most cases, also involve the pial layer. The main pathology is neuroinflammation of the nerve roots in the cauda equina and interfere with the spinal nerves.
Objective: The vast majority of cases described are secondary and are preceded by a known event, including trauma, infections, or irritative substances. Here, we present the case of primary spinal arachnoiditis.
Methods: A 75-year-old man was admitted to our hospital with a gradual and progressing tingling sensation in both his hips and legs, accompanied by a sense of weakness and some difficulties with voiding over a period of 10 days. Previously, he underwent surgery on his left leg about 30 years ago, and despite dealing with some lingering effects of motor weakness in his left ankle, he has managed to regain the ability to walk independently. He denied the recent back injury, non-surgical procedure at the lower back, and exposure to the irritative substances. On neurologic exam, he had a mild reduction in motor strength (approximately grade II~III) in bilateral hip flexion, abduction, and adduction and a slight decrease in motor strength (grade IV) in right ankle dorsiflexion and plantar flexion. Additionally, he had mild decrease in reflex responses in both knee and ankle joints. The finding of nerve conduction study could not explain the symptoms of the patient.

Results: The Spine magnetic resonance imaging (MRI) revealed the linear enhancement along the nerve roots in the conus medullaris and cauda equina without the cord lesion. These findings suggested the possibility of inflammatory changes such as arachnoiditis. Cerebrospinal fluid (CSF) examination showed elevated protein level (181 mg/dl) without pleocytosis. He was negative for oligoclonal band, anti-aquaporin 4, and anti-MOG antibodies. Workup for vasculitis showed positive antinuclear antibodies (1:160, cytoplasmic pattern), and anti SSA/Ro antibodies (45 IU/ml). He was managed with a 5-day course of methylprednisolone with gradual tapering of the dose over 12 weeks. The patient showed both leg motor grade V and no voiding difficulty with a mild leg tingling sensation.
Conclusion: Despite no history of preceding events including infections, trauma, and thecal sac contamination by intraspinal injection, we considered this case might be the primary spinal arachnoiditis associated with the autoimmune disease.

P-19
Neuro-Behcet's Unveiled: Simultaneous Unfolding of Brainstem Lesion and Cerebral Vasculitis - A Case Report
Oranuch Chuapakdee[1], Abhinbhen W. Saraya[2]
[1]*King Chulalongkorn Memorial Hospital, Chulalongkorn University*
[2]*Division of Neurology, Department of Medicine Faculty of Medicine, Chulalongkorn University*
Background: Behcet's disease is an inflammatory disorder in multiple systems. Neuro-Behcet's disease (NBD) is a rare occurrence, accounting for less than 10% of all cases of Behcet's disease. Although the phenotypic diversity of NBD includes both parenchymal and non-parenchymal manifestations, cerebral vasculitis remains uncommon in this context.
Objective: We aimed to report the case of a young Thai man diagnosed with NBD with concurrent cerebral vasculitis.
Methods: A 19-year-old Thai man presented to King Chulalongkorn Memorial Hospital with acute left hemiparesis and spastic dysarthria for five days. He was initially diagnosed with acute ischemic stroke. Brain MRI revealed an enhanced T2 hyperintense lesion in the left thalamus with restricted diffusion. In addition, T2 hyperintense lesions with patchy enhancement were observed in the bilateral midbrain and pons, as well as nodular leptomeningeal enhancement around the brainstem. MRA demonstrated severe stenosis of the M2 segment of the right MCA with focal fusiform dilatation in the Sylvian fissure, irregular narrowing of the bilateral PCA and bead-like appearance of the bilateral AICAs. These remarkable findings support the diagnosis of cerebral vasculitis.
Cerebrospinal fluid analysis showed lymphocytic pleocytosis with normal levels of protein and sugar, with no evidence of oligoclonal bands. All infectious diseases screenings yielded negative results. Serology tests for MOG-IgG and AQP4-IgG, as well as ANA, were negative. Considering the patient's history of recurrent aphthous ulcers and arthralgia in the past year, these findings are compatible with a diagnosis of NBD.
Results: The patient tested positive for Pathergy and met the ICBD diagnostic criteria for NBD. As a result, a diagnosis of NBD with concurrent cerebral vasculitis was established. The patient received timely treatment with corticosteroids and exhibited complete recovery after five days of intravenous methylprednisolone at a dose of 1 g/day. Subsequently, long-term immunosuppressive treatment with Azathioprine was initiated following acute management.
Conclusion: Although vasculitis is a mandatory pathological feature of Behcet's disease, cerebral vasculitis is rare. Our case highlights the NBD diagnosis with concurrent cerebral vasculitis, underscoring the complexity of this disease's presentation.
Disclosures: There is no conflict of interest.

P-20

Exploring Perspectives on Multiple Sclerosis Care: Insights from General Practitioners and Neurologists in Indonesia

Putri Widya Andini[1], Anyeliria Sutanto[2], Ahmad Rizal[3], Aih Cahyani[3], Kartika Maharani[1], Darma Imran[1], Riwanti Estiasari[1]

[1]*Department of Neurology, Faculty of Medicine Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Indonesia*

[2]*Department of Neurology, Faculty of Medicine Pelita Harapan University, Siloam Hospitals Lippo Village, Indonesia*

[3]*Department of Neurology, Faculty of Medicine Universitas Padjadjaran, Dr. Hasan Sadikin Hospital, Indonesia*

Background: Early detection and intervention of multiple sclerosis are crucial since the delay in diagnosis and treatment may exacerbate both the level of disability and the associated costs.

Objective: The preliminary study aims to provide insights and enhance our understanding of the complexities of MS care in Indonesia and pave the way for targeted interventions to address these challenges effectively.

Methods: This observational cross-sectional study used a structured questionnaire developed based on established literature, clinical guidelines, and expert consultations, and encompassed questions related to demographics, MS diagnosis, treatment approaches, and challenges on patient care. Participants were general practitioners (GPs) and neurologists who attended World Multiple Sclerosis Day 2023 in Indonesia. Data were grouped according to specialization and were summarized using descriptive statistics.

Results: A total of 118 GPs and 88 neurologists participated in this study. Among GPs, 53% were female, 44.1% practiced in primary care, and 26.3% were based in Jakarta. The median (IQR) career length was 10.5 (0.1-40) years. Among neurologists, 55% were female, median (IQR) age of 45 (37-52) years. They mostly worked in hospitals (98.9%; 46% in second-level health facilities), had a career length of 7 (2-17) years after residency, based in Jakarta (25.6%) and West Java (26.7%), facing 5 suspected MS patients a month (95.5%). Common challenges for GPs included difficult presentations (83.1%), diagnostic limitations (46.6%), and limited MS knowledge (37.3%). About 40% of GPs had not received MS education during medical school. Neurologists faced diagnostic and treatment limitations in terms of availability and costs (30% & 22.2%, respectively) along with difficulty in recognizing the manifestations (18.9%).

Conclusion: In Indonesia, GPs encountered challenges linked to the lack of comprehensive understanding of MS. Conversely, neurologists frequently encountered challenges concerning the availability and costs of diagnosis and treatment.

Disclosures: The authors have no conflicts of interest to declare

P-21

Relaxing Rituximab infusion intervals may be a cost effective and safe recommendation for management of Multiple Sclerosis in resource poor settings.

Suhan Alva[1], Lekha Pandit[1], Akshatha Sudhir[1], Anitha D'Cunha[1]

[1]*Justice K. S. Hegde Charitable Hospital*

Refer to O-5 in Plenary Oral Presentation - 1

POSTER SESSION-4
Disease modifying therapies.

P-22
Iguratimod ameliorates a Th17 cell migration into the CNS by inhibiting IL-6 production via mitigating glial inflammation in animal model of multiple sclerosis.
Satoshi Nagata[1], Ryo Yamasaki[1], Ezgi Takase[1], Kotaro Iida[1], Mitsuru Watanabe[1], Katsuhisa Masaki[1], Hiroo Yamaguchi[2], Jun-ichi Kira[3], Noriko Isobe[1]
[1]Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University
[2]School of Physical Therapy, Faculty of Rehabilitation, Reiwa Health Science University, Fukuoka, Japan
[3]Translational Neuroscience Center, Graduate School of Medicine, and School of Pharmacy at Fukuoka, International University of Health and Welfare
Background: We previously reported the efficacy of iguratimod (IGU), an anti-rheumatic drug, on experimental autoimmune encephalomyelitis (EAE) through suppressing glial inflammation. We also reported a progressive EAE (pEAE) model, which has prominent glial inflammation and pathogenic T cell migration into the CNS, by oligodendroglia-specific Cx47 knockout.
Objective: We hypothesized that the effects of IGU on a pathogenic T cell migration might be through inhibiting glial inflammation. We aimed to elucidate the effects of IGU on CD4+ T cell migration using mixed glial cell culture.
Methods: Conventional EAE or pEAE was induced by injecting MOG35-55 peptide subcutaneously. After pEAE mice were administered with IGU or vehicle from 17 to 50 days postimmunization, flow cytometric analyses, CSF cytokine/chemokine assay, and immunostaining were performed. For the migration assay, primary mixed glial cell cultures were prepared from the brains of newborn WT mice. The lower transwell chambers were filled with or without mixed glial cells, stimulants (IL-1α, C1q, TNF-α, and LPS), and IGU, while CD4+ T cells from conventional EAE mice were loaded in the upper chamber. After 24 h incubation, migrating T cells to the lower chambers were counted using flow cytometry and cytokine/chemokine levels in the culture supernatant were measured.
Results: Clinical signs of pEAE and demyelinated areas were ameliorated in IGU-treated mice compared to vehicle-treated mice ($p < 0.0001$ and $p = 0.011$, respectively). Areas of proinflammatory microglia and A1 astroglia in the CNS tissues were decreased by IGU treatment (both $p < 0.05$). Flow cytometric analyses of the CNS tissues from pEAE mice revealed that migrated Th17 cells into the CNS were decreased by IGU treatment ($p < 0.05$). CSF IL-6 levels of pEAE mice were decreased by IGU treatment ($p < 0.01$). In the migration assay, migrating Th17 cell numbers from the upper chamber to the lower chamber, which was increased by cytokine stimulants, was decreased by IGU treatment ($p < 0.001$). Cytokine assay revealed the decrease of IL-6 and CCL2 levels, which was accumulating over time after cytokine stimulation, in the glial cell culture supernatant by IGU treatment (both $p < 0.01$).
Conclusion: IGU mitigates Th17 migration via inhibiting glial inflammation and IL-6 production from glial cells, which ameliorates clinical signs of pEAE. IGU might be a promising drug for multiple sclerosis to suppress both acute and chronic disease activities.

P-23

Effect Of Glatiramer Acetate in Pregnancy, and Infantile Outcomes

Masoud Etemadifar[1], Mahboubeh Kaji Esfahani[1], Mehri Salari[2]
[1]*Isfahan University of Medical Sciences*
[2]*Shahid Beheshti University of Medical Sciences*

Background: Multiple sclerosis (MS) is the most common autoimmune disease that is mainly present in females. MS has some clinical effects on childbearing, and females with MS face different problems in becoming pregnant. Glatiramer acetate (GA) is shown to be relatively safe during pregnancy.
Objective: We aimed to investigate the safety profile of GA before and during pregnancy and infantile outcomes.
Methods: This is a prospective cohort study on the childbearing ages females who received GA before and during pregnancy who were referred to Isfahan MS clinics from January 2020 to January 2023. The patients were followed up for six months after pregnancy, and the maternal characteristics were investigated as an infant condition before, during, and after pregnancy.
Results: A total of 20 women treated with Glatiramer acetate during pregnancy were enrolled. The mean age of patients at the start of the study was 30.55±4.31, and the mean age at MS diagnosis was 25.2±3.88 years. The mean duration of using DMT was 2.26±1.51 years. The EDSS score of patients prior to pregnancy and six months after pregnancy was 1.225±0.25 and 1.275±0.30. New onset enhancing plaque after pregnancy was seen in one patient (5%). Moreover, three patients experienced one episode of relapse within 12 months before pregnancy, and no relapse was evident during pregnancy. No significant adverse event related to the exposure to GA was recorded.
Conclusion: Our findings showed that GA is not associated with significant pregnancy or newborn adverse events. Moreover, our data supported that a washout period before pregnancy is not obligatory before starting a pregnancy.

P-24

Efficacy of Eculizumab in Acute Phase of Neuromyelitis Optica Spectrum Disorder: A Case Series Study

Mitsuru Watanabe[1], Katsuhisa Masaki[1], Takuya Matsushita[2], Noriko Isobe[1]
[1]*Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University*
[2]*Department of Neurology, Kochi Medical School, Kochi University; Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University*

Background: Eculizumab (ECU), a monoclonal antibody against complement C5, has been approved to prevent relapse of neuromyelitis optica spectrum disorder (NMOSD). Because complement activation leads to neuroinflammation and tissue necrosis in attacks of NMOSD, ECU is expected to be also effective to ameliorate the symptoms in acute phase.
Objective: Because clinical reports on the efficacy of ECU in acute phase of NMOSD are limited, the aim of this study is to clarify its effectiveness on disease course and clinical symptoms in NMOSD attacks through our clinical experiences.
Methods: We described the clinical course of five cases with anti-aquaporin-4 antibody positive NMOSD who were administered ECU soon after the treatment for attack.

Results: Four cases were female and the other was male. Age of patients ranged from 50 to 93. The index attacks include optic neuritis in three cases, myelitis in one case, and brainstem encephalitis and myelitis in one case. Three of them had not received any maintenance therapy. Although all cases had received one or two courses of intravenous methylprednisolone (IVMP) and 3 to 5 times of plasma exchange (PE), which was not enough to improve their symptoms. Thereafter, ECU was initiated between 35 to 61 days after the attack onset. ECU ameliorated visual acuity or visual field in the three cases with optic neuritis. One case with myelitis experienced improvement of left-sided hemiparesis and hypoalgesia in her right leg. The other case with relapse in the pons and spinal cord had improvement of left medial longitudinal fasciculus syndrome, facial numbness, and weakness in her right leg.
Conclusion: Here we reported five cases with NMOSD for whom ECU administration soon after acute phase treatment improved their symptoms. Although IVMP and PE will be introduced as a first therapy, ECU could be a useful treatment option in severe NMOSD attacks.
Disclosures: Mitsuru Watanabe has received grant supports, consultant fees, speaking fees and/or honoraria from Japan Society for the Promotion of Science (JSPS KAKENHI: Grant number JP22K07351), Alexion Pharma, Novartis Pharma, Biogen Japan, Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, argenx, and UCB Japan. Katsuhisa Masaki has received grant supports and/or speaking fees from Japan Society for the Promotion of Science (JSPS KAKENHI: Grant number 23K06965), Mitsubishi Tanabe Pharma, Alexion Pharma, Chugai Pharmaceutical, Biogen Japan, Novartis Pharma, and Takeda Pharmaceutical. Eizo Tanaka has received speaking fees from Novartis Pharma. Takuya Matsushita has received grant supports and/or speaker honoraria payments from Japan Society for the Promotion of Science (JSPS KAKENHI: Grant number 20K07869), Alexion Pharma, Mitsubishi Tanabe Pharma, Takeda Pharmaceutical Company and Biogen Japan. Noriko Isobe has received grant support, consultant fees, speaking fees and/or honoraria from JSPS KAKENHI, Mitsubishi Tanabe Pharma, Alexion Pharma, Chugai Pharmaceutical, Biogen Japan, Novartis Pharma, UCB Japan, Takeda Pharmaceutical, Sumitomo Pharma, Japan Blood Products Organization, Daiichi Sankyo, CSL Behring, FP Pharmaceutical, EA Pharma, Kyowa Kirin, Amgen.

P-25

Efficacy and Safety of Rituximab in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder

Tatchaporn Ongphichetmetha[1], Jiraporn Jitprapaikulsan[1]
[1]Siriraj Neuroimmunology Center, Division of Neurology

Refer to O-7 in Plenary Oral Presentation - 2

P-26

OLIKOS Study: 6-Month Interim Efficacy and Safety in Patients With Relapsing Multiple Sclerosis Who Switched to Subcutaneous Ofatumumab From Intravenous Anti-CD20 Therapies

Jihan Talib[1], Le Hua[2], Brandon Brown[3], Benjamin Greenberg[4], Roland Henry[5], Rebecca Piccolo[3], Elizabeth Camacho[3]
[1]Novartis Pharmaceuticals Corporation, Sydney, Australia
[2]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, NV, United States
[3]Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States
[4]Department of Neurology, University of Texas Southwestern Medical Center, Neurology, Dallas, TX, United States
[5]UCSF Weill Institute for Neurosciences, Department of Neurology, University of California, San Francisco, CA, United States

Background: Anti-CD20 therapies are effective in the treatment of relapsing multiple sclerosis (RMS). Ofatumumab (OMB) is the only anti-CD20 administered subcutaneously as opposed to intravenous (IV) administration. Maintenance of efficacy, safety and satisfaction with OMB in RMS patients switching from IV anti-CD20 therapies were assessed in the OLIKOS study.
Objective: Describe interim efficacy and safety results for patients enrolled in OLIKOS who completed the first 6 months of the study.
Methods: OLIKOS a phase 3b, single arm, open label study, enrolled patients (18-60 years) with RMS who received ≥2 courses of IV anti-CD20 therapy (ocrelizumab (OCR) or rituximab). Patients were required to be stable on their previous therapy and switched for reasons other than safety or lack of efficacy. Eligible patients received OMB 20 mg SC via autoinjector, with standard loading and monthly maintenance doses over 1 year. Patient demographic and clinical characteristics were recorded at baseline (BL). The primary endpoint was the proportion of patients with no change or reduction in the number of gadolinium-enhancing (Gd+) lesions on magnetic resonance imaging (MRI) from BL to Month 12. Safety endpoints included treatment-emergent adverse events (TEAEs). Exploratory endpoints included change in immunoglobulin (Ig) G and IgM levels.
Results: This abstract reports on 65 of 111 enrolled OLIKOS patients with completed 6-month data. In this subset (n=65) the mean (SD) age at BL was 43 (8.4) years and most patients were White (72.3%) and female (64.6%); all patients previously received OCR before switching to OMB. Median (range) BL
Expanded Disability Status Scale score and mean (SD) disease duration were 3.5 (0.0–5.5) and 8.8 (7.0) years, respectively. At BL, mean (SD) number of Gd+ T1 lesions was 0.02 (0.1), and IgG and IgM levels (g/L) were 10.3 (3.0) and 0.5 (0.3), respectively. At 6 months, all patients with available Gd+ T1lesion data (n=51) met the primary endpoint (95% CI: 0.93-1.00). TEAEs occurred at the same frequency as in the phase 3 clinical trials, with no new safety signals identified. 6-month mean (SD)IgG and IgM levels (g/L; n=63) were 10.1 (3.0) and 0.5 (0.3), respectively. Interim results for all 111patients will be presented.
Conclusion: OMB 20 mg SC maintained efficacy at 6 months in patients with RMS transitioning from IV anti-CD20 therapies, as demonstrated by no new MRI activity. No new safety signals were identified, and Ig levels remained stable.
Disclosures: Jihan Talib: Employee of Novartis Pharmaceuticals Corporation.
Le H. Hua: Received personal fees for speaking, consulting, and advisory board activities from Alexion, Bristol Myers Squibb, EMD Serono, Genentech, Genzyme, Greenwich Biosciences, Horizon Therapeutics and Novartis; and has had research support paid to her institution from Biogen.
Brandon Brown: Employee of and stockholder in Novartis Pharmaceuticals Corporation.
Elizabeth Camacho: Employee of and stockholder in Novartis Pharmaceuticals Corporation.
Benjamin M. Greenberg: Received consulting fees from Alexion, Arialys, Bayer, Clene, Cycle Pharma, EMD Serono, Genentech/Roche, Genzyme, Horizon Therapeutics, Immunovant, Intervenn, IQVIA, Janssen, Novartis, PHAR, PRIME Education, Sandoz, Signant, Syneos and TG Therapeutics; received grant funding from Anokion, National Institutes of Health and Regeneron; serves as an unpaid member of the board of the Siegel Rare Neuroimmune Association; has equity in Clene and GenrAb; and receives royalties from UpToDate.
Roland G. Henry: Received consulting fees and/or research funding from Atara Biotherapeutics, Boston Pharmaceuticals, Celgene, Genentech/Roche, MedDay, Neurona Therapeutics, Novartis, QIA Consulting and Sanofi Genzyme.
Rebecca Piccolo: Employee of and stockholder in Novartis Pharmaceuticals Corporation.
Enrique Alvarez: Received consulting fees from Actelion/Janssen, Alexion, Bayer, Biogen, Celgene/Bristol Myers Squibb, EMD Serono/Merck, Genentech/Roche, Genzyme, Horizant, Novartis and TG Therapeutics; and has received research grants and/or participated in studies sponsored by Biogen, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Institute, Rocky Mountain MS Center and TG Therapeutics.

P-27

Satralizumab for Relapse In Patients With NMOSD In Japan: Analysis Of Real-World Data

Ichiro Nakashima[1], Jin Nakahara[2], Hideo Yasunaga[3], Masami Yamashita[4], Nobuo Nishijima[4], Atsushi Satomura[4], Mariko Nio[4], Kazuo Fujihara[5]
[1]*Tohoku Medical and Pharmaceutical University*
[2]*Keio University School of Medicine*
[3]*The University of Tokyo*
[4]*Chugai Pharmaceutical., Co. Ltd.*
[5]*Fukushima Medical University*

Background: Satralizumab reduced relapse risk in patients with neuromyelitis optica spectrum disorder (NMOSD) in two randomized, phase 3 trials (NCT02028884/NCT02073279).
Objective: To assess the relapse rates in patients with NMOSD who received satralizumab prescription in Japanese hospital claims database.
Methods: Medical Data Vision provided data of ICD10 based patients with NMOSD (April 2008-March 2022). Patients with ≥1 satralizumab prescription in the study period were included; index date was the date of first prescription. Relapse was defined as any one of these acute-phase treatments: steroid pulse for ≥3 days, plasma exchange, or intravenous immunoglobulin.
Results: Of 131 patients with NMOSD who were prescribed satralizumab, 6 patients relapsed during the continuous satralizumab prescription. All 6 patients were female, treated with oral glucocorticoid at the index date, and 5 were also on immunosuppressants. The median (interquartile range) time to first relapse from index date was 38 (8-69 days) days; 2/6 patients relapsed within 7 days. Annualized relapse rates (95% CI) in 30 patients with ≥360 days observation both pre- and post-index date, were 0.70 (0.40-1.00) and 0.17 (0.02-0.31), respectively.
Conclusion: Majority of patients were relapse-free after initiating satralizumab. Annualized relapse rates reduced in patients with ≥360 days follow-up pre- and post-index.
Disclosures: This study was funded by Chugai Pharmaceutical Co, Ltd. Statistical analysis was conducted by INTAGE Healthcare. Editorial assistance was provided by MedPro.

P-28

Immunosuppressive Therapy Used For Patients With NMOSD Treated With Satralizumab In Japan: A Real-World Study

Ichiro Nakashima[1], Jin Nakahara[2], Hideo Yasunaga[3], Masami Yamashita[4], Nobuo Nishijima[4], Atsushi Satomura[4], Mariko Nio[4], Kazuo Fujihara[5]
[1]*Tohoku Medical and Pharmaceutical University*
[2]*Keio University School of Medicine*
[3]*The University of Tokyo*
[4]*Chugai Pharmaceutical., Co. Ltd.*
[5]*Fukushima Medical University*

Background: In two randomized trials (NCT02028884, NCT02073279), satralizumab significantly reduced relapse risk vs placebo in patients with neuromyelitis optica spectrum disorder (NMOSD).
Objective: To assess the use of concomitant immunosuppressants as maintenance therapy in NMOSD patients prescribed with satralizumab in Japanese claims database.
Methods: Medical Data Vision provided data of ICD10 based NMOSD patients (April 2008-March 2022). We included patients with NMOSD prescribed ≤15 mg/day of oral glucocorticoid (GC) at the first satralizumab prescription (index date), ≥1 satralizumab prescription, and no relapse defined with acute-phase therapy within 90 days pre-index.

Results: Among 85 included patients, the mean (standard deviation) period of continuous prescription of satralizumab was 215.6 (159.7) days; 78 (91.8%) and 3 (3.5%) patients were prescribed oral GC at index and eculizumab at pre-index, respectively. At the last satralizumab prescription, 44/78 (56.4%) patients had reduced oral GC dose without relapse. Of 21 patients on continuous satralizumab prescription for ≥360 days, 2 (9.5%) had no oral GC prescription at index and 6 (28.6%) had achieved steroid-free status without relapse at 360 days post-index.
Conclusion: Oral GC and/or immunosuppressant therapy can be likely tapered without relapse in patients with ongoing satralizumab prescription.
Disclosures: This study was funded by Chugai Pharmaceutical Co, Ltd. Statistical analysis was conducted by INTAGE Healthcare. Editorial assistance was provided by MedPro.

P-29
Ofatumumab Effectiveness and Safety In Relapsing Multiple Sclerosis Patients With Breakthrough Disease On Oral Fumarates Or Fingolimod: Artios Interim Analysis
Susan Agland[1], Riley Bove[2], Matthew Craner[3], Dawn Langdon[4], Daniel Sienkiewicz[5], Javier Ricart[6], Soudeh Ansari[7], Sophie Arnould[8], Ibolya Boer[8], Tobias Derfuss[9]
[1]*John Hunter Hospital and Hunter Medical Research Institute*
[2]*University of California San Francisco*
[3]*John Radcliffe Hospital, Oxford University Hospitals NHS Trust Oxford*
[4]*Royal Holloway, University of London*
[5]*Novartis Pharmaceuticals Corporation*
[6]*Novartis Farmaceutica*
[7]*Novartis Institutes for Biomedical Research*
[8]*Novartis Pharma AG*
[9]*University Hospital and University of Basel Neurology Clinic and Policlinic and Research Center for Clinical Neuroimmunology and Neuroscience, Departments of Medicine and Biomedicine*
Background: In the ASCLEPIOS 1/11 Phase 3 trials, there was a limited number of patients with relapsing multiple sclerosis (RMS) switching to ofatumumab from oral therapies due to breakthrough disease. The ARTIOS study aims to bridge this gap.
Objective: To assess the effectiveness and safety of subcutaneous ofatumumab 20 mg in RMS patients with breakthrough disease on oral fumarates/fingolimod.
Methods: ARTIOS, an ongoing Phase 3b open-label, single-arm, non-comparative study, includes adult RMS patients with breakthrough disease on fumarates/fingolimod who transitioned to ofatumumab at the start of the study (planned enrollment, N=555). Patients receive ofatumumab once every 4 weeks (following an initial dose regimen in the first month) for up to 96 weeks. This interim analysis was conducted after ~50% of planned enrolled subjects completed the Week 48 visit + 28 days of follow up for relapses and adverse events (AEs). Annualized relapse rates (ARR), MRI lesion activity, disease progression, serum neurofilament light chain (NfL), IgG/IgM levels, and safety including AEs were analyzed. Safety data were also analyzed by fumarate or fingolimod subgroups.
Results: This analysis included 278 patients (mean age: 37.4 years; mean exposure: 52 weeks). Adjusted ARR was low at 0.12 (95% CI: 0.08, 0.181) and met the nominal threshold for significance (p=0.023 [null hypothesis ARR≥0.181). Ofatumumab significantly reduced Gd+T1 (by 97% versus baseline) and new/enlarging T2 lesions; EDSS remained stable.
Conclusion: This ARTIOS interim analysis indicates that ofatumumab reduces disease activity in RMS patients with breakthrough disease activity on oral fumarates/fingolimod. No new safety signals were observed compared with the ASCLEPIOS results.

P-30

A Multicentre Retrospective Observational Study To Investigate The Current Natalizumab Treatment Status In Japan - REFIND Study

Ichiro Nakashima[1], Takashi Ohashi[2,3], Michihiro Kanda[4], Yumiko Tani[4], Kazumasa Yokoyama[5,6]

[1] *Tohoku Medical and Pharmaceutical University*

[2] *Yachiyo Medical Center, Tokyo Women's Medical University*

[3] *Kamagaya General Hospital*

[4] *Biogen Japan Co., Ltd.*

[5] *Tohsei Center for Neurological Diseases*

[6] *Juntendo University*

Background: Natalizumab (NTZ) extended interval dosing (EID) has gradually started to be used in clinical practice in Japan around 2018. However, there is no data on Japanese multiple sclerosis (MS) patients treated with NTZ EID.

Objective: To investigate NTZ treatment status and disease activity in MS patients in actual clinical settings in Japan.

Methods: The REFIND study was a multicenter, retrospective, observational study in which data were collected between October 2021 and April 2022, from MS patients aged 20 years or older who consented to this study. For the primary endpoint, NTZ treatment patterns in patients with relapsing-remitting MS (RRMS) treated with NTZ for at least 1 year were analyzed for the standard interval dosing (SID) only, EID only and SID followed by EID (SID/EID) group. For each dosing pattern group, the annualized relapse rate (ARR) before and after administration of NTZ was compared using a negative binomial regression model.

Results: 206 MS patients from 20 facilities nationwide were enrolled in this study, of whom 121 RRMS patients were treated with NTZ for at least 1 year. Among these patients, 13 had an SID-only NTZ dosing pattern, 49 had EID-only, and 59 had SID/EID, with mean (SD) dosing intervals of 30.8 (1.6) days, 45.7 (3.4) days, and 38.7 (3.4) days, respectively. The ARR at one year before vs one year after initiation of NTZ in each group were: overall: 1.04, 0.13 (87.5% reduction, $p<0.0001$); SID-only: 1.08, 0.62 (42.6% reduction, $p=0.265$); EID-only: 0.95, 0.02 (97.9% reduction, $p=0.0075$); SID/EID: 1.10, 0.12 (89.1% reduction, $p=0.0058$).

Conclusion: The dosing pattern and efficacy of NTZ in Japanese MS patients under actual clinical settings were confirmed. Although the sample size was limited in this analysis, effectiveness of NTZ was also suggested in EID only group or SID/EID group.

Disclosures: This study is funded by Biogen.

IN: Honoraria for lectures from Biogen, Novartis, Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, Alexion Pharmaceuticals; support for attending meetings from Biogen, Novartis Pharma, Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, Alexion Pharmaceuticals; grants for commissioned/joint research from LSI Medience Corporation.

TO: Honoraria for lectures from Biogen, Novartis Pharma, Takeda Pharmaceutical Company, Eisai; support for attending meetings from Biogen, Novartis Pharma, Takeda Pharmaceutical Company, Eisai.

MK, YT: Employees of and may hold stock/stock options in Biogen.

KY: Honoraria for lectures from Biogen, Chugai Pharmaceutical; support for attending meetings from Biogen, Chugai Pharmaceutical.

P-31

Long-term Effect of Ofatumumab On Serum Immunoglobulin Levels In Patients With Relapsing Multiple Sclerosis

Suzanne Hodgkinson[1], Heinz Wiendl[2], Jerome De Seze[3], Amit Bar-Or[4], Jorge Correale[5], Anne Cross[6], Tobias Derfuss[7], Krzysztof Selmaj[8], Kevin Winthrop[9], Paul Giacomini[10], Francesco Sacca[11], Xixi Hu[12], Roseanne Sullivan[12], Valentine Jehl[13], Alit Bhatt[14], Stephen Hauser[15]

[1]*University of New South Wales*
[2]*University of Muenster*
[3]*University Hospital of Strasbourg*
[4]*University of Pennsylvania*
[5]*Dr Raul Carrea Institute for Neurological Research*
[6]*Washington University School of Medicine*
[7]*University Hospital and University of Basel*
[8]*University of Warmia and Mazury*
[9]*Oregon Health and Sciences University*
[10]*McGill University*
[11]*Universita Degli Studi di Napoli Federico II*
[12]*Novartis Pharmaceuticals Corporation*
[13]*Novartis Pharma AG*
[14]*Novartis Healthcare Pvt. Ltd*
[15]*University of California, San Francisco*

Background: Safety data from core clinical trials and ongoing ALITHIOS extension study up to 4 years of ofatumumab treatment have shown that most patients had serum immunoglobulin (Ig) levels remaining > lower limit of normal (LLN); mean serum IgG levels stayed similar to baseline values, and the mean IgM levels decreased over time but stayed above LLN.

Objective: To evaluate the effect of ofatumumab on serum IgG/IgM levels up to 5 years during the core and open-label extension studies.

Methods: Change in IgG/IgM levels from baseline for up to 5 years (cut-off: 25-Sep-2022) of ofatumumab treatment was analysed in the overall (N=1969), continuous (ofatumumab in core+extension; N=1292) and switch (teriflunomide in core, ofatumumab in extension; N=677) groups. The analysis also included proportion of patients with IgG/IgM level.

Results: In the overall group (median time on ofatumumab: 3.3 years), almost all patients (98%) had IgG levels that did not drop below the LLN at any assessment from the first dose of ofatumumab for up to 5 years. Additionally, the mean IgG levels remained stable for up to 5 years of treatment (mean % change from BL to Week 264, −2%). Serious infections were reported in 3/40 (7.5%) patients with IgG levels.

Conclusion: Up to 5 years on ofatumumab treatment, the majority of patients (IgG 98%, IgM 69.4%) did not have Ig levels that dropped below LLN at any time. Overall, the number of serious infections was low in patients with Ig levels that did drop below the LLN.

P-32

Five-Year Efficacy Outcomes of Ofatumumab in Relapsing MS Patients: Insights From ALITHIOS Open-label Extension Study

John Parratt[1], Ludwig Kappos[2], Jeffery Cohen[3], Ralf Gold[4], Jerome De Seze[5], Derrick Robertson[6], Heinz Wiendl[7], Sibyl Wray[8], Ronald Zielman[9], Amit Azmon[10], Jing Xi[11], Ibolya Boer[10], Stephen Hauser[12]
[1]*The University of Sydney, Royal North Shore Hospital*
[2]*University Hospital Basel*
[3]*Cleveland Clinic*
[4]*St. Josef-Hospital\/Ruhr-University Bochum*
[5]*University Hospital of Strasbourg*
[6]*University of South Florida*
[7]*University of Muenster*
[8]*Hope Neurology MS Center*
[9]*Novartis Pharma BV*
[10]*Novartis Pharma A.G.*
[11]*China Novartis Institutes For Biomedical Research Co*
[12]*University of California, San Francisco*

Background: In the Phase 3 ASCLEPIOS I/II trials, ofatumumab reduced clinical and MRI disease activity versus teriflunomide in relapsing multiple sclerosis (RMS) patients. Sustained reductions were observed with extended treatment (up to 4 years) in the ongoing, open-label ALITHIOS extension study.
Objective: Longer-term efficacy and safety assessments are important to further understand ofatumumab's benefit–risk profile in RMS patients. Here, we report ofatumumab efficacy outcomes for up to 5 years.
Methods: This analysis included participants randomised to ofatumumab/teriflunomide in the ASCLEPIOS I/II trials (core study) and who received ofatumumab in ALITHIOS extension study (data cut-off: 25-Sep-2022). Endpoints analysed by year included annualized relapse rates (ARR), MRI lesion activity (Gd+T1 and new/enlarging T2lesions) and NEDA-3 for up to 5 years in the continuous (ofatumumab [core+extension]; N=690) and switch (teriflunomide [core]/ofatumumab [extension]; N=677) groups.
Results: Patients in the continuous group maintained a low ARR over Years 1–5; while in the switch group, a marked reduction was observed from Year 2–3 (0.15–0.07) and maintained through Years 3–5 (0.05). Profound suppression of MRI lesion activity was maintained in the continuous group up to Year 5; while in the switch group, suppression was observed from Year 3–5. In the continuous group, the odds of achieving NEDA-3 increased from Year 2 (80%) and reached maximum at Year 5(93.4%) (Figures 1-3).
Conclusion: Continuous ofatumumab showed sustained efficacy on relapses and an almost complete suppression of MRI lesion activity for up to 5 years. Teriflunomide-to-ofatumumab switch resulted in pronounced reductions in these outcomes through Years 3–5.

P-33

Employing Novel Indirect Treatment Comparison Methodologies to Differentiate the Efficacy of Ofatumumab and Other High Efficacy Therapies versus Orally Administered Disease Modifying Therapies for Relapsing Multiple Sclerosis

Morag Nelson[1], Helmut Butzkueven[2], Anneke Van der Walt[3], Simon Broadley[4], Nicholas Riley[1], Nicholas Adlard[5], Martin Merschhemke[5], Dee Stoneman[5], Pamela McCombe[6], Michael Barnett[7], Rob Walker[1], Imtiaz Samjoo[8], Anja Haltner[8], Chris Drudge[8]

[1]*Novartis Pharmaceuticals Australia*

[2]*Monash University*

[3]*Monash University, Central Clinical School, Department of Neuroscience*

[4]*Griffith University, Menzies Health Institute Queensland*

[5]*Novartis Pharma AG, Basel, Switzerland*

[6]*University of Queensland*

[7]*Royal Prince Alfred Hospital Sydney and Brain and Mind Centre, University of Sydney*

[8]*EVERSANA*

Background: Emerging evidence challenges whether oral disease modifying therapies (DMTs) achieve similar efficacy to high efficacy therapies (HETs) for relapsing multiple sclerosis (RMS). Without head-to-head randomised controlled trial (RCT) data, indirect treatment comparisons (ITCs) can be used to estimate the relative efficacy between HETs and oral DMTs.

Objective: To differentiate HETs from oral therapies based on efficacy measures (annualised relapse rate (ARR), 3 and 6 month confirmed disease progression (3mCDP) (6mCDP)) using different ITC approaches.

Methods: Propensity score (PS) analyses were conducted to compare ofatumumab (OFA) to fingolimod (FIN) using inverse probability of treatment weighting (IPTW) to balance the trial populations for both therapies. The PS analyses used pooled individual patient-level data (IPD) from ASCLEPIOS I/II for OFA and from FREEDOMS I, II and TRANSFORMS for FIN. Unanchored simulated treatment comparisons (STCs) were conducted to compare OFA to each of the oral treatments by fitting a regression model for outcomes of interest. The STCs leveraged pooled IPD from ASCLEPIOS I/II and summary-level data (SLD) from individual phase 3 RCTs for cladribine (CLA), FIN and ozanimod (OZA). A network meta-analysis was also conducted to broadly compare the efficacy of DMTs for RMS, including HETs and oral therapies, using SLD from relevant RCTs.

Results: PS analyses demonstrated statistically significant superiority of OFA over FIN for reducing ARR (Rate Ratio 0.60, 95%CI 0.45-0.81) and delaying time to 3mCDP (HR 0.54, 95%CI 0.29-0.99), and numerical superiority over FIN for delaying time to 6mCDP (HR 0.59, 95%CI 0.31-1.12). Unanchored STCs demonstrated that OFA was (i) significantly superior to CLA, FIN, and OZA for reducing ARR, (ii) significantly superior to CLA, FIN and OZA for delaying 3mCDP and (iii) significantly superior to FIN and OZA for delaying 6mCDP; OFA was numerically superior to CLA for delaying 6mCDP. A network meta-analysis (NMA) analysis also demonstrated that alemtuzumab, natalizumab, ocrelizumab and OFA were each at least numerically superior to CLA, FIN and OZA.

Conclusion: The present ITC analyses consistently found evidence supporting the separation and therapeutic superiority of OFA and other HETs (NMA only) over oral therapies with respect to reducing relapses and delaying disease progression.

P-34

Effectiveness of Dimethyl Fumarate After Switching from Non-Specific Immunosuppressants

Timothy Spelman[1], Madifar Etemadifar[2], Sara Eichau[3], Raed Alroughani[4], Serkan Ozakbas[5], Samia J Khoury[6], Francesco Patti[7], Eva K Havrdova[8], Jens Kuhle[9], Jeannette Lechner-Scott[10], Orla Gray[11], Maria Pia Amato[12], Guy Laureys[13], Robert Hyde[14], Ivan Bozin[14], Haijue Wang[15], Nick Belviso[15], Feng Zeng[15], Anneke van der Walt[16], Helmut Butzkueven[17]

[1]*Royal Melbourne Hospital, University of Melbourne, Parkville, Victoria, Australia*
[2]*Al Zahra Hospital, Isfahan, Iran*
[3]*Hospital Universitario Virgen Macarena, Sevilla, Spain*
[4]*Amiri Hospital, Sharq, Kuwait*
[5]*Dokuz Eylul University, Konak\/Izmir, Turkey*
[6]*American University of Beirut Medical Center, Beirut, Lebanon*
[7]*Department of Medical and Surgical Sciences and Advanced Technologies, GF Ingrassia, Catania, Italy*
[8]*Charles University in Prague and General University Hospital, Prague, Czech Republic*
[9]*University Hospital Basel, Basel, Switzerland*
[10]*University of Newcastle, Newcastle, NSW, Australia*
[11]*South Eastern HSC Trust, Belfast, UK*
[12]*University of Florence, Florence, Italy*
[13]*University Hospital Ghent, Ghent, Belgium*
[14]*Biogen, Baar, Switzerland*
[15]*Biogen, Cambridge, MA, USA*
[16]*Monash University, Melbourne, Australia*
[17]*The Alfred Hospital, Melbourne, Australia*

Background: 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.

Objective: 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, 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), 100% (26/26), and 100% (15/15) at 12, 24, and 36 months of DMF. DMF discontinuation rate was 18.66/100 person-years (12.49, 26.79); TTFR (95% CI) was 9.01/100 person-years (4.92, 15.11); 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).

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.

P-35

Characterizing up to 2 years of Ofatumumab onboarding and utilization among real-world relapsing multiple sclerosis patients in Australia - the EAFToS Secondary Use of Data Study

Morag Nelson[1], Anneke Van der Walt[2], Simon Broadley[3], Jason Burton[4], Todd Hardy[5], Clare Kemp[1], Rob Walker[1], Patricia Berry[1], Kate Martel[1], Lien Lam[1]

[1]*Novartis Pharmaceutical Australia*

[2]*Central Clinical School, Monash University*

[3]*Griffith University, Menzies Health Institute Queensland*

[4]*Nexus Neurology*

[5]*Concord Hospital, University of Sydney*

Background: Ofatumumab (OFA) is approved for the treatment of adults with relapsing forms of multiple sclerosis (RMS). This Real-World Evidence study will analyse onboarding data, determine factors impacting treatment compliance and identify the OFA patient profile, through secondary use of data (SUD) from the integrated digital patient support program MSGo.

Objective: The primary objective is to characterize the onboarding experience and utilization of OFA in RMS patients in Australia. Secondary objectives are to describe the profile of patients initiating OFA, evaluate patient demographics and prior therapy.

Methods: Retrospective and longitudinal SUD analyses were conducted on data in the MSGo patient digital support program. Key inclusion criteria include adult patients diagnosed with RMS with Expanded Disability Status Scale of 5.5 or lower, treatment with OFA and enrolment in the study via MSGo. The primary endpoint was proportion of doses not completed within 3 days of the expected date during initiation and during the first 3 months of maintenance. Key secondary endpoints will assess the patient demographics, prior therapy and whether the treatment administrator influences compliance to treatment.

Results: Data from 567 de-identified patients were extracted from MSGo under the SUD study protocol in the 2nd interim analysis. 25% were treatment naive, 93% self-administered OFA and 9.5% discontinued therapy. Adherence during initiation was analysed by initiation dose 2 and 3 administered within 7 days±3 days from the previous dose. Most patients were adherent within the expected timeframe (proportion 97.6%, (CI 0.96-0.988)). The proportion of adherent doses during maintenance doses 2 and 3 administered within 30±3 days from the previous dose, was 95.6% (CI 0.93-0.974) and 96.9% (CI 0.95-0.983) respectively. Compliance remained high over duration of treatment with 97.7% (464/475; CI 0.959-0.988) and 94.1% (447/475; CI 0.92-0.96) of the patients remaining at least 80% or 90% compliant to OFA, respectively.

Conclusion: OFA patients had high adherence during first 3 months of treatment and maintained high compliance throughout duration of treatment. Exclusive use of data from MSGo is a novel approach for understanding quality use of medicines in the real world.

P-36

Satralizumab in NMOSD with SLE and Sjogren's syndrome: A possible treatment option in drug refractory cases

Praveena Sundram[1]
[1]*Hospital Kuala Lumpur*

Background: We are describing 2 challenging young females who have seropositive Neuromyelitis Optica Spectrum Disorder with concomitant Systemic Lupus Erythematosus, Sjogren's Syndrome, Antiphospholipid syndrome and myasthenia gravis who were treatment refractory to conventional off label immunosuppressants achieved remission with s/c satralizumab for 2 years.
Objective: To highlight the therapeutic advantage of subcutaneous satralizumab as an immunosuppressant that can help achieve remission when the other conventional treatments failed in these patients with complex autoimmune disorders.
Methods: This was achieved through history taking, physical examination and radiological investigations done which include Magnetic Resonance Imaging of the Brain and Spine.
Results: The patients had been on off - label immunosuppressants azathioprine, mycophenolate mofetil and failed to achieve sustained remission with rituximab and +/- cyclophosphamide but achieved remission with add on subcutaneous satralizumab for two years. The addition of satralizumab also allowed the doses of prednisolone and mycophenolate mofetil to be tailed down and switched off as well. In one patient, the prednisolone was switched off for one year.
Conclusion: Targeted therapy with IL6 inhibitors is a treatment option in patients with multiple autoimmune disorders coexisting together such as NMOSD, SLE and SS. We look forward to expanding this therapeutic advantage and improvement in access to treatments.

P-37

Immunosuppressive therapy in elderly patients with neuromyelitis optica spectrum disorder

Ki Hoon Kim[1], Su-Hyun Kim[1], Jae-Won Hyun[1], Ho Jin Kim[1], Yeon Hak Chung[2], Ju-Hong Min[2], Hee Jo Han[3], Seung Woo Kim[3], Shin Ha Young[3], Yong Nam Kwon[3], Sung-Min Kim[4], Hyunjin Kim[5], Eun-Jae Kim[5]
[1]*National Cancer Center of Korea, Department of Neurology*
[2]*Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine*
[3]*Department of Neurology, Yonsei University College of Medicine*
[4]*Department of Neurology, Seoul National University College of Medicine*
[5]*Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine*

Refer to O-6 in Plenary Oral Presentation - 2

P-38

First Interim Report of Survey on Long-term Use of Inebilizumab for Neuromyelitis Optica Spectrum Disorders in Japan

Kazuo Fujihara[1], Kyoko Okumura[2], Hideaki Hida[3], Saori Yamauchi[4], Satoshi Yuki[5], Shinya Hirota[5], Yoshito Nagano[4]
[1]*Department of Multiple Sclerosis Therapeutics, Fukushima Medical University*
[2]*Global Pharmacovigilance Department, Mitsubishi Tanabe Pharma Corporation*
[3]*Data Science Department, Mitsubishi Tanabe Pharma Corporation*
[4]*Medical Affairs Department, Mitsubishi Tanabe Pharma Corporation*
[5]*Medical Intelligence Department, Mitsubishi Tanabe Pharma Corporation*

Background: Inebilizumab was approved in March 2021 as a drug for neuromyelitis optica spectrum disorder (NMOSD) in Japan. A special use results survey (UMIN000044431) has been conducted to collect and evaluate the information related to long-term effectiveness and safety in a real-world clinical practice since June 2021.
Objective: To report the patient characteristics and safety information as the first report from the survey which is ongoing.
Methods: The survey has been conducted for all patients with NMOSD who started receiving inebilizumab in accordance with Good Post-marketing Study Practice (GPSP). The patient characteristics and safety information for 72 cases whose data were locked and who consented to publication as of December 2022 were interimly tabulated.
Results: The safety analysis set included 72 patients. The age (mean±standard deviation [SD]) was 54.8±14.1 years. The symptoms of NMOSD were optic neuritis (55.6%), acute myelitis (72.2%), area postrema symptoms (nausea, vomiting, hiccups) (20.8%), acute brainstem syndrome (19.4%), symptomatic narcolepsy with MRI lesions of diencephalon or acute diencephalic syndrome (1.4%), and symptomatic cerebral syndrome with MRI lesions of brain (6.9%). The observation period (mean±SD) was 43.4±20.3 days. Adverse drug reactions (ADRs) occurred in 13 patients (18.1%). ADRs were infusion related reaction (n=6), urinary tract infection, depressive symptom, somnolence, tremor, visual impairment, interstitial lung disease, diarrhoea, glossitis, nausea, pruritus, injection site erythema, malaise, lymphocyte count decreased, and total complement activity increased (n=1 each), of which serious ADRs were depressive symptom, visual impairment, interstitial lung disease, lymphocyte count decreased (n=1 each).
Conclusion: The survey has been proceeding as planned, and we continue collecting the information and promote appropriate use of inebilizumab.
The data was first presented at 64th Annual Meeting of the Japanese Society of Neurology (May 31 to June 3, 2023).
Disclosures: Kazuo Fujihara has received grants or contracts from the Ministry of Health, Labour and Welfare Japan; consulting fees from Merck Biopharma, Japan Tobacco Inc, and AbbVie; and payment or honoraria for lectures, presentations, manuscript writing, or educational events from Viela Bio/ MedImmune, Biogen, Mitsubishi Tanabe Pharma, Novartis Pharma, Chugai Pharmaceutical, Eisai, Asahi Kasei Medical, Merck, and Takeda Pharmaceutical; has participated in a data safety monitoring board or advisory board of Viela Bio/Horizon Therapeutics, Mitsubishi Tanabe Pharma, Novartis Pharma, Chugai Pharmaceutical, Alexion Pharmaceuticals, Biogen, and UCB; and has a leadership or fiduciary role in Pan-Asian Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS), Japanese Society of Neuroimmunology, Japan Multiple Sclerosis Society, and European Charcot Foundation. Hideaki Hida, Saori Yamauchi, Satoshi Yuki, and Shinya Hirota are employees of Mitsubishi Tanabe Pharma Corporation. Yoshito Nagano and Kyoko Okumura are former employees.

P-39
Withdrawn

P-40
Risk of rituximab discontinuation in patients with optic neuromyelitis spectrum disorders: a multicenter retrospective cohort study
Hu Sheng Fei[1], Li Rui[1], Qiu Wei[1]
[1]*The Third Affiliated Hospital of Sun Yat-sen University*
Background: The duration of monoclonal antibody drugs in treating neuromyelitis optica spectrum disorders (NMOSD) is still inconclusive, and there is a lack of large-sample clinical studies on the clinical outcomes of discontinuation of monoclonal antibody therapy with NMOSD.
Objective: This study aimed to analyze the clinical outcomes of NMOSD patients after rituximab (RTX) withdrawal and to evaluate the relationship between clinical indicators and the risk of relapse after discontinuation.
Methods: This study retrospectively collected clinical data of NMOSD cohorts using RTX from four large clinical centers in central, western, and southern China from 2016 to 2023, including age, sex, baseline EDSS score, recurrence, first recurrence after baseline, and time to disability progression, followed up for at least 1 year. Kaplan-Meier method was used to analyze the risk of relapse. COX regression model was used to analyze the predictors of relapse after drug withdrawal.
Results: 67 NMOSD patients using RTX were included in this study, of which 35 patients discontinued and 32 patients continued to use. In the discontinuation group, 18 patients recurred after discontinuation. Relapse occurred in 5 patients in the continuous treatment group. Kaplan-Meier analysis showed that the risk of relapse and disability progression was significantly higher in the discontinuation group than in the continuous treatment group. Subgroup analysis showed that the risk of relapse was higher in the subgroup with RTX treatment for less than 1 year and 1-2 years than in the continuous medication group, while the risk of relapse was not significantly different in the subgroup with RTX treatment for more than 2 years. Cox regression analysis showed that the frequency of recurrence during medication was closely related to the high risk of recurrence after drug withdrawal. After using RTX in the continuous group, the ARR decreased gradually every year, then there was a slight rebound.
Conclusion: Patients who discontinue RTX (especially for less than 2 years) have a significantly increased risk of relapse and disability progression. Long-term maintenance of RTX is beneficial to patients.

P-41
Pitfalls and Challenges of Multiple Sclerosis Long-Term Treatment in Middle Income Country
Rocksy Fransisca Vidiaty Situmeang[1], Anyeliria Sutanto[1], Rosaria Oktafiani Darmawan[2], Gerald Djuanda[1]
[1]*Department of Neurology, Faculty of Medicine Universitas Pelita Harapan, Siloam Hospitals Lippo Village, Indonesia*
[2]*Department of Neurology, Siloam Hospitals Lippo Village, Indonesia*
Background: Long-term treatment could be considered as one of the main pillars for multiple sclerosis comprehensive care, to prevent the disease activity and damage.
Objective: This observational descriptive study aims to evaluate the rate and sustainability of MS long-term treatment realization in Indonesia as middle-income country with its challenging limitation.
Methods: Data was collected from MS patients who came to MS clinic in Siloam Hospitals Lippo Village, Tangerang, Indonesia and received long-term treatment from January 2021-December 2022. Recorded medications were the usage of interferon beta, fingolimod, azathioprine, and mycophenolic acid.

Results: Among 32 MS patients who received long-term treatment, 81% were female, with median (min-max) of age 32.5 (14-55 years), and 82% with relapsing-remitting (RRMS) phenotype. Half of the patients were prescribed interferon beta as the disease-modifying drug (DMD), with 7 out of 17 patients had no continuation of the drug during the study. Fingolimod were used by 3 patients, in which only 1 patient still remained on treatment. Other 11 and 1 patient(s), respectively were using azathioprine and mycophenolic acid as alternative and off-label treatment. The main burden and challenge to give and preserve the treatment were the availability along with economic issues since the registered DMD (interferon beta and fingolimod) were not readily covered by the government insurance.
Conclusion: Despite the well-known efficacy and importance of long-term treatment, the realization was still lack due to limited availability and economical challenge.
Disclosures: No conflict of interest.

P-42
The effect and mechanism of B-cell deletion therapy on HTLV-1-associated myelopathy
Aowei Lv[1], Ying Fu[1]
[1]*The First Affiliated Hospital of Fujian Medical University*
Background: Human T-cell lymphotropic virus type 1-associated myelopathy (HAM) is a chronic, progressive, inflammatory disease of the central nervous system (CNS) with no effective treatments. Rituximab, an anti-CD20 monoclonal antibody, can reduce CD20+ B lymphocytes in circulation.
Objective: The purpose of this study was to ascertain the effect of rituximab in HAM and potential mechanisms.
Methods: This was an open-label, single-arm clinical trial. Eligible participants recruited would receive rituximab (375mg/m2 IV) twice at baseline and 6 months. Five evaluations were performed throughout a twelve-month follow-up period at three-month intervals. All adverse events were recorded throughout the study. The primary outcome was improvement of pyramidal or bowel-bladder function score in EDSS, which was defined as one point decrease. This study was registered with ClinicalTrials.gov, NCT04004819. Peripheral blood mononuclear cells (PBMC) from patients were obtained to explore the mechanism of rituximab in treating HAM through evaluating the effect of B cell deletion on T cell proliferation and activation in vivo and in vitro.
Results: After assessment on clinical features and HTLV-1 infection, fourteen HAM patients were enrolled and received infusions of rituximab. No adverse events were observed. During the 48-week trial period, three patients (21·4%) who received rituximab throughout the 48-week study period failed to achieve remission, compared to twenty-four (85·7%) patients who received any other therapy (group difference 64·3%, HR = 0·267, 95%CI 9·6-74·3, logrank p = 0·008). For the mechanism part, number of B cells in HAM patients had positive correlation with the increase of viral load (r = 0·481, p = 0·023) and infected cell counts (r = 0·466, p = 0·029). Deleting B cell caused HTLV-1 PVL fall from 18·80% (12·15%-23·80%) to 15·40% (8·90%-20·10%) (p = 0·016). Furthermore, HTLV-1 was found to infect B cells as well and deletion of B cells could inhibit the proliferation and activation of T cells.
Conclusion: Depleting B lymphocytes may delay the progression of HAM by inhibiting T cell proliferation

P-43

A Single-Centre Retrospective Review of Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis in Singapore

Sarah Abu Hassan[1], Ratnagopal Pavanni[1], Tianrong Yeo[1], Kevin Tan[1], Kok Pin Yong[1]
[1]*National Neuroscience Institute*

Background: While the emergence of numerous highly efficacious disease modifying therapies (DMT) has revolutionised the treatment of multiple sclerosis (MS) in recent years, autologous hematopoietic stem cell transplant (AHSCT) remains an important therapeutic option, particularly in selected patients with highly active disease despite usage of approved DMTs.

Objective: This study was done to describe the clinical characteristics of MS patients who underwent AHSCT in Singapore.

Methods: This was a single-centre retrospective review of patients diagnosed with MS who underwent AHSCT at Singapore General Hospital from 2002 to 2022. Twenty-five patients were identified. Data on patient demographics, Expanded Disability Status Scale (EDSS), DMT use, Magnetic Resonance Imaging (MRI) lesions and mortalities were collated from available medical records. Annualized relapse rates before and after AHSCT were calculated.

Results: 72% (n=18) were female; median age was 38 years (range 23-56). Twenty-one patients had relapsing-remitting MS; 4 patients had secondary progressive MS. All except 1 patient were on at least 1 (range 1-3) approved DMT pre-AHSCT. Fifteen patients (60%) had at least 2 relapses (range 2-17) prior to AHSCT with ARR of 0.86. The median time from diagnosis to transplant was 3 years (range 1-17). Median EDSS was 6 (range 2-8) at AHSCT. There were 4 mortalities – 1 occurred 6 months post-transplantation due to pneumonia and 3 occurred between 1- 15 years post-AHSCT, attributed to infections (primarily urosepsis or pneumonia). Thirteen patients remained on active follow up. Ten patients had no MRI lesion accrual at their latest imaging, performed at a median of 8 years (range 1-11) post-AHSCT. Three patients had 1 or more new MRI lesions (1, 3, and 10 years from transplant).Of these, 2 patients had an associated clinical relapse (ARR 0.016) and were treated with fingolimod and dimethyl fumarate.

Conclusion: Patients with MS who underwent AHSCT were mostly less than 40 years of age with relapses while on DMT and EDSS of 6.0. Post-AHSCT, clinical and radiological relapses were fewer and primary cause of mortalities were infections.

POSTER SESSION-5

Epidemiology, Genetics, and Epigenetics

P-44

Racial differences in Multiple Sclerosis disease characteristics amongst Chinese, Malay and South Asian patients in Singapore

Min Jie Koh[1], Tianrong Yeo[2], Seyed Ehsan Saffari[1], Kevin Tan[2], Janis Tye[2], Jeanne Tan[2], Amelia Aw[2], Rachel Siew[2]
[1]*Duke-NUS Medical School*
[2]*National Neuroscience Institute (NNI)*

Refer to O-8 in Plenary Oral Presentation – 2

P-45

Pediatric Neuromyelitis Optica Spectrum Disorder

Masoud Etemadifar[1], Amir Hossein Akhavan Sighari[1], Ebrahim Hajizadeh[2], Mahboubeh Kaji Esfahani[3]

[1]*Isfahan University of Medical Sciences*

[2]*Salamat Farda Hospital*

[3]*Najaf Abad University of Medical sciences*

Background: Neuromyelitis Optica Spectrum Disorders (NMOSD) represent a distinctive autoimmune demyelinating disorder characterized by the inflammation not only of the optic nerve and spinal cord, but also of other critical sites, notably the hypothalamus and area postrema. Notably, 3 to 5% of NMOSD cases encompasses the pediatric population.

Objective: The principal objective of our investigation resides in probing the clinical attributes, with a particular emphasis on the underpinnings of NMOSD within the pediatric demographic.

Methods: This study is a case series encompassing individuals diagnosed with Neuromyelitis Optica Spectrum Disorder (NMOSD) of pediatric onset (≤18 of years). The investigation transpired within the confines of the Isfahan MS Center, spanning the temporal continuum from March 2021 to March 2022. Scrutiny was extended to encompass the medical records of all NMOSD patients referred to or diagnosed at the Isfahan MS Clinic, either as part of routine follow-up evaluations or in response to clinical exigencies.

Results: We examined 18 participants with confirmed NMOSD with pediatric onset, with a female to male ratio of 2.6:1. (Out of a total of 215 NMOSD cases). On average, the disease began around the age of 13. Moreover, 4 participants (22%), all female, had a family history of NMOSD.12 patients were positive for anti-aquaporin-4 (AQP4) antibodies. Six participants (33%) had a negative antibody assay for both anti-AQP4 and anti-MOG antibodies.

Conclusion: In pediatric patients present with optic neuritis, myelitis, area postrema and hypothalamic dysfunction, physician must think about NMOSD. In children with AQP4-positive NMOSD, the clinical features and MRI abnormalities align with those seen in adult.

P-46

Withdrawn

P-47

Psychiatric Prodrome in Multiple Sclerosis and Related Disorders: A Single Centre Retrospective Observational Study from Singapore

Yin Yin Tan[1,2], Seyed Ehsan Saffari[1,3], Janis Siew Noi Tye[1], Xuejuan Peng[1], Jeanne May May Tan[1], Kevin Tan[1,3], Tianrong Yeo[1,3,4]

[1]*National Neuroscience Institute, Singapore.*

[2]*Department of Neurology, Penang General Hospital, Penang, Malaysia.*

[3]*Duke-NUS Medical School, Singapore.*

[4]*Lee Kong Chian School of Medicine, Nanyang Technological University.*

Background: Psychiatric comorbidities are common in Multiple Sclerosis (MS), most frequently observed are depression and anxiety. It is increasingly recognised that these psychiatric conditions can precede the diagnosis of MS, sometimes even before the onset of classical MS symptoms, however, its prevalence in Singapore is unknown.

Objective: To determine the prevalence of psychiatric disorders prior to the formal diagnosis of MS, in comparison to AQP4-Ab NMOSD and MOGAD, and to identify potential predictors of psychiatric comorbidities.

Methods: Clinical data of all patients with MS, Aquaporin-4 antibody (AQP4-Ab) Neuromyelitis Optica Spectrum Disorders (NMOSD) and Myelin Oligodendrocyte Glycoprotein Antibody associated Disease (MOGAD) seen at the National Neuroscience Institute (NNI Singapore) were reviewed. Patients with psychiatrist-confirmed psychiatric disorders before and after neurological diagnosis were identified and analysed.

Results: Two hundred forty-nine patients with MS (mean age at diagnosis, 32.0 ± [SD] 9.5 years; 192 female), 102 with AQP4-Ab NMOSD (51.6 ± 14.1 years; 90 female), and 48 with MOGAD (43.2 ± 14.5 years; 25 female) were evaluated. Thirteen (5.2%) MS patients had pre-existing psychiatric illness, significantly higher compared to AQP4-Ab NMOSD (1%) and MOGAD (0%) combined ($p = 0.035$). Univariate logistic regression revealed that age, gender, race, MS subtype, and the interval between classical MS symptom onset to MS diagnosis were not associated with pre-existing psychiatric disorders within MS patients. Mean PHQ-9 (depression questionnaire) score within MS patients at their first visit to NNI was 4.4 ± 4.7 (no depression cut-off: ≤4). There was no difference in the prevalence of psychiatric illness after neurological diagnosis between MS (29/236, 12.3%) and AQP4-Ab NMOSD (9/101, 8.9%) ($p = 0.454$), while this was significantly higher compared to MOGAD (0/48, 0%) ($p = 0.021$).

Conclusion: Our findings suggest that there is a significant psychiatric burden prior to MS diagnosis, in comparison to AQP4-Ab NMOSD and MOGAD. We also highlight the increased risk of psychiatric comorbidity after NMOSD diagnosis which warrants further study.

Disclosures: There is no conflict of interest between the authors.

P-48

Early onset versus Late-onset MOGAD in a single center study: real-world data

Hyunjin Ju[1], Chung Yeon Hak[1,] Ju-Hong Min[1]

[1]*Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Refer to O-9 in Plenary Oral Presentation - 2

P-49

Characteristic and Clinical Outcome of Transverse Myelitis Patient in Indonesian National Referral Hospital

Monalisa Sitinjak[1], Riwanti Estiasari[1,] Darma Imran[1], Kartika Maharani[1], Anyeliria Sutanto[2], Putri Widya Andini[1], Aulia Candra[1], Shierly Sitanaya[1]

[1]*Departement of Neurology, Faculty of Medicine Universitas Indonesia, Dr.Cipto Mangunkusumo Hospital, Indonesia*

[2]*Departement of Neurology, Faculty of Medicine Pelita Harapan University, Siloam Hospitals Lippo Village, Indonesia*

Background: Transverse myelitis (TM) is a focal inflammation across the spinal cord along one or more levels in the absence of a compressive lesion. Recently, the number of cases of TM has increased in our hospital.

Objective: To identify TM patients' characteristics and clinical outcomes at Cipto Mangunkusomo Hospital Jakarta.

Methods: A retrospective cross-sectional study was conducted on TM patients at Cipto Mangunkusumo Hospital Jakarta. All patients initially diagnosed with transverse myelitis, admitted from February to August 2023, were recruited. Characteristics and discharge outcomes of patients were recorded from medical records.

Results: There were 33 subjects with myelopathy symptoms, and myelitis diagnosis was ruled out on six patients. Among 27 TM patients, 4(14%) had multiple sclerosis,10(37%) neuromyelitis optic, 2(7%) related to systemic lupus erythematosus, 2(7%) related to infection, 1(3%) related to neoplasm and 8(31%) other TM. The mean age was 33,7(±11,25) years old, ranging from 18 to 63 years old. Female was predominantly 21(77%). The clinical symptoms were motor weakness 77%, a sensory disturbance 59%, autonomy impairment 48%, and neuritis optic 33%. According to Magnetic Resonance Imaging, the most commonly affected region was cervical 14(51%), followed by thoracic region 8(29%). Treatment was rituximab 4(14%), plasmapheresis 2(7%), plasmapheresis and rituximab 4(14%), plasmapheresis dan intravenous immunoglobulin 1(3%) and 1(3%) got only methylprednisolone because of pregnancy. Complete recovery or minimal residual deficit was found in 13(48%), 9(33%) had partial recovery and 5(18%) had no recovery.

Conclusion: The most common etiology of TM in our hospital is NMOSD. The cervical region is frequently affected. The discharge outcome majority is good with complete recovery or minimal residual deficit.

P-50

Withdrawn

POSTER SESSION-6
Infection and patients with MS or its related disorders

P-51
Myelin Oligodendrocyte Glycoprotein Antibody-Positive Spontaneous Spinal Cord Infarction Mimicking Acute Longitudinal Extensive Myelitis
Jae-Young An[1], Sang-Mi Noh[1]
[1]*Department of Neurology, St. Vincent Hospital, The Catholic University of Korea*
Background: The clinical manifestations of myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) are heterogeneous. Isolated involvement of the spinal cord in MOGAD can mimic spinal cord infarction (SCI).
Objective: We report a case of spontaneous SCI in an MOG antibody-positive patient, who developed progressive paraplegia over 24 hours after prior upper respiratory infection symptoms.
Methods: A 65-year-old woman, with a history of hypertension, presented at the emergency room after manifesting acute bilateral lower limb weakness an hour after waking. Two weeks earlier, she had experienced fever, cough, and runny nose. Neurological examination revealed weakness in the lower limbs (MRC grade 3/3), reduced deep tendon in the lower limbs, and dissociative sensory loss below L1. Plantar responses were normal. Within 24 hours, the weakness progressed to MRC grade 1/1. Initial spinal MRI exhibited a subtle signal alteration in the conus medullaris region. Brain diffusion MRI and cerebrospinal fluid analysis yield normal results. An antiplatelet treatment was initiated after the diagnosis of spontaneous SCI. Follow-up spinal MRI conducted after 5 days revealed a more pronounced signal change in the conus medullaris area, along with a new signal change in the lower thoracic spinal cord. Serological studies for autoimmune disease returned negative findings, excluding MOG Ab, which was positive. She was treated with intravenous high-dose methylprednisolone with oral prednisolone, but the improvement was not remarkable (grade 2/2).
Results: A confident diagnosis of spontaneous SCI without an apparent precipitating event is challenging. While MOG antibody is important for the diagnosis of MOGAD, it is important to acknowledge the potential for false positive outcomes, even given the high specificity of cell-based assays for MOG antibody.
Conclusion: A merge of clinical-MRI manifestation should be undertaken to establish the diagnosis of MOGAD.

P-52
A Rare Case of Neurosyphilis Presenting with Myelitis
Sunjun Kim[1], JongSeok Bae[1], Yun-young Jung[1]
[1]*Kangdong Sacred Heart Hospital*
Background: Neurosyphilis is a syphilis infection involved in central nervous system. In the early course, meningitis is the most common presentation involving meningeal or vascular invasion. In late stage, parenchymal invasion can occur and progress to general paresis or tabes dorsalis. It is uncommon these days, since antibiotics are properly used.
Objective: There are numerous causes of myelitis. Infections, autoimmune diseases, demyelinating, vascular event, and paraneoplastic syndromes should be considered as differential diagnosis. Neurosyphilis can take diverse form and should always be considered.

Methods: A 35-year-old man with type 1 diabetes mellitus presented with progressive lower limb weakness over 3 months. On admission, he was on wheelchair and could not walk independently. On neurological examination, both hip flexion motor grade was MRC Grade 3. Cranial examination was normal. He had three 3cm sized discoid scaly skin lesions, each placed on his left eyebrow, glabella, and nose. Sensory examination revealed sensory loss below T8 level with back sparing. Proprioception was reduced in both lower limbs. Deep tendon reflexes were reduced with bilateral babinski signs. He did not complain voiding difficulty, but anal tone was slightly reduced. Brain MRI was normal and spine MRI showed myelitis extending through T1 to T3 level. Cerebrospinal fluid (CSF) examination revealed elevated opening pressure (26cm H2O) with white blood cell 64 /mm3(mononuclear dominant 100%) and increased total protein concentration(88mg/dL). Anti-aquaporin 4 antibody was negative. PCR tests for varicella zoster virus, herpes simplex virus, tuberculous were negative. Rapid plasma regain (RPR) was reactive in serum and Venereal disease research laboratory (VDRL) was reactive in CSF. Fluorescent treponemal antibody absorbed test (FTA-ABS) IgG and IgM was positive and treponema pallidum latex agglutination (TPLA) was positive, which confirmed neurosyphilis.
Results: Antibiotics (ceftriaxone 2g for 14days) and methylprednisolone (1g/day) therapy were started for 5 days, and prednisolone (60mg/day) was maintained. His motor and sensory symptoms and his skin lesion in his face improved the day after the steroid was started, implicating skin gumma on his face. After intravenous ceftriaxone treatments, he was finally discharged home, and he could walk independently with minimal support.
Conclusion: Myelitis is rare manifestation of neurosyphilis. Therefore, suspicion and treatment of neurosyphilis are needed if syphilitic patients show neurologic symptoms consistent with neurosyphilis and pleocytosis in CSF (more than 5) with increased protein.

P-53
Recurrent zoster myelitis without skin rash
Jung Im Seok[1]
[1]*Catholic University of Daegu, School of Medicine*
Background: Varicella zoster virus (VZV) infection of the central nervous system include meningoencephalitis, multifocal vasculopathy, and myelitis, all of which can occur without rash. Among them, myelitis is rare, and recurrent cases are even more rare.
Objective: Zoster myelitis with no shingles could be diagnosed with VZV DNA.
Methods: We describe a patient who developed recurrent myelitis in the absence of rash, serologically confirmed to be caused by VZV.
Results: In 2019, a 55-year-old man presented with paresthesia of right leg. He had fever, chill, and myalgia. Neurologic examination showed paresthesia below T10 dermatome. Cerebrospinal fluid (CSF) analysis revealed normal glucose, high protein 182.2 mg/dL, and white blood cells 95 mm3 (polymorphonuclear 60%, mononuclear 40%). Spine magnetic resonance imaging (MRI) showed abnormal signal extending from T8 to T10. Considering viral myelitis, the patient was treated with acyclovir and steroid. Over the weeks, his sensory change improved. In 2023, he presented with weakness of right leg for 2 days. Muscle power was decreased in the right lower limb and deep tendon reflexes were brisk on right knee and ankle. CSF analysis revealed normal glucose, high protein 123.5 mg/dL, white blood cells 100 mm3 (polymorphonuclear 10%, mononuclear 90%). PCR for VZV was positive. Spine MRI showed inflammation at T8. Considering the possibility of zoster myelitis, he was treated with acyclovir and steroid.
Conclusion: Zoster infection without shingles often leads to misdiagnosis due to the lack of typical clinical manifestations. In this case, VZV DNA detection or rising anti-VZV antibody titers serve as a marker for active viral infection.
Disclosures: No potential conflict of interest

P-54

MOGAD: A Steroid-Responsive Meningoencephalitis Mimicking Infections

Amy May Lin Quek[1], Yihui Goh[1], Derek Soon[1]
[1]*National University Hospital*

Background: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), an inflammatory demyelinating disorder typically associated with opticospinal disease and acute disseminated encephalomyelitis, should be considered in the differential diagnosis of patients who present with fever and meningoencephalitis.

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), an inflammatory demyelinating disorder typically associated with opticospinal disease and acute disseminated encephalomyelitis, should be considered in the differential diagnosis of patients who present with fever and meningoencephalitis.

Objective: To describe three patients with steroid-responsive aseptic meningoencephalitis associated with MOGAD, whose clinical presentations were initially highly suspicious of an infectious aetiology.

Methods: This is a case series of three patients with meningoencephalitis.

Patient 1: A 27-year-old traveler who returned from India presented with headache, fever and seizures. She had dysphasia with right hemiplegia. Cerebrospinal fluid (CSF) examination showed lymphocytic pleocytosis (WBC,367, lymphocytes,85%; protein 0.89 g/dL). She was empirically treated for meningitis. MRI brain showed left-sided leptomeningeal enhancement. Pulsed methylprednisolone was initiated as infectious screens returned negative.

Patient 2: A 42-year-old diabetic male with fever, cough, headache and dysphasia was initiated on meningitic doses of antibiotics. Electroencephalogram showed left temporal ictal activity. After testing SARS-CoV-2-positive, he received dexamethasone for COVID-19 pneumonia. CSF was inflammatory (WBC,5; lymphocytes,87%; protein 1.56g/dL); MRI brain showed left-sided leptomeningeal enhancement. He received pulsed methylprednisolone for presumed COVID-19 encephalitis.

Patient 3: A 16-year-old female developed fever, headache and left faciobrachial weakness. MRI brain showed diffuse leptomeningeal enhancement; CSF was inflammatory (WBC,96; lymphocytes,42%; protein 0.48g/dL). She deteriorated despite meningitic doses of antibiotics and improved only after steroid initiation.

Results: All three patients' cerebrospinal fluid and serological tests returned negative for an infectious aetiology. They were subsequently found to have MOG-IgG seropositivity (serum titres of 1:100 for all 3 patients).

Patients 1 and 2 continued to improve on tapering doses of oral prednisolone, with resolution of their symptoms. Patient 3 discontinued steroids after 2 months, at which point she also developed COVID-19 infection associated with headache recurrence and right-hand automatisms. Repeat neuroimaging showed a more extensive left-sided leptomeningeal enhancement with cortical swelling. Her symptoms resolved after another course of steroids.

Conclusion: MOGAD-associated meningoencephalitis, a steroid-responsive immune-mediated condition, may be clinically indistinguishable from infectious aetiologies. MOG-IgG testing should be considered in aseptic cases with focal clinico-radiological findings.

P-55

Latent tuberculosis infection in Korean patients with multiple sclerosis and neuromyelitis optica spectrum disorder

Ki Hoon Kim[1], Su-Hyun Kim[1], Jae-Won Hyun[1], Ho Jin Kim[1]

[1]National Cancer Center of Korea, Department of Neurology

Background: Latent tuberculosis infection (LTBI) is defined as an immune response to a previous Mycobacterium tuberculosis infection that does not manifest clinically as active tuberculosis (TB). Since some immunotherapies can alter cellular immunity, LTBI screening has been recommended for patients with multiple sclerosis (pwMS) before long-term immunotherapy

Objective: In this study, we investigated the frequency of LTBI in Korean pwMS and patients with neuromyelitis optica spectrum disorder (pwNMOSD) and reported the long-term observation of untreated LTBI under various immunotherapies.

Methods: We enrolled pwMS or pwNMOSD patients who visited the Neurology department of the National Cancer Center between 2017 and 2021. LTBI was determined based on positive results of the interferon-gamma release assay (IGRA) using the QuantiFERON Gold Plus test and no evidence of active TB. Annual chest X-rays and careful monitoring for TB symptoms were performed until April 2023, or the time of follow-up loss.

Results: Among the 531 patients who underwent the IGRA test, 25 pwMS (10.5%) and 42 pwNMOSD (14.3%) were diagnosed with LTBI. Of the 67 patients with LTBI, 59 patients (24 pwMS and 35 pwNMOSD) declined to receive preventive anti-TB drugs. None of the 59 patients with untreated LTBI demonstrated TB reactivation during the 74.8 person-years in pwMS and the 166.1 person-years in pwNMOSD. In addition, eight patients who completed the treatment for LTBI experienced no TB reactivation for a median of 5.5 years.

Conclusion: The LTBI prevalence in Korean pwMS and pwNMOSD was 10.5% and 14.3%. Notably, none of the 59 patients with untreated LTBI showed TB reactivation over 240 person-years even under long-term immunotherapies.

Disclosures: KH Kim received speaker fees from Merck Serono. S-H Kim has lectured, consulted, and received honoraria from Bayer Schering Pharma, Biogen, Genzyme, Merck Serono, and UCB and received a grant from the National Research Foundation of Korea. J-W Hyun has received a grant from the National Research Foundation of Korea. HJ Kim received a grant from the National Research Foundation of Korea and research support from Aprilbio and Eisai; received consultancy/speaker fees from Alexion, Aprilbio, Altos Biologics, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, Handok, Horizon Therapeutics (formerly Viela Bio), Kaigene, Kolon Life Science, MDimune, Mitsubishi Tanabe Pharma, Merck Serono, Novartis, Roche, Sanofi Genzyme, Teva-Handok, and UCB; is a co-editor for the Multiple Sclerosis Journal and an associated editor for the Journal of Clinical Neurology.

P-56

Efficacy of Rituximab for Neuromyelitis Optica Spectrum Disorders and Multiple Sclerosis in Indonesian National Referral Hospital

Desmita Siregar[1], Riwanti Estiasari[2], Darma Imran[2], Kartika Maharani[2]

[1]Departemen of Neurology, Faculty of Medicine, Universitas Indonesia

[2]Dr. Cipto Mangukusumo Hospital, Jakarta, Indonesia

Background: Neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis (MS) are inflammatory demyelinating central nervous system disease, that causes substantial disability, and a high mortality rate if not treated. Rituximab is an immunomodulatory agent that is used to prevent these recurrences. However, in Indonesia, its use is still limited.

Objective: To explore the use of Rituximab in NMOSD and MS patients in Indonesia regarding the recurrence rate and improvement of the patient's disability
Methods: This descriptive study reports 8 patients, who were diagnosed with NMOSD or MS, and received Rituximab. Therapy was initiated as a cycle of intravenous Rituximab 2 weeks apart of 1 gram each, followed by subsequent cycles every 6 months. The outcomes assessed were the number of relapses and disability rates. Disability rates are assessed using the expanded disability status scale (EDSS).
Results: Six NMOSD patients received Rituximab due to the ineffectiveness of previous immunosuppressants, while the reason for giving Rituximab to 2 progressive MS patients in this study was to prevent more severe disability. All NMOSD and progressive MS patients who received Rituximab did not experience relapse with an average of 10.1±5.05 months of Rituximab administration. Six out of 8 patients who received Rituximab, experienced improvement in EDSS with an average score of 1±0.92.
Conclusion: The treatment of NMOSD and MS with Rituximab in Indonesian national referral hospital patients prevents relapse and improves patients' disability.
Disclosures: Author has received grants from (None) no conflict of Interest, I declare that I have no conflict of interest.

P-57
Synchronous Autoimmune Disorders: Co-existing relationship between Connective Tissue Disease and Neuromyelitis Optica Spectrum Disorder (NMOSD), A Case Study.
Jayakiran Radhakrishnan[1], Joyce Pauline Joseph[1]
[1]*Neurology Department Kuala Lumpur General Hospital*
Background: Neuromyelitis Optica Spectrum Disorder Spectrum is a neurological autoimmune disease which is associated with optic neuritis or myelitis in the presence of Aquaporin 4 IgG Antibody. Despite a wide array of rheumatology disorders associated with NMOSD, there are not many cases of Rheumatoid arthritis co-existing with NMOSD.
Objective: Recently, juvenile RA was identified as a coexisting autoimmune disorder with NMOSD and a survey on optic neuritis showed a poor visual outcome associated with RA.
Methods: A 32-year-old lady of Indian ethnicity with underlying seropositive rheumatoid arthritis (Positive RF with anti-CCP >2000) presented with fever and vision loss for 1 week. Clinically her vision was impaired where the right eye was reactive to light perception and the left eye is reactive to finger counting with presence of right eye RAPD and brisk lower limb reflexes. Over the course of a year, she experienced two episodes of optic neuritis and one relapse of transverse myelitis last year. CT done showed multifocal infarcts with enhanced enlarged right optic nerve while MRI done revealed right optic neuritis with multifocal white matter lesion in juxtacortical and periventricular as well as corpus callosum and pons. CSF protein from lumbar puncture performed was 0.54. No oligoclonal bands were detected however the CSF IgG was raised indicating an inflammatory disorder.
Results: Repeated MRI in a year showed similar findings suggestive of atypical demyelinating disease and multiple old infarcts suggestive of vasculitis in view of seropositive rheumatoid arthritis. Serum Aquaporin 4 antibody was positive and hence initiated her immunosuppressive therapy. Patient clinically improved after a course of steroids and cycles of rituximab therapy. Overall, here we have a patient with underlying seropositive rheumatoid arthritis presenting with multiple episodes of optic neuritis and transverse myelitis and tested positive for anti-AQP4-positive which confirms the diagnosis of NMOSD.
Conclusion: This raises the potential of RA to co-exist in the autoimmune spectrum of NMOSD.
Disclosures: NONE

P-58

Acute Flaccid Myelitis in Neuro-Melioidosis: A MOGAD mimic

Salika Kumari Karunanayaka[1], Shanindra De Alwis[1], Arjuna Fernando[1]
[1]*National Hospital of Sri Lanka*

Background: Myelin oligodendrocyte glycoprotein (MOG)–associated disorders are known to cause acute onset bilateral quadriparesis with a long segment cord lesion. A subset of MOGAD presents acute flaccid myelitis and demonstrates flaccid areflexia instead of the more common upper motor neuron syndrome.

Objective: We present a case with serologically confirmed Neuro-Melioidosis presenting with acute flaccid paralysis that mimicked a MOG antibody-associated disorder to highlight MOGAD and its mimics as causes of acute flaccid paralysis.

Methods: A 34-year-old male presented with bilateral quadriparesis of 5 days duration along with urine retention and a prodrome of severe back pain. His medical history was significant for diabetes mellitus and a wound in his left foot. He had gone on a fishing expedition with exposure to muddy water 2 weeks prior. Examination revealed a bilateral flaccid areflexic quadriparesis.

After admission, his condition deteriorated, and the weakness progressed to involve the bulbar and respiratory muscles. He was electively intubated and mechanically ventilated.

Results: MR imaging of the spine revealed a very long segment T2/FLAIR hyperintensity from the medulla to the conus. IV Methylprednisolone and Immunoglobulins were urgently started but the response to above was poor. CSF analysis showed a significant lymphocytic reaction. Furthermore, his MRI of the brain showed symmetrical T2/FLAIR hyperintensities in the bilateral corona radiata, posterior limbs of the internal capsule and brain stem suggestive of corticospinal tract involvement.

His melioidosis antibodies were strongly positive. He was started on a 6-week course of high-dose IV Meropenem and was subjected to 5 cycles of Plasma Exchange. His limb power significantly improved with the above regimen.

Conclusion: This is a very rare manifestation of Neuro-Melioidosis and the utilization of plasma exchange as treatment hasn't been described previously.

POSTER SESSION-7

Neuroimaging and Neurophysiology

P-59

Withdrawn

P-60

Association of Iron Deposition in Early-Stage Multiple Sclerosis Lesion with Remyelination Capacity

Woojun Kim[1], Hyeong-Geol Shin[2], Jung Hwan Lee[1], Hyun-soo Lee[3], Yoonho Nam[4], Jiwoong Kim[5], Xu Li[6], Peter van Zijl[6], Peter Calabresi[7], Jongho Lee[8], Jinhee Jang[9]
[1]*Dept. of Neurology, Seoul St. Mary's Hospital, The Catholic Univ. of Korea*
[2]*Department of Radiology, School of Medicine, Johns Hopkins University*
[3]*MR Research Collaboration, Siemens Healthineers*
[4]*Division of Biomedical Engineering, Hankuk University of Foreign Studies*
[5]*Department of Mathematics and Statistics, University of South Florida*
[6]*Department of Radiology, School of Medicine, Johns Hopkins University*
[7]*Department of Neurology and Neuroscience, Johns Hopkins University School of Medicine*
[8]*Department of Electrical and Computer Engineering, Seoul National University*
[9]*Department of Radiology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea*

Background: Assessing histopathological features of myelin and iron in multiple sclerosis (MS) lesions is crucial for understanding disease progression and treatment response. However, current in-vivo imaging techniques lack the ability to simultaneously visualize these key features.
Objective: To investigate longitudinal changes in tissue iron and myelin in MS lesions from their early stage using susceptibility source-separation (χ-separation) MRI and assess its potential implication for remyelination and clinical courses.
Methods: From a longitudinal observation cohort of participants with MS (October 2017 to February 2023), we identified 17 participants (age 30.6±8.3 years, 13 women) with early-stage lesions and 34 participants (age 32.9±8.3 years, 27 women) with various clinical courses. Using χ-separation MRI, we assessed diamagnetic myelin (χ_{dia}) and paramagnetic iron (χ_{para}) signals in lesions and characterized their longitudinal outcomes. Clinical status, Expanded Disability Status Scale, and treatment status were analysed. From them, clinicoradiological factors related to remyelination were evaluated.
Results: Total 48 lesions that showed their early-stage characteristics with the following MRI scan(s) were identified. Compared to normal-appearing white matter, 23 lesions exhibited early-stage hyperintense χ_{para} (iron deposition in any part of the lesion), which is referred to as a hyper-paramagnetic sign (HPS). During follow-up (26±14 months), the lesions showed various longitudinal outcomes in myelin signal (18: remyelinating, 12: stable, 18: demyelinating). After adjusting confounders, later successful remyelination outcome was associated with the absence of early-stage HPS (P=.004). Quantitatively, lesions with early HPS showed myelin signal loss over time (-1.49 ppb/year), while lesions without HPS during the extended early stage (lesion detection time to next MRI time within a year after it) exhibited myelin signal recovery (0.29 ppb/year). The number of lesions with early HPS in clinically relapsing group (6.9±6.5) was higher than that (2.5±3.0) in clinically stable group (P=.045).
Conclusion: There was significant association between presence of HPS in early-stage MS lesions and impaired remyelination capacity. In-vivo assessment of iron within MS lesions is potential clinical avenues to predict future remyelination and clinical courses.

P-61
Enlarged Choroid Plexus in Multiple Sclerosis Can Be an Indicator of Neuroinflammation but Not Neurodegeneration
Juichi Fujimori[1], Tetsuya Akaishi[2], Ichiro Nakashima[1]
[1]*Tohoku Medical and Pharmaceutical University*
[2]*Tohoku University*
Background: Enlargement of the choroid plexus (CP) is reported to associate with inflammatory activity and contribute to brain atrophy in patients with multiple sclerosis (pwMS). However, a recent study in healthy volunteers (HVTs) has suggested that CP enlargement can be attributed to ventriculomegaly.
Objective: To clarify the pathological significance of the enlargement of CP in multiple sclerosis (MS).
Methods: A total of 102 pwMS (89 with relapsing-remitting MS and 13 with secondary progressive MS) and 41 HVTs were cross-sectionally evaluated using brain volumetry. The CP volume was compared between disease groups and investigated for the relationships with other brain regional volumes.
Results: In the univariate analysis, CP volume was significantly larger in pwMS than in HVTs. However, in multivariable analysis, significant volume changes in pwMS compared with HVTs or among different stages of MS were observed not in the CP but mainly in the deep gray matter (GM), such as the thalamus and pallidum. Meanwhile, the CP and lateral ventricle (LV) volumes were significantly correlated. CP enlargement was significantly associated with increased lesion load, even after adjusting for LV volume, but not with disability or disease severity. In contrast, multivariable analyses revealed that LV enlargement, but not CP enlargement, was associated with total GM atrophy.

Conclusion: CP enlargement was closely associated with LV enlargement. After adjusting for LV volume, CP enlargement in pwMS was associated with increased lesion load but not GM atrophy.

P-62

Functional and microstructural brain changes associated with speech in people with multiple sclerosis

Katherine Kenyon[1], Myrte Strik[2], Angela Morgan[3], Adam Vogel[2], Scott Kolbe[4], Frederique Boonstra[1], Anneke van der Walt[1]

[1]*Monash University*

[2]*The University of Melbourne*

[3]*Murdoch Childrens Research Institute*

[4]*Royal Melbourne Institute of Technology*

Background: Over 40% of people with multiple sclerosis (pwMS) develop dysarthria, a motor speech disorder. Dysarthria in MS is associated with higher disease severity and lower quality of life. Despite this, little is still known about the underlying mechanisms of dysarthria in pwMS.
Objective: To evaluate the pathophysiology of motor speech impairment in MS using functional and diffusion magnetic resonance imaging (MRI).
Methods: Sixty-two pwMS (mean EDSS=4.3, 74% female) and 14 healthy controls (HC, 64% female) underwent 3T MRI with functional and diffusion components while completing a word repetition task. All participants completed an array of clinical and speech measures. We used a general linear model through FSL Feat to complete functional MRI analysis, and fixel-based analysis through MRTrix for diffusion data. Mann-Whitney U tests and Spearman correlations were used for statistical analyses.
Results: Functional MRI show that pwMS have significantly lower widespread activation during speech preparation and higher activation during speech production, than HC ($p<.05$). This increase during speech production is seen in the left Brodmann area 45 (BA45-L). Further, we see significant reduction in fibre density and cross section in pwMS compared to HC ($p<.05$). Both function and diffusion MRI changes in pwMS correlate with measures of dysarthria and cerebellar function.
Conclusion: This study provides new insights into the underlying mechanisms of dysarthria in pwMS that have implications for the development of monitoring strategies for cerebellar function in MS.
Disclosures: None

P-63
Altered diffusion MRI metrics in cortico-thalamic-striatal tracts associated with fatigue and disability in people with MS
Oun Al-iedani[1], Abdulaziz Alshehri[1], Nikitas Koussis[1], Ibrahim Khormi[1], Rodney Lea[1], Saadallah Ramadan[2], Jeannette Lechner-Scott[3]
[1]*University of Newcastle*
[2]*Hunter Medical Research Institute*
[3]*John Hunter Hospital*
Background: Diffusion MRI is highly sensitive to microstructural changes in the white matter of people with multiple sclerosis (pwMS), which are linked to the development of progressive disability. Despite the clinical significance of fatigue in pwMS and extensive research using conventional MRI, the link between neurodegeneration and fatigue remains unclear.
Objective: In a prospective study, we investigated how the microstructural neural integrity of cortico-thalamic-striatal (CTS) tracts correlates with fatigue and disability over time.
Methods: 76 people with stable Relapsing-remitting MS (RRMS) were age and sex-matched to 43 healthy controls (HCs). Participants completed disability, cognitive, fatigue, and mental health assessments, and underwent structural and diffusion scans on a 3T-MRI at baseline (BL) and 2-years follow-up (2Y-FU). The primary outcome was the change in diffusion metrics over time; the secondary was the correlation of diffusion metrics with fatigue (MFIS) and disability (EDSS) scores. We estimated fractional anisotropy (FA), mean, radial and axial diffusivities (MD, RD, AD) of normal-appearing white matter (NAWM) and white matter lesions (WML) in nine tracts-of-interests (TOIs) segmented by TractSeg, using MRtrix3 in-house pipeline.

Results: Significant differences in diffusion metrics in TOIs were found in RRMS compared to HCs at BL and 2-YFU ($p \leq 0.001$). WML diffusivities decreased, and FA increased significantly over time in most TOIs ($p \leq 0.001$), but no changes in diffusion metrics were observed in NAWM in pwMS. AD and MD positively correlated with fatigue scores ($r \leq 0.33$, $p \leq 0.01$) in NAWM-TOIs, while EDSS was negatively correlated with FA in most NAWM-TOIs ($|r| \leq 0.31$, $p \leq 0.01$) and EDSS correlated with all diffusivity parameters ($r \leq 0.29$, $p \leq 0.05$) in most WML-TOIs at both time-points.
Conclusion: Significant changes in WML diffusivities may indicate integrity improvement in CTS tracts over time in stable treated RRMS. This suggests potential repair of damaged tracts and a possible outcome measure for future remyelination clinical trials.
Disclosures: Oun Al-iedani: OA's salary was supported by another investigator-initiated grant from Biogen. Jeannette Lechner-Scott: institution receives non-directed funding as well as honoraria for presentations and membership on advisory boards from Sanofi Genzyme, Biogen, Merck KGaA, Teva, Roche and Novartis Australia.

P-64

Temporal And Topological Properties of Dynamic Networks Reflect Disability in Patients With Neuromyelitis Optica Spectrum Disorders

Yao Wang[1], Fuqing Zhou[1]
[1]*The First Affiliated Hospital of Nanchang University*

Background: Approximately 36% of patients with neuromyelitis optica spectrum disorders (NMOSD) suffered from severe visual and motor disability (blindness or light perception or unable to walk) with abnormalities of functional networks. However, it remains unclear how functional networks are related to clinical disability in patients with NMOSD.
Objective: Therefore, our study aims to explore the static strength, time-varying and topological properties of large-scale functional networks and their association with disability in patients with NMOSD
Methods: A total of 30 NMOSD patients (37.70±11.99 years) and 45 healthy controls (HCs, 41.84±11.23 years) were recruited. All subjects underwent functional MRI and disability assessments. We constructed resting-state functional networks for subjects and evaluated between-group differences in the static strength and network temporal and topological properties of networks using analysis of variance. We also assessed their association with disability severity with Spearman's correlation coefficients. A receiver operating characteristic (ROC) curve was also generated to investigate the efficacy of abnormal measures in diagnosing NMOSD.
Results: Compared to HCs, NMOSD patients showed significant alterations in dynamic networks rather than static networks. Three dynamic states were defined, and State 1 was characterized by overall hypoconnectivity within and between networks. NMOSD patients showed increased fractional times (P
Conclusion: Dynamic network might better explain disability than static network in NMOSD. Specifically, increased fractional time, higher dwell times with fewer transitions of hypoconnectivity state in dynamic networks were related to higher disability in NMOSD.
Disclosures: no

P-65

χ-separation Imaging in Myelin Oligodendrocyte Glycoprotein Antibody Associated Disease

Jean Hee Kim[1], Hyeong-Geol Shin[2], Jinhee Jang[3], Woojun Kim[1]
[1]*Dept. of Neurology, The Catholic University of Korea*
[2]*Johns Hopkins University*
[3]*Dept. of Radiology, The Catholic University of Korea*

Background: Magnetic susceptibility source separation (χ-separation) imaging can provide surrogates for iron and myelin, which have paramagnetic and diamagnetic characteristics, respectively. Those two components are associated with pathologic changes in brain lesions of MS or NMOSD, However, χ-separation imaging has not been applied to MOGAD.

Objective: We aimed to examine the appearance of the brain lesions in MOGAD on χ-separation maps.

Methods: This study included all consecutive individuals with MOG-IgG seropositive MOGAD who underwent MRI with the protocols for χ-separation imaging among those who visited the neurology clinic of our hospital from October 2017 to May 2023. Ten people with MOGAD underwent 3T MRI brain scans, including FLAIR and χ-separation imaging. For χ-separation maps, paramagnetic (χ-para) and diamagnetic susceptibility (χ-dia) were separately estimated by using local frequency shifts and calculating R2' (R2' = R2* − R2). R2 mapping was performed with a machine learning approach. In the lesions assessed in FLAIR image, signal characteristics on the χ-separation maps were evaluated and classified into three categories: hypointense, isointense, and hyperintense. From follow-up MRI scans, longitudinal outcomes of each lesion in T2 FLAIR and χ-separation images were assessed. Participant demographic and clinical characteristics were collected from the medical records.

Results: The mean age was 36.0 ± 16.6 years (range 13 – 59 years) and the mean disease duration was 24.7 ± 18.8 months (range 8 days – 63.5 months) at their first MRI scans. Among the 10 patients, 8 showed brain lesions during follow-up. Two of the patients showed multiple confluent white matter lesions, with a variety of neurological symptoms related to the lesions. The lesions had hypointensities on both χ–dia and χ–paramagnetic maps, suggesting demyelination with iron loss. They tended to regress in the follow-up MRI scans with symptomatic improvement. Six of the patients showed 8 small bran lesions, without corresponding neurological symptoms. Five of these lesions exhibited no changes in χ–separation maps, while the other three lesions showed hypointensity on the χ–dia maps, suggesting demyelination (two with hyperintensity on χ–para maps, suggesting iron deposition).

Conclusion: Brain lesions of MOGAD showed various patterns on χ–separation maps. Large edematous lesions showing demyelination without iron deposition tended to regress with time. Some of the small lesions showed demyelination with or without iron deposition.

P-66

Diencephalon Syndrome: Extending the Spectrum of GFAP-Astrocytopathies?

Ting Yoong Tee[1], Yin Yin Tan[1], Md Hanif Md Arif[2], Kartika Salwah Abd Latif[2], Mohd Sufian Adenan[1]
[1]*Neurology Department, Hospital Kuala Lumpur, Malaysia*
[2]*Radiology Department, Hospital Kuala Lumpur, Malaysia*

Background: Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy is a novel autoimmune astrocytopathy mainly presented with meningoencephalomyelitis and is often accompanied by a hallmark brain linear perivascular radial enhancement on magnetic resonance imaging (MRI). It lacks diagnostic criteria and often misdiagnosed as seronegative NMOSD or multiple sclerosis. Diencephalic involvement in GFAP astrocytopathy is an unusual occurrence.

Objective: We report a case of GFAP astrocytopathy presented with hypersomnia and symptomatic narcolepsy with hypothalamus involvement.
Methods: A 61-year-old gentleman presented with subacute onset of hypersomnia and symptomatic narcolepsy. Over 6 months duration, he developed progressive cognitive decline, gait instability and generalised myoclonus. No history of infection or vaccination prior to disease onset. On examination, he was encephalopathy, dysautonomia, tetraparesis with frequent myoclonus required intubation.
Results: His electroencephalogram (EEG) showed diffuse theta-delta slowing. Lumbar puncture revealed mild lymphocytic pleocytosis with elevated protein of 1.22g/L. His connective tissue disease, infection and malignancy workup were negative. There was no oligoclonal band found in his cerebral spinal fluid (CSF). Serum Aqouporin-4 IgG, Myelin Oligodendrocyte Glycoprotein (MOG) IgG, autoimmune and paraneoplastic encephalitis panels were unremarkable. His neuroimaging showed T2/FLAIR symmetrical hyperintensities in hypothalamus, thalamus, brainstem, periventricular white matter and spinal cord with subtle bilateral linear perivascular radial enhancement seen in T1 post contrast. Further CSF for GFAP Cell Based Assay (CBA) was positive with immunofluorescence (IFA) titre of 1:16. He was then diagnosed with GFAP astrocytopathy and was treated with intravenous methylprednisolone followed by oral steroid and azathioprine. He responded well with 90-day Modified Rankin Score (MRS) of 4.
Conclusion: Our case illustrated that diencephalon syndrome may be a novel phenotype in GFAP astrocytopathy.
Disclosures: None

P-67
Differences Of MRI Enhancement Patterns Between Patients with MOGAD And MS
Hiroshi Kuroda[1], Yoshiki Takai[1], Kimihiko Kaneko[1], Yuki Matsumoto[1], Chihiro Namatame[1], Hirohiko Ono[1], Toshiyuki Takahashi[1], Tatsuro Misu[1], Kazuo Fujihara[2], Masashi Aoki[1]
[1]*Tohoku University Graduate School of Medicine*
[2]*Fukushima Medical University School of Medicine*
Background: MOG antibody-associated disease (MOGAD) is clinically characterised by optic neuritis, acute disseminated encephalomyelitis, etc.; characterised by existence of MOG antibody in sera and/or cerebrospinal fluid. Although distinct clinical course and treatment, the differences between MRI characteristics of MOGAD and MS have not been fully clarified.
Objective: To elucidate differences of MRI enhancement patterns between patients with MOGAD and MS.
Methods: We retrospectively reviewed characteristics of gadolinium-enhanced MRI scans during acute phase in patients with MOGAD and MS. The enhancement patterns were categorised into 5 patterns as open ring, linear, punctate, pia-arachnoid, and perivascular enhancement.
Results: A total of 26 patients [15 MOG patients and 11 RRMS patients, median age 37 years, 77% female] were enrolled. Among these patients, a total of 64 enhanced lesions (22 in MOGAD and 42 in MS) were detected. The number of each enhancement pattern [MOGAD, MS] was open ring [3, 14], linear [3, 5], punctate [3, 23, $P < 0.01$], pia-arachnoid [7, 0, $P < 0.001$], and perivascular [6, 0, $P = 0.001$], respectively.
Conclusion: The pia-arachnoid and perivascular enhancement patterns on MRI are characteristic for MOGAD, compared to MS.
Disclosures: None

P-68

Clinical Features of Eight Patients Presenting with Concentric Lesions like Baló's Concentric Sclerosis

Kazunori Iwao[1,2], Katsuhisa Masaki[1], Yuu-ichi Kira[1], Eizo Tanaka[1], Mitsuru Watanabe[1], Koji Shinoda[1], Takeshi Miura[3], Noriko Isobe[1]

[1]Departments of Neurology, Graduate School of Medical Sciences, Kyushu University, Japan
[2]Department of Anatomy and Cell Biology, Graduate School of Medical Sciences, Kyushu University, Japan
[3]Department of Anatomy and Cell Biology, Graduate School of Medical Sciences, Kyushu University, Japan

Background: Baló's concentric sclerosis (BCS) is an extremely rare condition characterized by concentric demyelinating lesions. It is not understood under what pathophysiological conditions concentric lesions develop. Furthermore, there is no established evidence regarding the clinical course and treatment.
Objective: We aimed to describe the clinical features of cases presenting with concentric lesions.
Methods: We investigated cases at Kyushu University Hospital from 2010 to 2022 that showed concentric lesions on brain MRI and identified 8 cases for further assessment of their characteristics.
Results: All the cases satisfied the 2017 McDonald criteria. The average age at onset was 31.0 ± 7.5 years and concentric MRI lesions were observed in one to four lesions per individual. In cerebrospinal fluid, the white cell counts, and protein levels were elevated in 75% and 25% of the cases, respectively. Oligoclonal bands were detected in 7 cases (87.5%). No patient was positive for anti-aquaporin 4 antibody and anti-myelin oligodendrocyte glycoprotein antibody was also negative in all the 4 cases whose sera were tested. Corticosteroid was used in 7 cases as acute phase treatment and effective in all the cases. Several cases were initially diagnosed with multiple sclerosis (MS) before concentric lesions appeared and had been treated with dimethyl fumarate or fingolimod as disease modifying drugs (DMDs). All of these patients treated as MS experienced new brain MRI lesions during the course and required DMD switch to natalizumab or ofatumumab, which resulted in no further relapses since then.
Conclusion: We described the characteristics of patients presenting with concentric lesions like BCS. The relationship between BCS and MS, as well as treatment strategies in Baló's concentric sclerosis will be discussed.

P-69

The Tendency of Multiple Sclerosis Lesions Locations: MRI-based Evaluations

Anyeliria Sutanto[1], Rosaria Oktafiani Darmawan[2], Gerald Djuanda[3], Rocksy Fransisca Vidiaty Situmeang[1]

[1]Department of Neurology, Faculty of Medicine Universitas Pelita Harapan, Siloam Hospitals Lippo Village, Indonesia
[2]Department of Neurology, Siloam Hospitals Lippo Village, Indonesia
[3]Department of Neurology, Faculty of Medicine Universitas Pelita Harapan, Indonesia

Background: The specific MRI findings hold crucial part as one of the diagnostic criteria in diagnosing multiple sclerosis, as stated in McDonald's criteria 2017.
Objective: This descriptive study aims to elaborate the MS lesion locations throughout 10 locations in brain and spinal cord.
Methods: Data was collected from brain and spinal cord MRI of MS patients who came to MS clinic in Siloam Hospitals Lippo Village, Tangerang, Indonesia from January 2021-December 2022. There were 10 specific locations in brain (nerve root entry zone, middle cerebellar peduncle, medial longitudinal fasciculus/MLF, brainstem, cerebellar hemisphere, inferior temporal lobe, periventricular, corpus callosum, arcuate fibers, cortical/juxtacortical) and spinal cord which noted to find its tendency.

Results: Among 32 MS patients, 88% were female, with median (min-max) of age 35 (20-51 years), and 81% with relapsing-remitting (RRMS) phenotype. Cortical/juxtacortical lesion was the most common that was found in all patients, 96% in frontal lobes. Dawson's fingers, corpus callosum lesions, and inferior temporal lobes lesions were found in more than half of the patients (91%, 66%, 60%). The least frequent locations were MLF and nerve root entry zone, that were none to be found in this study. No particular difference was seen in various MS phenotypes.
Conclusion: The knowledge of MS lesion location tendency was hoped to be able to improve the accuracy in determining and differentiating MS lesions to support the solid diagnosis of MS.
Disclosures: No conflict of interest.

P-70
Symptomatic MS-like Brain Lesions in An AQP4 Positive Neuromyelitis Optica: A Case Report
Shanindra De Alwis[1], Arjuna Fernando[1]
[1]*Institute of Neurology, National Hospital of Sri Lanka, Colombo, Sri Lanka*
Background: Neuromyelitis optica (NMO) is an immune-mediated demyelinating CNS disease classically associated with optic neuritis and longitudinally extensive transverse myelitis. It is widely accepted that brain involvement is rare in NMO and in some instances the diagnosis is questioned when MRI abnormalities are detected in the brain.
Objective: Asymptomatic brain lesions are common in NMO, and symptomatic brain lesions do not exclude its diagnosis.
Methods: A 46-year-old female patient had a 5-year history of recurrent acute limb weakness that resolved spontaneously within a period of two weeks. She was diagnosed to have recurrent lacunar infarcts given the MR imaging of the brain showing multiple white matter hyperintensities that was attributed to cerebral small vessel disease. She continued to have such episodes despite being on anti-platelet therapy. She presented to our unit with sub-acute deterioration of visual acuity in both eyes. Fundoscopy revealed bilateral optic atrophy. Visual Evoked Potentials showed delayed P100 latencies bilaterally. A clinical diagnosis of optic neuritis was made and Treatment with high dose intravenous methylprednisolone was commenced. AQP4 IgG antibodies were subsequently positive.
Results: Analysis of the MR imaging of the brain showed multiple foci of T2/FLAIR hyper-intensities bilaterally in the periventricular, centrum semiovale, corpus callosal and cerebellar regions without diffusion restriction; suggestive of Multiple Sclerosis. After an initial response to immunosuppression, she relapsed with an episode of long segment myelitis in the cervical & thoracic cord.
Conclusion: This case highlights the varied presentation of NMO spectrum disorders and the heterogeneity of cerebral lesions that can be seen; some of which can be MS-like.
Disclosures: None

P-71

Different activation pattern of late complement pathway in the CSF between MOGAD and AQP4+N-MOSD.

Kimihiko Kaneko[1], Hiroshi Kuroda[2], Hirohiko Ono[1], Yuki Matsumoto[3], Naoya Yamazaki[1], Naoki Yamamoto[1], Shu Umezawa[1], Chihiro Namatame[1], Yoshiki Takai[1], Toshiyuki Takahashi[4], Juichi Fujimori[5], Ichiro Fujimori[5], Yasuo Harigaya[6], Kazuo Fujihara[7], Tatsuro Misu[1], Masashi Aoki[1]

[1]Tohoku University
[2]Southern Tohoku Research Institute for Neuroscience Southern Tohoku General Hospital
[3]NHO Miyagi National Hospital
[4]NHO Yonezawa national hospital
[5]Tohoku Medical and Pharmaceutical University
[6]Japanese Redcross Maebashi Hospital
[7]Fukushima Medical University

Refer to O-10 in Plenary Oral Presentation - 2

P-72

Structural and functional MRI markers for cognitive impairment in neuromyelitis optica spectrum disorders

Xiaolu Xu[1], Xinli Wang[2], Yunyun Duan[1], Zhizheng Zhuo[1], Ningnannan Zhang[2], Fenglian Zheng[1], Decai Tian[5], Sven Haller[3], Chunshui Yu[2], Frederik Barkhof[4], Fudong Shi[5], Yaou Liu[1]

[1]Department of Radiology, Beijing Tiantan Hospital, Capital Medical University
[2]Department of Radiology and Tianjin Key Laboratory of Functional Imaging, Tianjin Medical University General Hospital, Tianjin, China
[3]Department of Imaging and Medical Informatics, University Hospitals of Geneva and Faculty of Medicine of the University of Geneva, Geneva, Switzerland
[4]Centre for Medical Image Computing, Department of Computer Science, University College London, London, UK
5Department of Neurology, Beijing Tiantan Hospital, Capital Medical University

Background: Cognitive impairment (CI) develops in 35%-67% of patients with NMOSD, severely impacting their quality of life. Identifying the imaging predictors of CI can help early detect, objectively assess, and choose optimal therapy for NMOSD patients.

Objective: To identify the structural and functional predictors of CI in NMOSD using multimodal MRI.

Methods: In this cross-sectional study, 101 NMOSD patients and 43 age- and gender-matched healthy controls (HC) from two centers were prospectively recruited between January 2015 and May 2019. All patients underwent comprehensive neuropsychological assessments and multimodal MRI including T2/FLAIR, 3D-T1, diffusion images, and resting-state functional MRI. Structural MRI measures, including white matter (WM) lesion volume, WM integrity (fractional anisotropy, FA), gray matter volume (GMV), and functional MRI measure (amplitude of low-frequency fluctuation, ALFF) were compared between CI and cognitive preserved (CP) groups. The receiver operating characteristic curve and binary logistic regression model were performed to determine the power of clinical and MRI measures for predicting CI status.

Results: Thirty-four patients (33.7%) with NMOSD were classified as CI. Both CI and CP patients showed decreased FA, decreased GMV and functional abnormalities compared to HC. Compared to CP patients, the CI patients showed decreased FA in the anterior corpus callosum, decreased GMV in several brain regions including bilateral thalamus, parahippocampal gyrus, gyrus rectus and right middle temporal gyrus. While CP patients showed increased ALFF in the bilateral inferior parietal lobule (IPL) and left superior parietal lobule, CI patients had decreased ALFF in the right IPL, compared to HC. A combination of structural and functional MRI measures with education level and age exhibited fair to excellent discriminative power (AUC>0.8) for the discrimination between CI and CP. Binary logistic regression analysis predicted CI including GMV in the right middle temporal gyrus (β=11.92, P=0.014) and ALFF in the right IPL (β=-12.56, P=0.002).
Conclusion: CI developed as the structural damage in deep GM, frontal and temporal lobes progressed and functional adaption failed. MRI measures of GMV in right middle temporal gyrus and ALFF in right IPL are promising imaging markers for predicting CI in NMOSD.

POSTER SESSION-8
Neuropathology

P-73
A 3-year Longitudinal Study of Cognition in Multiple Sclerosis (MS)
Angel Ng[1], Lin Zhao[2]
[1]*The Chinese University of Hong Kong*
[2]*Beijing Shijitan Hospital, Capital Medical University*
Background: MS studies have traditionally been centered on progressive physical disabilities, while cognitive impairments are often neglected.
Objective: The present study aims to evaluate the cognitive functions and cerebral magnetic resonance imaging (MRI) features in Hong Kong Chinese patients with relapsing-remitting MS (RRMS) over a period of 3 years.
Methods: RRMS patients and healthy controls (HC) were enrolled between 2019 to 2021. A neuropsychological battery was performed by using a comprehensive set of cognitive measures that have been validated in the Hong Kong Chinese population. Subjects with >=3 impaired cognitive domains were defined as cognitively impaired (CI); with <3 impaired cognitive domains were defined as cognitively preserved (CP).
Results: 68 RRMS patients (78% females, meanage: 35.9 years) and 18 healthy controls (78% females, meanage: 39.2 years) were recruited. Compared with HC, RRMS patients performed significantly worse in processing speed (median (IQR): 0.06 (-0.29 to 0.49) vs. -0.45 (-1.26 to 0.20), p<0.05). Overall, CI-MS patients were more frequently male, with a lower year of education, and higher EDSS scores than CP-MS patients. 10 RRMS patients were reassessed at a 3-year interval. 20% of patients who were originally CP-MS converted to CI-MS at follow-up. A detailed investigation was conducted and mixed patterns of cognition evolution were observed over time: 1) Patients failed in fewer cognitive domains or failed at different cognitive domains at follow-up compared to baseline; 2) Patients initially impaired showed improvements at follow-up, while the opposite trend was observed for patients unimpaired at baseline.
Conclusion: This study suggests that cognitive impairments in MS do not always direct to progressive decline, which contradicts to the traditional belief in MS that cognitive impairments would inevitably deteriorate as MS progresses.

POSTER SESSION-9
Patient Reported Outcomes and Programs that Support Quality of Life

P-74
Steps Are A Candidate Digital Biomarker For Fatigue And Mood In Multiple Sclerosis
Kenzo Sakurai[1], Kenji Isahaya[1], Takeshi Imai[1], Yoshihisa Yamano[1]
[1]*St. Marianna University School of Medicine*
Background: Improving patient QoL in addition to suppressing disease activity to enhance long-term prognosis is important in the treatment of multiple sclerosis (MS). While biomarkers such as MRI and spinal fluid testing are used to assess disease activity, there are no established biomarkers for fatigue and mood, which affect QoL.
Objective: The purpose of this study is to assess the disease burden among patients with MS using electronic Patient-Reported Outcomes, as well as to identify potential factors that could serve as indicators of disease burden in Personal Health Records.
Methods: A web-based questionnaire survey was conducted among MS patients attending St. Marianna University School of Medicine. The survey included patient information such as age and employment status, disease information such as duration of illness and degree of disability, subjective symptoms such as fatigue and mood, and digital biomarkers. Digital biomarkers included the number of steps taken per day and time spent using smartphones.
Results: The study included 27 patients with a mean age of 41.0 ± 14.6 years, 18 of whom were female, and 17 of whom were unaware of their disability. Ten patients were aware of moderate or greater fatigue, 8 had depression, 4 had sleep disorders, and 15 were able to achieve rewarding results. The average number of steps taken per day was 5113 ± 3274, and the average time spent operating a smartphone was 259.4 ± 157.3 minutes. Perceived fatigue and depressive tendencies significantly decreased the number of steps taken ($p=0.02$, <0.01). The number of steps was negatively correlated with the Fatigue Assessment Scale (FAS) ($r=-0.47$, $p=0.02$), while smartphone operation time was not correlated with each factor.
Conclusion: The daily step count may reflect fatigue and mood and may be a useful digital biomarker in QoL-aware practice in MS.

P-75
The Prevalence of Stroke in Multiple Sclerosis Patients
Ebrahim Hajizade[1], Masoud Etemadifar[2]
[1]*Salamat Farda Hospital*
[2]*Isfahan University of Medical Sciences*
Background: Multiple Sclerosis (MS) is associated with numerous comorbidities such a include cardiovascular disease, psychiatric diseases, ischemic and hemorrhagic stroke, diabetes, hypertension, autoimmune diseases, and metabolic disorders. Comorbid disease is an important consideration for clinicians treating patients with MS.
Objective: The objectives of our study are to estimate the risk of stroke in patients with MS and to review related studies to draw preliminary conclusions that may improve clinical practice.

Methods: This case series study was conducted from year 2018 to year 2022 in the Isfahan MS clinic. A total of 2465 MS cases who referred to the clinic for routine follow ups were screened for stroke attack. Diagnosis of stroke attacks using MRI and CT scan analysis and their relation to the underlying MS was made by a board-certified neurologist. All the patients who had MS confirmed by experienced neurologist according to McDonald's, criteria having symptoms for more than one year and had ischemic or haemorrhagic stroke attack were included in the study.
Results: Out of 2465 MS patients, 10 (0.4%) of them had stroke attack, 6 (60%) had haemorrhagic attack and 4(40%) had ischemic attack. Among these patients, 7(70%) were females, 3(30%) were males, mean age MS patients that had stroke attack was 51.8 ± 9.28 years, mean age at MS start was 38.8 ± 10.23 years, mean duration between MS and stroke was 6.5 ± 2.91, mean EDSS was 2.05 ± .3 , 7 (70%) were of RRMS type , 3 (30%) were of SPMS type and the most common first MS sign was paresthesia.
Conclusion: The stroke prevalence is greater in MS patients than in general population. Most patient with stroke had RRMS type and the most type of stroke was haemorrhagic type.

P-76

Efficacy of cladrabine in RRMS patient in Singapore – real world evidence from a single centre in Singapore

Jeanne May May Tan[1,2], Janis Siew Noi Tye[1], Amelia Yun Yi Aw[1], Rachel Wan En Siew[1], Xuejuan Peng[1], Kevin Tan[1,2], Tianrong Yeo[1,2]
[1] National Neuroscience Institute (NNI) Singapore
[2]Duke-NUS Medical School, Singapore

Background: Cladribine is a synthetic purine analog with selective lymphotoxic specificity. It is currently FDA-approved for highly active relapsing remitting multiple sclerosis (RRMS) with the CLARITY trial showing 58% reduction in annualized relapse rates (ARR) at 2 years, lower accrual of MRI lesions, and decreased disability progression.
Objective: To determine the efficacy of cladrabine in patients with RRMS in NNI, Singapore.
Methods: Data from RRMS patients who received cladrabine were collected. Clinical efficacy was determined by: (1) calculating ARR before and after cladrabine completion, and (2) measuring EDSS score at cladrabine initiation and at 6-12 months after year 2 Cladribine, with disability progression confirmed by a subsequent clinical visit ≥3 months after. Radiological activity was defined as the presence of ≥2 new T2 lesions (referenced to rebaseline MRI) and/or any gadolinium-enhancing lesion on MRI performed at least 6 months after year 2 Cladribine.
Results: 33 RRMS patients who received cladribine were identified; 28 patients completed the full prescribed course. A total of 7 patients relapsed (21.2%, 7/33); 4 relapsed within year 1 of cladribine use while 4 patients relapsed in year 3 (including 1 patient who had relapsed in year 1). Four patients switched to anti-CD20 therapy while 1 was given a 3rd dose of cladribine. Follow-up data was available from 19 patients who completed ≥2 years monitoring post cladrabine: (1) ARR 2 years after Cladribine initiation was significantly lower than ARR 2 years prior [0.07 (SD 0.18) vs 0.87 (0.66), $p<0.001$], (2) 3 (15.8%, 3/19) had clinical relapse, (3) 4 (21.1% 4/19) had radiological activity, and (4) none had disability progression.
Conclusion: Our results, similar to CLARITY trial, showed significantly reduced relapse rates, low MRI activity and no disability progression in RRMS patients on cladribine.

P-77

Depression Screening in MS clinic - A comparative analysis of Beck's Depression Inventory (BDI 2) and Yale single question (YSQ) Screen in Indian Population

Parthvi Ravat[1], Sangeeta Hasmukh Ravat[1], Surabhi Garg[2], Sheela Chitnis[3]
[1]*Seth GS Medical College and King Edward Memorial Hospital, Mumbai*
[2]*St. John's National Academy of Health Sciences*
[3]*MS Society of India*

Background: The care of a depressed MS patient is more complex than that of a non-depressed MS patient. With the majority of patients being young and the high prevalence of depression in MS, it is vital to address this mental health issue at every clinical visit. Standardized tools exist for depression assessments but are scarcely used in every clinic visit.

Objective: To find an efficient way to screen for depression in clinical outpatient settings in Multiple Sclerosis in India.

Methods: We formulated a structured questionnaire that included Patient demographic details, disease details, the YSQ screen, and validated BDI 2 patients. The entire form was translated into Hindi (including a published, validated BDI translation), Marathi, and Gujarati, which are the widely spoken local languages. 2 native language speakers for each language were appointed who used the forward-backward translation method. No consent was involved in order to avoid bias in the patients.

All patients were initially screened for depression by asking patients the YSQ--' Do you frequently feel sad or depressed?', followed by BDI administration. 207 successive patients, who fulfilled the criteria for MS, regardless of type, filled out these forms. The BDI forms were analysed during the same clinic visit. Depression was defined as a score of > or = 13 on the BDI.

Results: The results are under processing, and we expect to get done with the analysis soon. Expected results are the YSQ sensitivity, Positive predictive value, Negative predictive value, comparison with BDI 2, assessment of these 2 scales in patients already on antidepressants, and analysis of variables like age, gender, time elapsed since diagnosis of MS, and the prevalence of depression in this Indian Cohort of MS patients. We hope to address whether YSQ is a substitute for the lengthy BDI 2 screening tool and whether it will help us accurately in referring the right patients to the psychiatry clinic, thus improving care without increasing the burden on healthcare or causing undue stress to the patient.

Conclusion: This study aims to highlight the importance of at least one appropriately selected screening tool becoming a mandatory and regular practice in each clinical visit for MS patients.

P-78

The disease burden among Neuromyelitis Optica patients in Taiwan

Chia-Yi Tian[1], Chen-Shu Chang[1], Kai-Chen Wang[2]
[1]Changhua Christian Hospital
[2]Cheng Hsin General Hospital

Background: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory disease of the central nervous system. The Real-World data of NMOSD in Taiwan is limited.

Objective: To delineate the demographic, clinical, and risk factors predictors of disease burden such as infection or relapse for hospitalization in NMOSD in Taiwan.

Methods: We retrospectively identified NMOSD patients by diagnostic codes or being positive for AQP4 autoantibody, and then confirmed through physician chart reviews based on the 2015 NMOSD criteria with a diagnosis of NMOSD between 2014 and 2021. The patients were divided into three groups based on their history of emergency room visits or hospitalizations in the observation period: Group A, patients who had no hospitalizations or emergency room visits; Group B, patients who had only one hospitalization or emergency room visit; and Group C, patients who had two or more hospitalizations or emergency room visits. Statistical analyses were performed to find out the risks such as hospitalization, infection, or relapsing among these patients in the follow-up period.
Results: During a median follow-up period of 3.5 years, 59 NMOSD patients were identified and analysed. Our findings indicated that higher doses of Azathioprine (54.6mg, P=0.04) and a higher trend of oral steroids (P=0.048, mean 14.1mg) were associated with higher frequent hospitalizations or emergency room visits. The disease severity of the first two years can't determine the later frequency of hospitalization(P=0.10) and emergency visits(P=0.58). Furthermore, the adjusted Cox regression analysis revealed that NMOSD patients who were older or had comorbid Sjogren's syndrome were more likely to experience infections (Hazard ratios of 1.1 [95% CI 1.0-1.2] and 31.7 [95% CI 1.5-693.5], respectively). Male gender was associated with a higher risk of relapse, with a hazard ratio of 3.8 [95% CI 1.0-18].
Conclusion: Our study reports the demographic, clinical, and risk factors predictors of disease burden such as infection or relapse for hospitalization in Taiwan NMOSD.

P-79

Insights from Patients and Caregivers in Coping with Multiple Sclerosis: A Preliminary Study

Anyeliria Sutanto[1], Putri Widya Andini[2], Kanya Puspokusumo[3], Sutji Windari[3], Febriani Yahya[3], Ahmad Rizal[4], Aih Cahyani[4], Kartika Maharani[2], Darma Imran[2], Riwanti Estiasari[2]
[1]*Department of Neurology, Faculty of Medicine Universitas Pelita Harapan, Siloam Hospitals Lippo Village, Indonesia*
[2]*Department of Neurology, Faculty of Medicine Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Indonesia*
[3]*Indonesian Multiple Sclerosis Society*
[4]*Department of Neurology, Faculty of Medicine Universitas Padjadjaran, Dr. Hasan Sadikin Hospital, Indonesia*
Background: Understanding the perspectives of patients and caregivers is crucial as multiple sclerosis (MS) can have a significant impact on their lives.
Objective: This preliminary study aims to explore perspectives from MS patients and caregivers to identify barriers and gather suggestions for their resolution.
Methods: Data was collected from MS patients and caregivers using structured questions related to demographics, challenges, and aspirations. The questionnaire was developed based on literature, clinical guidelines, and expert consultations. The survey was conducted on World MS Day 2023 in Indonesia.
Results: Among 31 MS patients, 87.1% were female, with higher degree qualifications (64.5%) and median (IQR) age of 32 (17-55) years. Most patients (58.1%) had been living with MS for less than 5 years, with 96.8% maintaining their productivity across various roles.
The prevalence of financial constraints was evident, as 61.3% reported an income less than minimum regional wage (<330 USD). Fatigue, coordination disorder, and motoric weakness were the three most debilitating symptoms. Patients hope for the implementation of disability-friendly public transportation, enhanced inclusivity in education and the workplace, increased availability of diagnostic tools and treatments, and a robust support system from family and community. Among, 9 caregivers, over 50% acknowledged moderate to severe impacts on their lives due to caregiving responsibilities. However, 78% did not view their role as a burden. Primarily being immediate family members, caregivers hoped for better access to both diagnosis and treatment.

Conclusions: The findings from this preliminary study highlight the significance of addressing individuals' expectations, and comprehensive treatment approach to help MS patients reintegrate into their normal activities, particularly related to inclusivity, diagnostic tools and treatment availability, and a robust support system. Subsequent research is necessary to gain deeper insights and elaboration on these findings.
Disclosures: No conflict of interest.

POSTER SESSION-10
Symptom Management; Rehabilitation Research and Strategies

P-80
The Prevalence of Gustatory Dysfunctions in Multiple Sclerosis And Neuromyelitis Optica Spectrum Disorders
Mahboubeh Kaji Esfahani[1], Masoud Etemadifar[2], Farzaneh Montazeri[2]
[1]*Najaf Abad University of Medical Sciences*
[2]*Isfahan University*
Background: Gustatory dysfunction is a rare manifestation of the central nervous system (CNS) inflammatory demyelinating diseases (CNSIDDs). Different CNSIDDs have different anatomical lesion distribution patterns. Comparative data on gustatory dysfunction frequency in patients with different CNSIDDs are scarce.
Objective: To investigate and compare the frequency of gustatory dysfunction in multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) patients.
Methods: Patients with taste impairment were identified through their medical records in the Isfahan Multiple Sclerosis Center. Included participants were asked to take a gustatory function test, and the frequency of gustatory dysfunction was measured in both groups of MS and NMOSD patients.
Results: We collected data of 5,190 MS patients and 163 NMOSD patients from the registry of the Isfahan MS center. Patients were evaluated for taste function, and finally,47 MS patients (n=42 women, n=5 men) with a mean age of 37.7±11.8 years and a mean disease duration of 9.3±6.8 years and 5 NMOSD patients (n=5 women) with a mean age of 36.7±9.3 years and a mean disease duration of 11.3±11.1 years were identified. Therefore, the prevalence of gustatory dysfunctions was significantly different among MS and NMOSD patients (about 0.01 and 0.03, respectively, p-value = 0.02). in the next step, further investigations were applied in these patients to reach a clearer view of taste disorders in MS and NMOSD patients.
Conclusion: We showed that dysgeusia occurred in a fraction of NMOSD and MS patients, necessitating including the entity of these two diseases in the differential diagnoses. On the other hand, according to the obtained results, these two groups varied in many as

European Charcot Foundation Symposium

Understanding and Treating Progression

ECF-1

Hans-Peter Hartung, M.D., Ph.D
Immunopathology of Progressive MS
Professor of Neurology, Heinrich Heine University Düsseldorf, Germany

Histological and imaging studies have contributed in recent years to a better understanding of the pathobiology of progressive MS. Compartmentalized CNS inflammation located subpially involves B cells but also various T lymphocytes populations. Microglia appears fundamental in driving the pathological process. Thus, peripheral aberrant cognate immune responses, CNS intrinsic innate immunity, as well as antigen-specific inflammation, heightened production of e.g., oxygen radical species, mitochondrial energy breakdown, disturbed iron hemostasis and failure of effective remyelination all synergize to produce the inflammatory neurodegenerative changes. Superimposed may be the changes accompanying aging.

Currently, there are only 2 drugs approved for the treatment of progressive MS, the S1PR modulator siponimod for SPMS and the anti-CD20 B cell depleting monoclonal antibody ocrelizumab for PPMS. Their effects are moderate. A promising strategy currently widely explored are BTK inhibitors that may target B cells in both the periphery and CNS and microglia.

A range of remyelinating drugs are being studied. A reset of disordered immune responses. Clearly, the pressing unmet needs of progressive MS mandate intense investigation of agents disrupting the multiple pathomechanisms underlying progressive MS.

ECF-2

Detection and monitoring of progressive MS

Giancarlo Comi
Honorary Professor Vita Salute San Raffaele University (Milan, Italy)

The traditional classification of multiple sclerosis courses in relapsing-remitting, primary progressive and secondary progressive has been recently challenged by the evidence that a silent progression may occur quite early, perhaps already in the preclinical phase of the disease. Early detection of the progression is very important because the pathophysiological mechanisms underlying progression are different from those operating in the relapsing phase of the disease and require a different therapeutic approach. The values and limits of the different approaches for the ascertainment of silent progression will be discussed.

The recent availability of disease modifying treatments for primary and secondary progressive multiple sclerosis requires the availability of tools for assessment of treatment response. The expanded disability status scale (EDSS) is the gold standard in clinical trials and also in clinical practice, however in a recent study it was demonstrated that EDSS is more amenable to measurement error and less sensitive to changes than other outcome measures, such as T25FW and 9HPT. These alternative outcome measures are mostly used for research purposes, as a consequence the detection of a treatment failure in progressive MS patients can be late and incorrect. This is a relevant problem because patients with PMS are more exposed to risks of adverse effects of DMTs due to age, more frequent comorbidities and disability. The contribution of imaging, functional and body fluid biomarkers in progressive multiple sclerosis monitoring will be examined.

ECF-3

Treatment of progressive MS

Kazuo Fujihara, MD
Professor, Department of Multiple Sclerosis Therapeutics, Fukushima Medical University School of Medicine, Fukushima, Japan

Clinical disability in progressive MS (PMS) progresses independently of relapse activity and the pathogenesis of PMS is a complex, multifactorial process including neurodegeneration. Thus, PMS is difficult to treat and in fact, the efficacy of approved anti-inflammatory drugs for PMS, such as ocrelizumab and siponimod, is limited. Younger patients with shorter duration of PMS and more active disease at baseline appear to benefit the most from the available treatments. But other modes of therapy including drugs with neuroprotective or remyelinating effects, stem cell transplantation and other types of cell therapy, etc. are also being evaluated in PMS. In a recent position paper, European experts recommended making treatment decisions in PMS based on the individual patient's pattern of disease progression, as well as functional, clinical, and imaging parameters, rather than on their clinical phenotype. In this presentation, therapeutic evidence of PMS, novel therapies and the challenges in research and clinical practice will be discussed.

ECF-4

Neuromodulation

Letizia Leocani, MD, PhD
Associate Professor of Neurology, University Vita-Salute San Raffaele, Milan

Repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) are non-invasive brain stimulation techniques widely explored as a potential treatment in several neuropsychiatric disorders. While rTMS is routinely used as a therapeutic intervention for major depression and obsessive-compulsive disorder not responsive to a first pharmacologic treatment, several evidence points to an additional use of non-invasive brain stimulation, based on the possibility to enhance brain plasticity, and thus potentiate the effects of rehabilitation. Several studies point to the benefits of combining rehabilitation – physical, cognitive – with non-invasive brain stimulation in movement disorders, stroke, multiple sclerosis and neurodegenerative dementing diseases. Further randomized, controlled studies are needed to strengthen this evidence and provide information about the criteria to identify the modalities of administration in terms of dosing, schedule, and brain target, and to identify the best potential responders.

Pharma Educational Symposia

MITSUBISHI TANABE PHARMA SYMPOSIUM
Thursday, 23 November 2023, 17:30 – 19:00

Epidemiology of NMOSD in Taiwan - Perspective from a Southern Medical Center
Chairperson: Kazuo Fujihara, MD (Japan)
Speaker: Lin, Chou-Ching, M.D. (Taiwan), Department of Neurology, National Cheng Kung University Hospital

This scientific lecture delves into the epidemiological landscape of Neuromyelitis Optica Spectrum Disorder (NMOSD) in Taiwan, with a specific focus on insights gathered from a prominent southern medical center. NMOSD, a rare autoimmune disorder affecting the central nervous system, poses unique challenges in diagnosis and management. Drawing on extensive data collected over years, the lecture sheds light on the prevalence, clinical characteristics, and demographic patterns of NMOSD within the Taiwanese population. By examining cases from a southern medical center, the lecture unravels regional variations, allowing a comprehensive understanding of the disease's impact. Insights derived from this study hold pivotal implications for healthcare strategies, emphasizing the need for tailored interventions and heightened awareness campaigns, ultimately enhancing the overall management of NMOSD in Taiwan.

Inebilizumab, B cells, and NMOSD: lessons learned in N-MOmentum study
Chairperson: Lin, Chou-Ching, M.D. (Taiwan)
Speaker: Kazuo Fujihara, MD (Japan), Department of Multiple Sclerosis Therapeutics, Fukushima Medical University School of Medicine

B cells contribute to the pathogenesis of neuromyelitis optica spectrum disorders (NMOSD) in multiple ways including aquaporin-4 (AQP4)-antibody production, enhancing proinflammatory B cell and plasmablast activity and impaired B cell regulatory function. Inebilizumab is a humanized anti-CD19 monoclonal antibody. CD19 is broadly expressed on B-lineage cells and in experimental studies, inebilizumab depletes >90% of CD19-positive B cells. N-MOmentum, a pivotal phase II/III placebo-controlled randomized controlled trial, and the open label extension clearly demonstrated high efficacy and safety of the B cell depleting therapy in NMOSD. Moreover, the post hoc analyses revealed additional evidence of immunopathological effects of inebilizumab in NMOSD and new aspects of the disease. In this presentation, those clinical and experimental findings and the challenges that lie ahead will be discussed.

NOVARTIS PHARMACEUTICALS SYMPOSIUM
Friday, 24 November 2023, 08:00 – 09:30

Evolving treatment strategies in MS – perspectives from Asia and Australia
Chairperson: Professor Noriko Isobe MD, PhD (Department of Neurology, Kyushu University, Japan)

Speakers:

Prof. Kazuo Fujihara MD (Fukushima Medical University School of Medicine and Southern TOHOKU Research Institute for Neuroscience (STRINS), Koriyama, Japan)

Dr John Parratt, MBChB, MD, FRACP (Royal North Shore Hospital and North Shore Private Hospital, Australia)

Susan Agland, RN (John Hunter Hospital and Hunter Medical Research Institute, Australia)

In recent years there have been great advances in the treatment of multiple sclerosis (MS). Early intervention with high efficacy therapy for relapsing forms of MS, in particular with the B cell depleting anti-CD20 monoclonal antibody therapies, has been building in adoption based on growing evidence from across clinical trials, real world registry data and longer-term safety data. A coordinated and holistic approach is important in ensuring the best clinical outcomes for patients treated with these therapies.

This Symposium will bring together a faculty of MS experts from across Japan, Australia and China to share their perspectives on the unique challenges that they face in treating patients with MS in their countries and share their learns to guide treatment practice across the Asia Pacific region. The session will focus on MS treatment strategies, treating with the aim of NEDA and experience of managing progression independent of relapse activity (PIRA), highlighted with patient case studies with a focus on Kesimpta (ofatumumab). The session will also delve into the importance of a holistic approach to treatment management and safety monitoring and the critical role of the MS nurse to ensure optimal patient outcomes.

Throughout the session, the faculty will be sharing their perspectives through a panel discussion and will welcome audience questions on the topics discussed during the Symposium to foster exchange of experience and learning.

CHUGAI PHARMACEUTICAL CO., LTD. SYMPOSIUM
Friday, 24 November 2023, 16:30 – 18:00

Role of IL-6 in NMOSD
Chairperson & Speaker: Jin Nakahara
Professor, Department of Neurology, Keio University School of Medicine, Tokyo, Japan

Dr. Nakahara will give a lecture on the role of IL-6 in NMOSD

Treatment Strategy of NMOSD – Focus on IL-6
Chairperson & Speaker: Ichiro Nakashima
Professor, Department of Neurology, Tohoku Medical and Pharmaceutical University, Sendai, Japan.

Dr. Nakashima will give a lecture on NMOSD treatment strategies focusing on IL-6 inhibition.