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

THE 16th PAN-ASIAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS CONGRESS

30 OCT - 2 NOV 2024 BANGKOK, THAILAND

ULTOMIRIS
(ravulizumab)
100 mg/mL concentrate for solution for infusion

For the treatment of adult patients with anti-aquaporin-4 (AQP4) antibody-positive **Neuromyelitis Optica Spectrum Disorder (NMOSD)**[1]

Strive for Zero

- All patients treated with ULTOMIRIS were relapse-free at a median treatment period of 73.5 weeks*[2]
- No relapses were observed at a follow-up period of 90.9 weeks[3]
- 98.6%[‡] reduction in the risk of relapse vs placebo[2]

ULTOMIRIS: Give your patients the **chance of zero relapses** as soon as possible[2,3]

* The safety and efficacy of ULTOMIRIS were studied in CHAMPION-NMOSD, a global, externally placebo controlled, open-label, multicentre trial of 58 adults with AQP4 Ab+ NMOSD. The placebo group of the PREVENT trial was used as an external comparator (n=47). [2] [‡]p<0.0001; HR=0.014 (95% CI: 0.000, 0.103).[2] [‡]No patients had an adjudicated on-trial relapse during the study period, real-world data for ULTOMIRIS outcomes in NMOSD are not available.

Ultomiris (Ravulizumab) Abbreviated Prescribing Information (API)

Ultomiris (Ravulizumab) concentrate for solution for infusion (100 mg/mL). **Ultomiris is indicated in the treatment of adult patients with NMOSD who are anti-aquaporin 4 (AQP4) antibody-positive.** The doses to be administered are based on the patient's body weight. Maintenance doses should be administered at a once every 8-week interval, starting 2 weeks after loading dose administration. **Body weight range: ≥ 40 to < 60 kg:** Loading dose: 2,400 mg, Maintenance dose: 3,000 mg. **Body weight range: ≥ 60 to < 100 kg:** Loading dose: 2,700 mg, Maintenance dose: 3,300 mg. **Body weight range: ≥ 100** kg: Loading dose: 3,000 mg, Maintenance dose: 3,600 mg. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in SmPc. Patients with unresolved Neisseria meningitidis infection at treatment initiation. Patients who are not currently vaccinated against Neisseria meningitidis unless they receive prophylactic treatment with appropriate antibiotics until 2 weeks after vaccination. **Special warnings and precautions for use:** all patients must be vaccinated against meningococcal infections at least two weeks prior to initiating ravulizumab. **Undesirable effects:** The most common adverse reactions with ravulizumab (intravenous formulation) are headache. The most serious adverse reactions are meningococcal infection including meningococcal sepsis and encephalitis meningococcal. Shelf life: chemical and physical stability of the diluted product have been demonstrated for up to 24 hours at 2 °C - 8 °C and up to 4 hours at room temperature. **Date of Revision: October 2024.** This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Please report any adverse reactions via your national reporting systems. Adverse events can be also reported to AstraZeneca Thailand by email at medinfo.th@astrazeneca.com

Marketing Authorization Holder: AstraZeneca (Thailand) Ltd. Asia Centre Bldg., 173/20, South Sathorn Rd. Thungmahamek, Sathorn, Bangkok 10120 (Thailand) T: +66 2 739 7400 - F: +66 2 729 7498

1. Full Ultomiris SmPC: Ultomiris (Ravulizumab) summary of product characteristics. AstraZeneca (Thailand) 2024. 2. Pittock SJ, et al. Ann Neurol. 2023;93(6):1053–1068. 3. Pittock S, et al. Efficacy and safety of ravulizumab in adults with anti-aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder: outcomes from the phase 3 CHAMPION-NMOSD trial (S5.002). Presented at AAN April 2023 DOI: 10.1212/WNL.0000000000202922.

ULTOMIRIS®
SmPC
(English)

โปรดอ่านรายละเอียดเพิ่มเติมในเอกสารอ้างอิงฉบับสมบูรณ์และเอกสารกำกับยา
เป็นยาใหม่ใช้เฉพาะสถานพยาบาล
ความถูกต้องของโฆษณานี้เป็นความรับผิดชอบของผู้โฆษณา มิได้ดำเนินการโดยสำนักงานคณะกรรมการอาหารและยา
การโฆษณาตามใบอนุญาตนี้ต้องกระทำโดยตรงต่อผู้ประกอบโรคศิลปะ ผู้ประกอบวิชาชีพเวชกรรม หรือผู้ประกอบการบำบัดโรคสัตว์เท่านั้น ผู้ใดนำโฆษณานี้ไปเผยแพร่ต่อบุคคลอื่นที่ไม่ใช่ผู้ประกอบโรคศิลปะ ผู้ประกอบวิชาชีพเวชกรรม หรือผู้ประกอบการบำบัดโรคสัตว์ มีอาจเป็นการฝ่าฝืนมาตรา 88 และมาตรา 88 ทวิ ต้องระวางโทษปรับไม่เกินหนึ่งแสนบาท ตามมาตรา 124 แห่งพระราชบัญญัติยา พ.ศ. 2510 และฉบับแก้ไขเพิ่มเติม
ใบอนุญาตโฆษณาเลขที่ ธศ. 2-3418/2567

AstraZeneca
TH-20953 Exp Oct 2026

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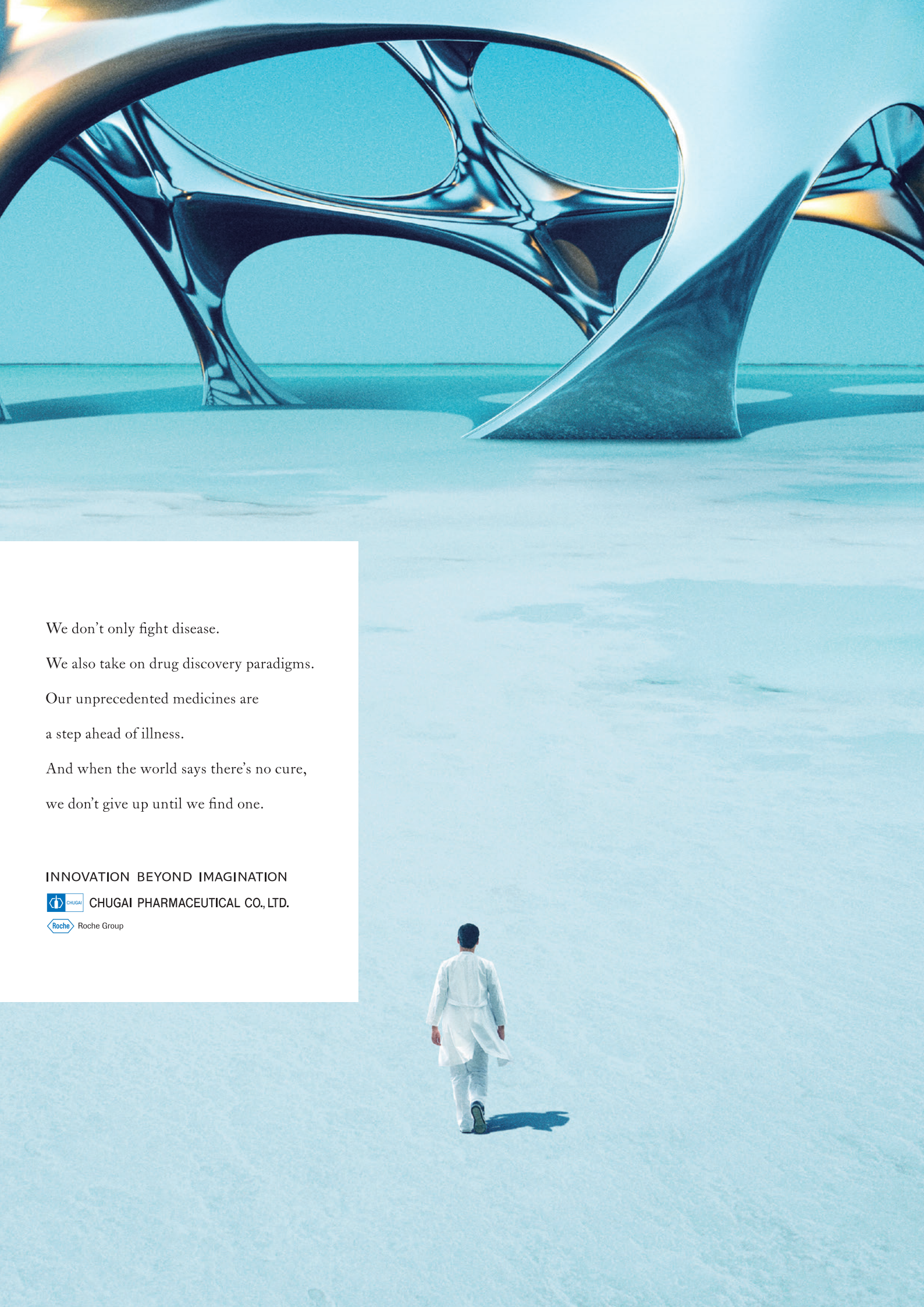

We don't only fight disease.

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 Esteemed Guests,

With utmost respect for the Thai people, the traditional custodians of the land upon which we gather, and in recognition of their enduring culture, we extend our warmest greetings. It is with great pleasure and anticipation that we welcome you to the 16th Congress of the Pan-Asian Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS), set to unfold in the dynamic city of Bangkok, Thailand, from October 30th to November 2nd,2024.

Bangkok, with its rich cultural heritage, bustling streets, and exquisite cuisine, provides an ideal backdrop for this esteemed gathering of minds. As you immerse yourselves in the intellectual discourse and collaborative sessions over the coming days, we trust that you will also find time to explore the enchanting sights and sounds that our city has to offer.

As we convene for PACTRIMS 2024, our focus remains steadfast on addressing the diverse challenges encountered by patients within our region's healthcare landscape. This year's congress, guided by five pivotal themes:

1. Updated pathophysiology of CNS demyelination
2. Early diagnosis of MS and related disorders: Current and emerging criteria
3. Treatment associated risks in MS: Regional strategies for mitigation.
4. Pediatric CNS inflammatory diseases
5. Artificial Intelligence (AI) in neurological diagnosis

We are confident that the discussions and exchanges during the conference will be both enlightening and enriching, fostering new connections and paving the way for future collaborations.

In addition to the stimulating conference sessions, we have organized various social events and networking opportunities to allow you to interact with your peers in a relaxed and informal setting. These gatherings will not only facilitate knowledge sharing but also create lasting memories of your time in Bangkok.

On behalf of the organizing committee, I extend a heartfelt welcome to each of you. May your time at PACTRIMS 2024 be both enriching and rewarding, as we collectively embark on this journey of discovery and collaboration in the heart of Bangkok. Once again, welcome to Bangkok! May your time here be filled with productive discussions, memorable experiences, and meaningful connections.

Yours sincerely,

Dr. Sasitorn Siritho Chair,
Local Organizing Committee PACTRIMS 2024
Bangkok, Thailand

WELCOME NOTE

PACTRIMS
Committee Members 2024

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16TH PACTRIMS LOCAL ORGANIZING COMMITTEE

Chairperson
Sasitorn Siritho, Thailand

PROGRAM OVERVIEW

PACTRIMS-ECTRIMS JOINT TEACHING COURSE
Advances in MS and Related Conditions

Wednesday, 30 October 2024				
Time	**Duration**	**Topics**	**Speakers**	**Chairpersons**
09:00-09:05	5 mins	Welcome to the Inaugural PACTRIMS-ECTRIMS Joint Teaching Course	Todd Hardy (Australia), Jyh Yung Hor (Malaysia), Waqar Rashid (UK)	
09:05 - 10:15	1 hr 10 min	Session 1: Diagnosis and Treatment of MS		Todd Hardy (Australia) & Waqar Rashid (UK)
09:05 - 09:40	35 min	TL1: Diagnosis of MS - Update on the McDonald criteria	Waqar Rashid (UK)	
09:40 - 10:15	35 min	TL2: How to treat MS - including discontinuation/de-escalation	Vincent Van Pesch (Belgium)	
10:15 - 10:45	30 min	Coffee Break		
10.45 - 12:30	1 hr 45 min	Session 2: Special Considerations in MS and Optic Neuritis Update		Simon Ling (Singapore) & Cheryl Hemingway (UK)
10:45 - 11:20	35 min	TL3: Challenges of MS in childhood and adolescence	Cheryl Hemingway (UK)	
11:20 - 11:55	35 min	TL4: Approach to Optic Neuritis	Shweta Singhal (Singapore)	
11:55 - 12:30	35 min	TL5: MS Nursing Lecture: Vascular Co-Morbidities in MS	Meaghan Osborne (Australia)	
12:30 - 13:30	60 min	Lunch at Skyline Restaurant 11th Floor		
13.30 - 15.15	1 hr 45 min	Session 3: MS Immunology, Pathology and Biomarkers		Sean Riminton (Australia) & Martina Absinta (Italy)
13:30 - 14:05	35 min	TL6: Pathology of MS	Richard Reynolds (UK)	
14:05 - 14:40	35 min	TL7: Immunology of MS	Sean Riminton (Australia)	
14.40 - 15:15	35 min	TL8: MS Biomarkers - including newer MRI techniques and the role of neurofilaments	Martina Absinta (Italy)	
15:15 - 15:45	30 min	Coffee Break		
15.45 - 16.55	1 hr 10 min	Session 4: NMOSD and MOGAD		Jyh Yung Hor (Malaysia) & Ichiro Nakashima (Japan)
15:45 - 16:20	35 min	TL9: Diagnosis and Treatment of NMOSD	Jin Nakahara (Japan)	
16:20 - 16:55	35 min	TL10: Diagnosis and Treatment of MOGAD	Ichiro Nakashima (Japan)	
16:55 - 17:00	5 min	Closing	Todd Hardy (Australia), Jyh Yung Hor (Malaysia), Waqar Rashid (UK)	

PROGRAM OVERVIEW

Time	Duration	Topics	Speakers	Chairpersons
Thursday, 31 October 2024				
EUROPEAN CHARCOT FOUNDATION PRE-CONGRESS SYMPOSIUM				
12:30-13:00	30 mins	1. Treatment of progressive MS in practice	Hans-Peter Hartung (Germany)	
13:00-13:30	30 mins	2. Patient Reported outcomes in the assessment of treatment response	Giancarlo Comi (Italy)	
13:30-14:00	30 mins	3. Advances in neurorehabilitation	Letizia Leocani (Italy)	
14:00-14:30	30 mins	4. Symptomatic therapy	Kazuo Fujihara (Japan)	
14:45-21:30		**PACTRIMS CONGRESS DAY 1**		
14:45-14:50	5 mins	Welcome Address by the Local Organizing Chairperson	Sasitorn Siritho (Thailand)	
14:50-14:55	5 mins	Opening Address by the President	Kazuo Fujihara (Japan)	
14:55-15:00	5 mins	Special Address by the Guest of Honour	Deputy Director General Dr. Sakarn Bunnag (Thailand)	
15:00-16:30	1 hr 30 min	**Plenary 1: Updated pathophysiology of CNS demyelination**		**Jen Jen Su (Taiwan) & Sungmin Kim (Korea)**
15:00-15:25	25 mins	L1. Correlation of neuropathology with MRI	Martina Absinta (Italy)	
15:25-15:50	25 mins	L2. Pathomechanisms of NMOSD	Norio Chihara (Japan)	
15:50-16:15	25 mins	L3. Meningeal inflammation as a driver of cortical pathology in Multiple Sclerosis	Richard Reynolds (UK)	
16:15-16:30	15 mins	Q&A		
16:30-17:00	30 mins	Coffee Break/ Poster Viewing / Meet The Experts		Giancarlo Comi
17:00-18:00	60 mins	ORAL PRESENTATION PART ONE - 5 presentations		**Hans-Peter Hartung (Germany) & Sasitorn Siritho (Thailand)**
18:15-19:15	60 mins	Chugai Pharmaceutical Co., Ltd Sponsored Symposium - How Satralizumab changed treatment strategy in NMOSD	Yusei Miyazaki (Japan) Ichiro Nakashima (Japan)	**Jin Nakahara (Japan)**
19.30-21.30	2 hours	Welcome Reception at the Long Tail, Anantara Riverside		
Friday, 1st November 2024				
08:00-18:30		**PACTRIMS CONGRESS DAY 2**		
08:00-09:00	60 mins	Alexion Sponsored Symposium - Complement in Focus: Clinical and Real-World Evidence for the Prevention of Relapses in AQP4-Ab+ NMOSD -	Prof. Ho Jin Kim (Korea), Prof. Sasitorn Siritho (Thailand), Prof. Jin Nakahara (Japan)	
9:15-10:20	1 hr 05 mins	**Plenary 2: Pediatric CNS inflammatory diseases**		**Lekha Pandit (India) & Todd Hardy (Australia)**
9:15-9:40	25 mins	L4. Pediatric MS/NMOSD	Cheryl Hemingway (UK)	
9:40-10:05	25 mins	L5.Prevalence and Diagnosis of Pediatric MS/NMOSD in Taiwan	Wang-Tso Lee (Taiwan)	
10:05-10.20	15 mins	Q&A		
10:20-10:50	30 mins	Coffee Break/Poster Viewing / Meet The Experts		**Hans-Peter Hartung**
10:50-12:20	1 hr 30 min	**Plenary 3: Early diagnosis of MS and related disorders: Current and emerging criteria**		**Ichiro Nakashima (Japan) & Kevin Tan (Singapore)**
10:50-11:15	25 mins	L6. RIS and its revised criteria	Darin Okuda (USA)	
11:15-11:40	25 mins	L7. Importance of early diagnosis of MS and predict early non-disabling relapses	Anneke van der Walt (Australia)	

PROGRAM OVERVIEW

Time	Duration	Topics	Speakers	Chairpersons
11:40-12:05	25 mins	L8. Diagnosis of MOGAD: Tips for accurate diagnosis	Jae-Won Hyun (Korea)	
12:05-12:20	15 mins	Q&A		
12:20-13:20	60 mins	Lunch		
13:20-14:20	60 mins	ORAL PRESENTATION PART TWO - 5 presentations		**Kazuo Fujihara (Japan) & Allan Kermode (Australia)**
14:20-15:50	1 hr 30 mins	**Plenary 4: Treatment associated risks in MS: Regional strategies for mitigation**		**Metha Apiwattanakul (Thailand) & Thomas Mathew (India)**
14:20-14:45	25 mins	L9. Treatment strategy for PML in daily practice	Jin Nakahara (Japan)	
14:45-15:10	25 mins	L10. Risk mitigation in multiple sclerosis immunotherapy - the Indian perspective	Sruthi Nair (India)	
15:10-15:35	25 mins	L11. Treatment strategies for MS/NMOSD in Thailand	Metha Apiwattanakul (Thailand)	
15:35-15:50	15 mins	Q&A		
15:50-16:05	15 mins	Coffee Break		
16:05-17:20	75 mins	Poster Presentation Session		**Letizia Leocani (Italy)**
17:30-18:30	60 mins	Mitsubishi Tanabe Sponsored Symposium- CD19-targeted therapy for NMOSD	Chung-Hsing Chou (Taiwan), Yusei Miyazaki (Japan)	**Kazuo Fujihara (Japan)**
Saturday, 2nd November 2024				
09:45-11:35		**PACTRIMS CONGRESS DAY 3**		
09:45-11:15	1 hr 30 mins	**Plenary 5: Artificial Intelligence (AI) in neurological diagnosis**		**Yaou Liu (China) & Yeo Tianrong (Singapore)**
9:45-10:10	25 mins	L12. Overview of machine learning approaches	Wilson Goh (Singapore)	
10:10-10:35	25 mins	L13. Future with AI-based MRI monitoring in MS	Chenyu (Tim) Wang (Australia)	
10:35-11:00	25 mins	L14. AI for imaging MS and NMOSD	Yaou Liu (China)	
11:00-11:15	15 mins	Q&A		
11:15-11:35		**Closing and Award Ceremony**		
11:15-11.30	15 mins	Poster Award ceremony	Noriko Isobe (Japan)	
11:30-11.35	5 mins	Closing Remarks by the Vice-President	Ho Jin Kim (Korea)	

SOLIRIS
(eculizumab)
300 mg/30 mL concentrate for solution for infusion

THE PROSPECT OF MORE RELAPSE-FREE DAYS

for adult NMOSD patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing course of the disease[1]

Soliris (Eculizumab) Abbreviated Prescribing Information (API)
Soliris (Eculizumab) concentrate for solution for infusion. **Soliris is indicated of adults for the treatment of Neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing course of the disease.** Initial phase: 900 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every week for the first 4 weeks. Maintenance phase: 1,200 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion for the fifth week, followed by 1,200 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every 14 ± 2 days. Soliris has not been studied in paediatric patients with NMOSD. Contraindications: Hypersensitivity to eculizumab, murine proteins or to any of the excipients listed in SmPC. Special warnings: Meningococcal Infection. To reduce the risk of infection, all patients must be vaccinated at least 2 weeks prior to receiving Soliris unless the risk of delaying Soliris therapy outweighs the risks of developing a meningococcal infection. Vaccines against serogroups A, C, Y, W 135 are recommended in preventing the commonly pathogenic meningococcal serogroups. Vaccine against serogroup B where available is also recommended. Undesirable effects: The most common adverse reaction was headache, and the most serious adverse reaction was meningococcal infection. Shelf life: After dilution, the medicinal product should be used immediately. However, chemical and physical stability has been demonstrated for 24 hours at 2°C – 8°C. Date of Revision: October 2024
This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Please report any adverse reactions via your national reporting systems. Adverse events can be also reported to AstraZeneca Thailand by email at medinfo.th@astrazeneca.com

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1. Full Soliris SmPC: Soliris (Eculizumab) summary of product characteristics. AstraZeneca (Thailand) 2024.

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เป็นยาใหม่ใช้เฉพาะสถานพยาบาล
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ใบอนุญาตโฆษณาเลขที่ ฆศ. 2-3420/2567

SOLIRIS® SmPC (English)

AstraZeneca

TH-20952 Exp Oct 2026

PACTRIMS-ECTRIMS JOINT TEACHING COURSE

SESSION 1: Diagnosis and Treatment of MS

TL1: Diagnosis of MS - Update on the McDonald criteria

Waqar Rashid, MBBS, Bsc, MRCP(UK), PhD
Consultant Neurologist St George's University Hospitals NHS Foundation Trust, London and Honorary Senior Clinical Lecturer, Brighton and Sussex Medical School, University of Sussex.
Multiple Sclerosis Clinical Lead at St George's Hospital
Consultant Neurologist since 2008 with research and clinical sub-specialist interest in Multiple Sclerosis and related neuroinflammatory disorders.

The diagnosis of multiple sclerosis (MS) continues to evolve with advances in technology and increasing recognition of the benefits of earlier diagnosis and treatment to achieve improved longer term clinical outcomes.
MS remains a clinical diagnosis but the increased sensitivity of Magnetic Resonance Imaging (MRI) in demonstrating inflammatory activity is well established as a diagnostic aid without compromising on accuracy.
The previous McDonald criteria in 2017 simplified the imaging requirements to demonstrate dissemination in space and incorporated the finding of unmatched oligoclonal bands in spinal fluid testing to confirm dissemination in time.
In my talk I will discuss the recent update of the McDonald criteria in 2024 and looks at the potential of newer MRI analytical techniques such as the Central Vein Sign (CVS) and the value of optic nerve involvement as well. In addition, I will outline the latest evidence on Radiological Isolated Syndromes (RIS) and what additional investigation changes are required to confirm a diagnosis of MS in this group of patients. The role of other potential biomarkers will be discussed as the McDonald criteria continue to evolve to facilitate an earlier but accurate clinical diagnosis.

TL2: How to treat MS - including discontinuation/de-escalation

Vincent Van Pesch, MD, PhD
Associate Chief of Neurology Department, Cliniques Universitaires Saint-Luc,
UCLouvain University, Brussels, Belgium

Multiple Sclerosis (MS) is increasingly recognized as a continuum rather than a disease with distinct phases, driven by both inflammatory and neurodegenerative processes. Current treatment strategies are centered around disease-modifying therapies (DMTs), which aim to reduce relapse rates, prevent new lesion formation, and slow disability progression.

Treating MS throughout the lifecycle of the disease requires an integrated and evolving approach, tailored to the changing needs of patients, such as pregnancy planning. Early intervention with high-efficacy DMTs in well selected patients is critical. Optimizing MS treatment involves not only selecting the appropriate therapies early in the disease course but also considering de-escalation strategies as patients age. As the disease evolves, the balance between treatment efficacy and long-term safety becomes increasingly important, particularly in older patients who may be at higher risk for adverse effects from high-efficacy DMTs. Discontinuing DMT or de-escalation, defined as the process of

transitioning from highly potent immunosuppressive therapies to treatments with a more favourable safety profile, can be a key strategy in long-term MS management.

Finally, MS care includes comprehensive care extending beyond pharmacological intervention. Addressing fatigue, mobility issues, and quality of life is essential for optimal management of the disease, in a multidisciplinary and personalized fashion.

SESSION 2: Special Considerations in MS and Optic Neuritis Update

TL3: Challenges of MS in childhood and adolescence

Cheryl Hemingway, MBChB (UCT), BA. (Hons) (Oxon), MRCP (UK) FRCPCH (UK), FCPaed (SA), M.Med (UCT), PhD (UCL)
Consultant Neurologist, GOSH
Hon Ass Professor Institute of Child Health, University College London
Consultant Paediatric Neurologist at Great Ormond Street Hospital (GOSH)

MS is the commonest underlying cause in **adult** patients presenting with optic neuritis and CNS demyelination. In contrast, in paediatrics more than 70% of acute demyelination is not due to MS and presentations can look quite different from adult onset. In particular, the antibody (Ab) driven disorders such as Myelin Oligodendrocyte Glycoprotein Ab (MOG-Ab) and Aquaporin 4 Ab (AQP4-Ab), are important to consider. Accurate diagnosis and an in-depth understanding of the important differentials is crucial, as there can be significant overlap in many of the presenting features. During the 35-minute lecture, I will give a brief update highlighting the main differences seen in paediatric and adult onset MS and then through the use of clinical vignettes, I will explore the spectrum of presentations in young people which can mimic MS demyelination.

TL4: Approach to Optic Neuritis

Shweta Singhal
Senior Consultant, Department of Neuro Ophthalmology, Singapore National Eye Centre(SNEC)
Assistant Professor, Duke-NUS Medical School Eye Academic Clinical Program
Clinician-Scientist, Singapore Eye Research Institute (SERI)
Clinical Lecturer, NUS Yong Loo Lin School of Medicine

Over the last decade, it has been established that multiple sclerosis (MS) related optic neuritis is less prevalent in the Asia Pacific region compared to the west. With the increasing availability of Aquaporin 4 (NMO) and Myelin Oligodendrocyte Glycoprotein (MOG) antibody tests, our understanding of these entities in optic neuritis has also improved. Nevertheless, optic neuritis remains a common first presentation in patients with MS. This talk will review the clinical presentation, disease course, treatment response and overall prognosis of optic neuritis associated with MS as well as the most prevalent non-MS optic neuritis presentations. The aim of this lecture is to provide the managing physician with the diagnostic framework to identify and appropriately manage the more sinister and poor prognosis variants of optic neuritis to prevent irreversible visual loss in these patients

TL5: MS Nursing Lecture: Vascular Co-Morbidities in MS

Meaghan Osborne
Neurology and Stroke Nurse Practitioner, Royal Brisbane and Women's Hospital

Managing comorbidities and maintaining brain health in people living with Multiple Sclerosis (MS) remains an important component of holistic care. Multiple studies have indicated that people living with MS have an increased risk of cardiovascular disease, peripheral vascular disease, cerebrovascular disease, diabetes, hyperlipidaemia, obesity, diabetes, smoking and hypertension. These comorbidities significantly impact the overall health and vitality of an individual leading to increase morbidity with higher Expanded Disability Status Scale (EDSS), lower quality of life and higher relapse rate. Preserving brain health, maintaining function through medical management, lifestyle modification and person centred care is an integral role within the MS nurse practitioner clinic to positively impact the quality of life of those living with MS.

SESSION 3: MS Immunology, Pathology and Biomarkers

TL6: Pathology of MS

Richard Reynolds, BSc, PhD
Professor of Cellular Neurobiology, Faculty of Medicine, Division of Brain Sciences, Imperial College London, UK

The pathology of progressive MS is classically characterised by multiple foci of perivenular inflammation in the white matter (WM) accompanied by primary demyelination. Axon transection can be observed in active inflammatory lesions, but there is relative sparing of axons in the majority. Demyelination is also present in the cerebral cortical and deep grey matter (GM), often more extensive than in the WM. Lymphocytes are only present in small numbers in progressive MS brains, predominantly restricted to the WM perivascular spaces. T and B-cells are rare in the GM parenchyma and perivascular spaces, although substantial numbers are found in the overlying leptomeninges of a significant proportion of cases, often in tertiary lymphoid-like aggregates. Many diffuse pathological changes are present in the normal appearing WM and GM, including axon damage/loss, microglial activation, node of Ranvier abnormalities and neuronal and synaptic loss. Quantitative analysis of pathological features and clinical outcomes in a large post-mortem cohort indicates that, whereas the degree of demyelination correlates only weakly with measures of progression, neuronal loss in the thalamus and pons are strongly correlated with disease duration and time to wheelchair use, suggesting that neurodegeneration is driving the accumulation of disability in progressive MS.

TL7: Immunology of MS

Assoc Prof Sean Riminton, MBChB (Dist, Otago) PhD (Sydney) FRACP FRCPA
Head of Department of Immunology and Cofounder of the Neuroimmunology Service at Concord Hospital in Sydney

This teaching session will review major advances in the immunology of MS in a manner that allows the generation of hypotheses about unknown mechanisms of disease and the selection of individually targeted therapies for our patients. We will look at the immunogenomics of patient susceptibility, immune surveillance of the brain, the nature, timing and location of CNS lesions, the meaning of oligoclonal bands, the EBV story, putative roles of immune cell subsets, the search for target autoantigens, and what can be learnt from the therapeutics that have succeeded in clinical practice. We will discuss how patients with a new diagnosis are confronted with a career of future immune interventions, and how the integrity of immunity can be managed for safer as well as efficacious outcomes.

TL8: MS Biomarkers - including newer MRI techniques and the role of neurofilaments

Martina Absinta, MD, PhD
Associate Professor of Neurology at Humanitas University in Milan

In this talk, we will explore the latest advancements in biomarkers for multiple sclerosis (MS), focusing on both i maging and molecular markers. As our understanding of MS deepens, the role of biomarkers in diagnosing, monitoring, and predicting disease progression has become increasingly vital. We will delve into innovative imaging techniques that enhance the detection and characterization of MS lesions, providing more precise insights into disease activity and progression. Special emphasis will be placed on the detection of chronic active/ smoldering lesions, which are now recognized as key contributors to disease progression in MS, using both MRI and/or PET approaches.

A significant portion of the discussion will center on fluid biomarkers, especially neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) levels, which have emerged as promising biomarkers for MS. Overall, this presentation will underscore the importance of combining imaging and molecular biomarkers to advance our understanding of MS and improve patient care. By leveraging these tools, we can move closer to a future where MS management is more predictive, personalized, and effective.

SESSION 4: NMOSD and MOGAD

TL9: Diagnosis and Treatment of NMOSD

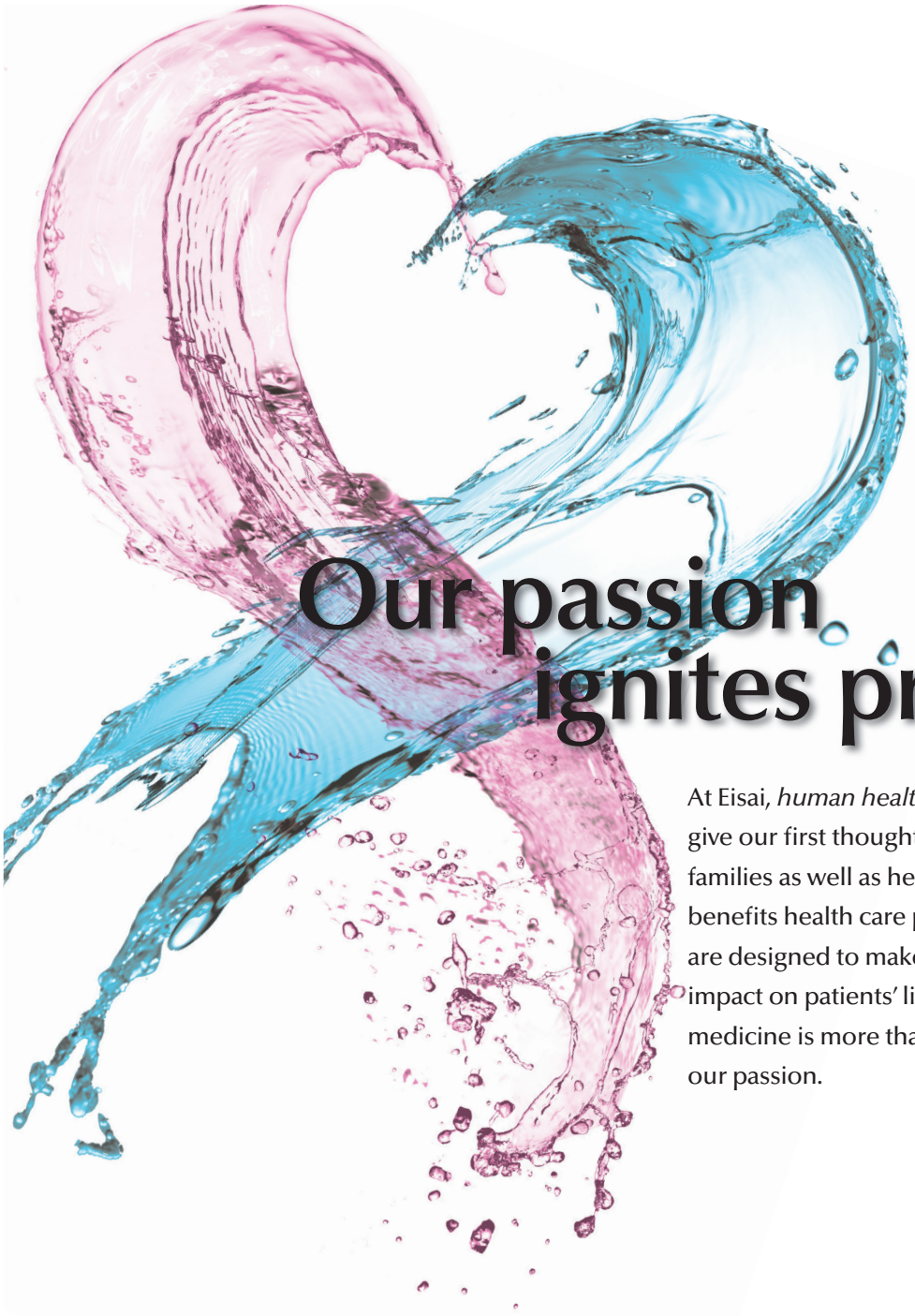
Jin Nakahara, MD, PhD
Professor and Chair of the Department of Neurology at Keio University School of Medicine
Department Head of the Department of Neurology at Keio University Hospital
Director of Keio University Hospital Stroke Center and Parkinson's Disease Center
Director of iPS Cell Research Center for Intractable NeurologicalDisorders at Keio University (KiND)
Visiting Professor of Kanazawa
University Graduate School of Medical Sciences

The pathogenic autoantibodies against aquaporin 4 (AQP4) were discovered in 2005 and became a clinically validated serum biomarker to distinguish neuromyelitis optica (NMO) from multiple sclerosis. In 2015, the International Panel for NMO Diagnosis (IPND) published the latest international consensus diagnostic criteria for NMO-spectrum disorders (NMOSD). A series of basic and clinical research revealed the role of anti-AQP4 antibodies in the pathophysiology of NMOSD, along with possible molecular targets for the therapeutic intervention. As a result, eculizumab (anti-complement C5 antibodies), the first biologic with firm evidence in NMOSD, was approved in 2019, followed by satralizumab (anti-interleukin-6 receptor antibodies) and inebilizumab (anti-CD19 antibodies) in 2020, and ravulizumab (anti-complement C5 antibodies) in 2023. The significant efficacy of these biologics in the NMOSD relapse prevention ultimately changed the prognosis and quality-of-lives of the patients, which might expose further unmet needs to light in the future. In this lecture, diagnosis, pathophysiology, and treatment of AQP4-NMOSD will be reviewed and discussed.

TL:10 Diagnosis and Treatment of MOGAD

Ichiro Nakashima, MD, PhD
Professor of Neurology at Tohoku Medical and Pharmaceutical University
President of the Japanese Society of Neuroimmunology
Board-Certified Member of the Japanese Society of Neurology and the Japanese Society of Internal Medicine
Councillor of the Japanese Society of Neurology, and the Japanese Society of Neuro Therapeutics

In recent years, myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), characterized by the presence of antibodies against myelin oligodendrocyte glycoprotein (MOG), has been recognized as a new demyelinating disease. In 2023, the International Panel on MOGAD established diagnostic criteria for the disease. Additionally, the results of a nationwide epidemiological survey on MOGAD in Japan were published in the same year. According to the survey in Japan, the estimated number of patients is 1,695 (range: 1,483-1,907), with an estimated crude prevalence rate of 1.34 (range: 1.18-1.51) per 100,000 people and an estimated crude incidence rate of 0.39 (range: 0.32-0.44) per 100,000 people per year. In pediatric cases, acute disseminated encephalomyelitis was common at onset, while in adult cases, encephalitis, brainstem encephalitis, and myelitis were more common. The response to immunotherapy, including corticosteroids, was favourable, consistent with reports from other countries, suggesting no significant regional or racial differences in MOGAD



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INVITED LECTURES

PLENARY 1: Updated pathophysiology of CNS demyelination

L1. Correlation of neuropathology with MRI

Martina Absinta, MD, PhD
Associate Professor of Neurology at Humanitas University in Milan

The pathological mechanisms driving clinical progression in multiple sclerosis (MS) remain incompletely understood and are therefore not fully addressed by current therapies. Recent studies have emphasized the significance of compartmentalized smoldering inflammation, particularly in chronic active or smoldering lesions, as a key factor in persistent clinical progression.
Given that MRI-neuropathological correlations are essential for advancing our understanding of this disease and developing personalized medicine approaches, this presentation will explore imaging techniques and provide a detailed correlative analysis of the neuropathology of MS lesion evolution, including chronic active lesions, utilizing multiplex immunostaining, single-cell analysis, and spatial transcriptomics. Special emphasis will be placed on the different microglia phenotypes present within chronic active/smoldering lesions. Additionally, recent advancements in imaging techniques for repair and remyelination will also be discussed.

L2. Pathomechanisms of NMOSD

Norio Chihara
Project Associate Professor of Neurology at Kobe University Hospital

Neuromyelitis optica spectrum disorder (NMOSD) is a relapsing inflammatory disease that often mimics multiple sclerosis (MS) due to its clinical presentation of optic neuritis and myelitis. Two decades of studies have shown that autoantibodies to the water channel protein aquaporin 4 (AQP4) on astrocytes are detected in a core group of patients. These autoantibodies are central to the inflammatory pathology of the disease, which involves proinflammatory cytokines, chemokines, and various immune cells. Anti-AQP4 antibody-positive NMOSD is fundamentally different from MS, particularly in its responsiveness to therapy and the neuropathology associated with astrocyte destruction. Advances in understanding the immunological mechanisms of NMOSD have led to the identification of therapeutic targets, such as the complement pathway and interleukin-6 (IL-6) receptor signalling. Randomized controlled trials have demonstrated the exceptional efficacy of therapies targeting complement C5, IL-6 receptors, and B cells in preventing relapses in patients with anti-AQP4 antibodies, although no such effects were found in anti-AQP4 antibody negative patients. These results suggest that anti-AQP4 antibody is a biomarker that predicts the efficacy of therapies and may guide the development of “personalized medicine” approaches tailored to individual patients.

L3. Meningeal inflammation as a driver of cortical pathology in Multiple Sclerosis

Richard Reynolds, BSc, PhD
Professor of Cellular Neurobiology, Faculty of Medicine, Division of Brain Sciences, Imperial College London, UK

Neuropathological studies of cortical pathology in progressive MS have identified a relationship between leptomeningeal immune cell infiltrates in the deeper cortical sulci and subpial demyelination of the grey matter. An increasing degree

and lymphoid-like organisation of meningeal infiltrates and extent of cortical demyelination are linked with increasing disease severity. Increased meningeal inflammation also correlates with increased loss of cortical neurons, independent of the presence of subpial demyelination. Analysis of diagnostic and post-mortem CSF demonstrated a link between a proinflammatory CSF milieu (levels of TNF, IFN-gamma and CXCL13), and the presence of meningeal inflammation and cortical demyelination. To test the hypothesis that proinflammatory molecules diffusing from the meninges into the underlying cortex can produce MS-like pathology, we induced chronic meningeal expression of combinations of TNF, LT-alpha and IFN-gamma in the rat subarachnoid space. This gave rise to rapid immune cell infiltration into the meninges and the development of lymphoid-like tissues, followed by accumulating sub-pial demyelination and neuronal loss. Subpial demyelination was dependent on the presence of a humoral anti-MOG immune response, whereas neurodegeneration was independent, as in the MS brain. These animal studies have demonstrated that chronic pro-inflammatory cytokine expression in the meninges alone can give rise to underlying cortical pathology.

PLENARY 2: Pediatric CNS inflammatory diseases

L4. Pediatric MS/NMOSD

Cheryl Hemingway, MBChB (UCT), BA. (Hons) (Oxon), MRCP (UK) FRCPCH (UK), FCPaed (SA), M.Med (UCT), PhD (UCL)
Consultant Neurologist, GOSH
Hon Ass Professor Institute of Child Health, University College London
Consultant Paediatric Neurologist at Great Ormond Street Hospital (GOSH)

Over recent years there have been significant advances in our understanding of the pathogenesis of Paediatric Multiple Sclerosis (MS) together with a growing recognition of the diverse range of disorders which can present as non-MS white matter lesions involving the brain, eye and spine in children and young people. Some of these, in particular the antibody (Ab) driven disorders such as Myelin Oligodendrocyte Glycoprotein Ab (MOG-Ab) and Aquaporin 4 Ab (AQP4-Ab), can have a range of different presentations and relapse and remit. Importantly though, best treatment options differ making an accurate diagnosis essential. There are also a range of other mimics of acute demyelinating syndromes which may appear steroid responsive, but which actually require a more targeted treatment. During the 25 minute lecture I will explore a selection of the spectrum of presentations in young people with CNS inflammatory disease.

L5. Prevalence and Diagnosis of Pediatric MS/NMOSD in Taiwan

Wang-Tso Lee, MD, PhD, EMBA
Superintendent, National Taiwan University Children's Hospital, Taipei, Taiwan
Chairman and Professor, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
Attending Physician, Department of Pediatric Neurology, National Taiwan University Children's Hospital, Taipei, Taiwan
Professor, School of Medicine and Graduate Institute of Brain and Mind Sciences, College of Medicine, National Taiwan University, Taipei, Taiwan
Executive Board, International Child Neurology Association
National Delegate of TCNS in Asian and Oceanian Child Neurology Association

The long-term outcome of optic neuritis (ON) is heterogeneous. Identification of determinants of natural history of ON would be helpful in therapeutic planning and prognostication, especially in Asia where those patients are less reported. Whether comorbidities and treatment in ON patients are associated with differential risks of subsequent development of multiple sclerosis (MS) or neuromyelitis optica spectrum disorder (NMOSD) is less investigated in

Taiwan. In our study in the past, ON could be the sentinel event linking several peripheral autoimmune comorbidities to distinct forms of central nervous system demyelination. By the way, the occurrence of combined central and peripheral demyelination (CCPD) is rare, and data are limited to small case, mainly in adults. However, it can also develop in children. The relationship between CCPD, MS, and NMOSD remains to be investigated, and is an emergent interesting topic to investigate. The long-term outcome is also remained to be clarified

PLENARY 3: Early diagnosis of MS and related disorders: Current and emerging criteria

L6. RIS and its revised criteria

Darin T. Okuda, M.D., M.Sc., F.A.A.N, F.A.N.A.

The original criteria for radiologically isolated syndrome (RIS) were first released in 2009, describing incidental MRI features highly suggestive of multiple sclerosis (MS) within healthy individuals lacking existing or prior clinical symptoms typical of central nervous system (CNS) demyelination. Key scientific advancements within the field of neuroimmunology have occurred since, resulting in enhanced knowledge related to techniques that improve upon the specificity of observed MRI anomalies along with factors that stratify risk for clinical evolution to a first acute or progressive symptom attributable to autoimmune injury to myelin and nerve fibers. In 2023, the revised diagnostic criteria for RIS were published, incorporating advances in scientific knowledge and creating harmonization with existing criteria for MS to enhance diagnostic accuracy and precision. More recently, the field has shifted focus towards even earlier disease identification, with anticipated revisions to the newly released criteria for MS expected to include asymptomatic individuals – an aspect filled both with significant opportunities and challenges. In this presentation, the original and updated criteria for RIS will be reviewed coupled with the projected impact of changes to the MS diagnostic criteria on those currently affected, those not yet diagnosed, and future research.

L7. Importance of early diagnosis of MS and predict early non-disabling relapses

Anneke Van Der Walt, MBChB, PhD, FRACP (Neur)

Early diagnosis of multiple sclerosis (MS) is crucial in improving patient outcomes and slowing disease progression. Prompt detection allows for the timely initiation of disease-modifying therapies (DMTs), which can reduce the frequency of relapses, delay disability, and improve the overall quality of life of people living with MS.
Identifying predictors of disability in MS is equally important for personalized treatment planning and long-term management. Key predictors include the patient's age at diagnosis, the number and severity of early relapses, the presence of certain biomarkers (such as oligoclonal bands in cerebrospinal fluid, s-neurofilament light chain), and magnetic resonance imaging (MRI) findings, particularly the presence of new or enlarging lesions. Additionally, lifestyle factors, such as smoking and obesity, also contribute to the trajectory of disability.
In this talk, we will review early diagnosis of MS and the efficacy of early and effective intervention. An overview of clinical and paraclinical factors associated with worse outcomes will be presented.

L8. Diagnosis of MOGAD: Tips for accurate diagnosis

Jae-Won Hyun, MD, PhD
Neurologist, Assistant Professor, National Cancer Center

Antibodies against myelin oligodendrocyte glycoprotein (MOG) are found in patients with acquired CNS demyelinating syndromes that are distinct from AQP4-IgG positive neuromyelitis optica spectrum disorder and multiple sclerosis. Recent refinement of MOG-IgG testing has led to the proposal of the International MOGAD Panel diagnostic criteria. The

presence of MOG-IgG, determined using a reliable assay, is a core criterion. Also, a thorough understanding of MOGAD characteristics allows for appropriate selection of candidates for MOG-IgG testing and accurate interpretation of the results. Both these components should be considered to ensure the accurate diagnosis of MOGAD. This talk reviews the clinical and radiological features typical of MOGAD to foster a comprehensive understanding of its characteristics and provides an overview of MOG-IgG testing.

PLENARY 4: Treatment associated risks in MS: Regional strategies for mitigation

L9. Treatment strategy for PML in daily practice

Jin Nakahara, MD, PhD
Professor and Chair of the Department of Neurology at Keio University School of Medicine
Department Head of the Department of Neurology at Keio University Hospital
Director of Keio University Hospital Stroke Center and Parkinson's Disease Center
Director of iPS Cell Research Center for Intractable NeurologicalDisorders at Keio University (KiND)
Visiting Professor of Kanazawa
University Graduate School of Medical Sciences

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system often associated with severe neurological sequelae, thought to occur almost exclusively in immunocompromised patients until an MS patient under natalizumab treatment first developed PML in 2005. Nowadays it is well recognized that various disease-modifying drugs, particularly of high efficacy, including fingolimod and anti-CD20 antibodies, could also cause PML in otherwise immunocompetent MS patients. Unfortunately, however, specific treatment for PML is lacking and the prognosis is largely dependent on the restoration of immune system by timely termination of causative agents as well as the management of immune reconstitution inflammatory syndrome (IRIS). In this lecture, the current PML management strategies will be reviewed based on the actual case from the lecturer's institute.

L10. Risk mitigation in multiple sclerosis immunotherapy - the Indian perspective

Sruthi S. Nair, MBBS, MD (General Medicine), DM (Neurology), FRCP (Edin.)
Additional Professor, Department of Neurology
In-Charge Neuromuscular and Multiple Sclerosis Divisions
Sree Chitra Tirunal Institute for Medical Sciences and Technology

The face of multiple sclerosis (MS) therapy in India has radically transformed in the recent years. Biosimilar disease modifying therapies (DMTs) and highly active agents are used extensively. A sizeable proportion of patients receive 'off-label', nonetheless efficacious, broad-spectrum agents including azathioprine, mycophenolate mofetil and rituximab. Safety protocols for newer DMTs have not kept pace with their therapeutic application. India has unique infection-related challenges due to high endemicity of tuberculosis, high risk of exposure to varicella zoster and other tropical microbes and low compliance with adult vaccination strategies. Natalizumab and Alemtuzumab are financially inaccessible to many, but have had a safe record in India, particularly the former with no reported cases of progressive multifocal leukoencephalopathy. Rituximab which is the most widely used highly active DMT, was associated with increased hospitalization during the COVID-19 pandemic as with increased risk of bacterial infections. Risk of oncogenesis is poorly quantified.

Adverse effects of DMTs can be minimized by appropriate patient selection, diligent clinical and laboratory monitoring and dosage adjustments. Mitigation strategies specific to the region focus on tuberculosis screening and vaccination tailored to the climate, pollution and local pathogens. More longitudinal and registry-based data from the region is required to inform decisions.

L11. Treatment strategies for MS/NMOSD in Thailand

Metha Apiwattanakul, MD
Head of the Neuroimmunology Unit, Department of Neurology, Neurological Institute of Thailand
Deputy Secretary General of the Neurological Society of Thailand

Epidemiological studies in Thailand show that neuromyelitis optica spectrum disorder (NMOSD) is more prevalent than multiple sclerosis (MS). While both conditions share clinical features like optic neuritis and myelitis, they differ significantly in imaging and biomarkers. NMOSD is often associated with longitudinally extensive transverse myelitis and long-segment optic nerve or chiasmatic involvement, unlike MS. AQP4-IgG is a key biomarker distinguishing NMOSD from MS.
In resource-limited settings like Thailand, access to disease-modifying therapies (DMTs) for MS is limited due to high costs, despite drug availability. On-label DMTs are not included in the National Essential Medicines List, leaving off-label options like azathioprine, cyclophosphamide, and rituximab as primary treatments. In non-aggressive MS, azathioprine is often the first choice, while aggressive cases or suboptimal responses prompt escalation to rituximab or cyclophosphamide. Rituximab is now favored due to its better efficacy and side-effect profile.
For NMOSD, first-line therapy includes steroids and steroid-sparing agents like azathioprine or mycophenolate. Rituximab is used for refractory cases, though newer drugs like eculizumab, inebilizumab, and satralizumab remain inaccessible.

PLENARY 5: Artificial Intelligence (AI) in neurological diagnosis

L12. Overview of machine learning approaches

Wilson Goh
Assistant Professor of Biomedical Informatics, Lee Kong Chian School of Medicine, School of Biological Sciences
Senior Lecturer (Honorary), Imperial College London
Chief Data Scientist, NTU Center of AI in Medicine
Academic Lead, Data Science Research Research Programme
Co-Director, Centre for Biomedical Informatics
Group Leader, Bio-Data Science and Education Laboratory

The healthcare landscape is rapidly evolving with the rise of Digital Health and AI, poised to be transformative forces. However, these advancements come with a complex set of challenges, including stakeholder engagement, data acquisition, and the development of multi-modal models. Understanding the needs and perspectives of both users and recipients is crucial to optimizing outcomes in digital health and AI initiatives. It's equally important to critically evaluate the significance of model outputs. In this presentation, I will share recent research on clinician trust and adoption attitudes, along with key lessons learned in developing AI models for diagnosis, prognosis, and research interventions. Lastly, I will explore how these advancements may impact MS management in the near future and the implications for both patients and doctors.

L13. Future with AI-based MRI monitoring in MS

Chenyu (Tim) Wang, B.Eng., M. Eng., PhD
MS Australia Fellow, Senior Research Fellow, University of Sydney

Modern management of Multiple Sclerosis (MS) targets No Evidence of Disease Activity (NEDA). While MRI remains the

primary tool for neurologists to monitor clinically silent MS disease activity and determine when to escalate treatment, standard radiology reports are often qualitative and may lack sufficient sensitivity to subtle yet important pathological changes in the brain. By leveraging recent advancements in Artificial Intelligence and imaging informatics, there is significant potential to address this challenge and accelerate the delivery of precision care in MS through quantitative imaging analysis.
In this session, we will share the latest MS AI research and development from the MS research group at the University of Sydney's Brain and Mind Centre, focusing on various approaches to improving the productivity and accuracy of MS disease activity detection via MRI. We will also discuss how these advancements can enhance the quality of care for MS patients by interpreting quantitative imaging outcomes within a clinical context and explore the future potential of AI in MS clinical management.

L14. AI for imaging MS and NMOSD

Yaou Liu, MD, PhD
Director of Department of Radiology, Beijing Tiantan Hospital, Capital Medical University
China National Neurological Disease Center
Professor in Neuroradiology

Artificial intelligence (AI) has emerged as a transformative tool in the imaging of neurological disorders, particularly Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD). This presentation will focus on the application of AI techniques, such as machine learning and deep learning, to enhance the accuracy and efficiency of diagnosing and monitoring these diseases.
AI significantly improves the interpretation of MRI scans, which are crucial in distinguishing MS from NMOSD by detecting subtle differences in brain and spinal cord lesions. Advanced algorithms assist in lesion segmentation, classification, and quantification, thereby reducing radiological assessment time and minimizing diagnostic errors. Furthermore, AI models analyze large datasets to predict disease progression and patient outcomes, aiding in the development of personalized treatment strategies.
While the primary focus is on AI, the presentation will also touch upon the role of large language models (LLMs) as part of the broader AI landscape. LLMs contribute by enhancing data processing and interpretation, complementing the deep learning algorithms used in imaging.
This session will highlight recent advancements, challenges, and future directions in integrating AI for imaging MS and NMOSD, emphasizing its potential to revolutionize patient care through improved diagnostic precision and individualized therapeutic approaches.

ORDINARY SUBMISSION

PLENARY ORAL PRESENTATION - 1

Advances in Technology in Diagnosis and Care

O-1

Serum Proteomics Distinguish Subtypes of NMO Spectrum Disorder and MOG Antibody-Associated Disease and Highlight Effects of B-Cell Depletion

Yang Mao-Draayer[1]
[1]*Oklahoma Medical Research Foundation*

Background: AQP4 antibody-positive NMOSD (AQP4-NMOSD), MOG antibody-associated disease (MOGAD), and seronegative NMOSD (SN-NMOSD) are neuroautoimmune conditions that have overlapping clinical manifestations. Yet, important differences exist in these diseases, particularly in B-cell depletion (BCD) efficacy.
Objective: Our study aims to clarify biological pathways distinguishing these diseases beyond autoantibodies and investigate variable BCD effects through proteomic comparisons.
Methods: In a retrospective study, 1,463 serum proteins were measured in 53 AQP4-NMOSD, 25 MOGAD, 18 SN-NMOSD, and 49 healthy individuals. To identify disease subtype-associated signatures, we examined serum proteins in patients without anti-CD20 B-cell depletion (NoBCD). We then assessed the effect of BCD treatment within each subtype by comparing proteins between BCD-treated and NoBCD-treated patients.
Results: In NoBCD-treated patients, serum profiles distinguished the 3 diseases. AQP4-NMOSD showed elevated type I interferon-induced chemokines (CXCL9 and CXCL10) and TFH chemokine (CXCL13). MOGAD exhibited increased cytotoxic T-cell proteases (granzyme B and granzyme H), while SN-NMOSD displayed elevated Wnt inhibitory factor 1, a marker for nerve injury. Across all subtypes, BCD-treated patients showed reduction of B-cell–associated proteins. In AQP4-NMOSD, BCD led to a decrease in several inflammatory pathways, including IL-17 signalling, cytokine storm, and macrophage activation. By contrast, BCD elevated these pathways in patients with MOGAD. BCD had no effect on these pathways in SN-NMOSD.
Conclusion: Proteomic profiles show unique biological pathways that distinguish AQP4-NMOSD, MOGAD, or SN-NMOSD. Furthermore, BCD uniquely affects inflammatory pathways in each disease type.
Disclosures: Y. Mao-Draayer has consulted for and/or received grant support from Acorda, Bayer Pharmaceutical, Biogen Idec, EMD Serono, Genzyme, Novartis, Horizon/Amgen, Questor, Genentech, and Teva Neuroscience.

O-2

Diagnostic Delay In MOGAD: Prevalence And Impact On Relapse In A Korean Nationwide Cohort

Seung Ho Choo[1], Hyunjin Ju[2], Ki Hoon Kim[3], Ho Jin Kim[3], Su-Hyun Kim[3], Ju-Hong Min[4]
[1]*Samsung Medical Center*
[2]*Department of Neurology, Soonchunhyang University Seoul Hospital*
[3]*Department of Neurology, Research Institute and Hospital of National Cancer Center*

[4]*Department of Neurology, Samsung Medical Center*
Background: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a CNS demyelinating disease characterized by presence of MOG-antibody. Therefore, MOG-IgG antibody testing is crucial for diagnosing MOGAD and planning treatment. However, the proportion of diagnostic delay and its clinical impact in MOGAD patients remain unclear.
Objective: This study investigates prevalence and consequences of diagnostic delay (DD) in patients with MOGAD and changes after 2020, where MOG-IgG cell-based assays (CBA) become widespread in Korea.
Methods: We retrospectively collected adult MOGAD patients, who had positive MOG-IgG from 28 hospitals in a Korean nationwide MOGAD cohort. We defined diagnostic delay (DD) as >6months elapsing between the first onset and MOG-IgG testing. Clinical and MRI features, including age at onset, relapse rates, types of attacks, and treatment details, were compared. Correlations between diagnostic latency and annualized relapse rate (ARR), or final Expanded Disability Status Scale (EDSS) score were evaluated. A sensitivity analysis was conducted for patients diagnosed after 2020 (post-2020 cohort).
Results: Among 359 patients, 148 had DD (41.2%) and 211 had non-DD (58.8%). DD group showed younger age at onset, higher myelitis prevalence, and more frequent brainstem/cerebellar deficits, with less frequent optic disc edema and more frequent central cord lesions or H-signs. Patients with DD received less acute treatment at onset (77.2% vs. 86.3%) and used long-term immunosuppressants less frequently (26.0% vs. 51.0%), than those with non-DD. They also had a higher proportion of relapsing course (72.3% vs. 24.6%) and higher ARR (0.21 vs. 0.00), compared to patients with non-DD. Moreover, in a total cohort, diagnostic latency correlated with ARR (Spearman's rho = .386, P<.001) but not with final EDSS score (P=.404). Post-2020 analysis showed diminished differences between groups, with prevalence of DD dropping from 80.7% to 14%, but differences in proportion of relapsing course (64.5% vs. 20.2%), ARR (0.39 vs. 0.00), and acute treatments (64.5% vs. 85.2%) remained statistically significant.
Conclusion: We demonstrate that diagnostic delay could impact clinical outcomes in MOGAD patients, particularly associated with higher relapse rates and less timely initial treatment.
Disclosures: JH Min is funded by and has received research support from the National Research Foundation of Korea (MIST and KHIDI) and SMC Research and Development Grant. She has lectured, consulted and received honoraria from Bayer Healthcare, Merk, Biogen Idec, Sanofi, UCB, Samsung Bioepis, Mitsubishi Tanabe, Celltrion, Roche, Janssen, and AstraZeneca.
Conflict of Interest
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O-3

Peripapillary Vessel Density and Visual Outcomes After Unilateral Optic Neuritis: An Optical Coherence Tomography Angiography Study

Natthapon Rattanathamsakul[1], Deena A. Tajifirouz[2], Kevin D. Chodnicki[3], Sean J. Pittock[4], Eoin P. Flanagan[4], John J. Chen[5]
[1]*Department of Ophthalmology, Mayo Clinic, Rochester, MN; Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok Thailand*
[2]*Department of Ophthalmology, Mayo Clinic, Rochester, MN; Department of Neurology, Mayo Clinic, Rochester, MN*

[3]*Department of Ophthalmology, Mayo Clinic, Rochester, MN*
[4]*Department of Neurology, Mayo Clinic, Rochester, MN; Center for MS and Autoimmune Neurology, Mayo Clinic, Rochester, MN; Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN*
[5]*Department of Ophthalmology, Mayo Clinic, Rochester, MN; Department of Neurology, Mayo Clinic, Rochester, MN; Center for MS and Autoimmune Neurology, Mayo Clinic, Rochester, MN*
Background: Optical coherence tomography angiography (OCTA) has been introduced in the care of optic neuritis (ON), potentially serving as an early biomarker. The relationship between peripapillary vessel density (pVD) and visual outcome has been scarcely investigated.
Objective: To study the correlation between the pVD and the visual parameters.
Methods: Patients diagnosed with unilateral ON seen consecutively over 1 year at the Mayo Clinic were recruited. All underwent comprehensive neuro-ophthalmologic examination. Peripapillary retinal nerve fiber layer (pRNFL) and ganglion cell-inner plexiform layer (GCIPL) thickness were measured using spectral-domain OCT (Cirrus), while pVD was assessed using the Optovue OCTA device. Patients with an ON attack within 3 months of the OCTA or history of bilateral ON were excluded.
Results: Of all 30 patients, 56.7% were female, with a median age of 38.1 (interquartile range (IQR) of [30.2, 50.9]) years at the time of evaluation. Multiple sclerosis was the most common etiology (60%). The median time from the last ON attack to OCTA was 13.7 (IQR [7.0, 24.4]) months. The affected eyes exhibited reductions in RNFL and GCIPL thickness ($p<0.001$), and a decrease in pVD compared to the unaffected eyes ($p=0.008$). Furthermore, the affected eyes in patients achieving full visual recovery (visual acuity of 20/20 or better) demonstrated higher pVD than those without (60.0±4.5 vs. 52.1±6.3%, $p=0.001$). The correlation between deficits on visual field mean deviation (MD) and the pVD reduction was strong ($r=0.683$, $p<0.001$), while the degree of RNFL and GCIPL thinning did not show significant correlation with the change in MD ($p=0.382$ and 0.113, respectively).
Conclusion: pVD was found to be decreased in eyes affected by ON, with higher pVD observed in those achieving complete visual recovery. pVD demonstrated a strong correlation with visual fields suggesting OCTA may be a better biomarker of visual outcome than OCT.
Disclosures: All authors report no relevant financial relationships pertaining to this abstract.

Basic Science

O-4
Predicting Relapse of Neuromyelitis Optica by Complement Factors
Katsuichi Miyamoto[1], Norimitsu Inoue[2]
[1]*Wakayama Medical University/Neurology*
[2]*Wakayama Medical University/Molecular Genetics*
Background: Although complement activation is involved in the pathogenesis of neuromyelitis optica spectrum disorders (NMOSD) and antibodies against C5 have been used to prevent relapse, the detailed mechanism of action is unknown. Recently, we have shown that activation of the complement alternative pathway is important for disease activity in NMOSD.
Objective: In this report, we will discuss the relationship between these complement factors and NMOSD prognosis and predict the risk of NMOSD recurrence based on complement factor measurements.
Methods: Thirty-five patients with NNOSD (32 women and 3 men, mean age 52.0) whose sera were collected at relapse and subsequently followed up for 3 years without biologics were included. Ba, a marker of activation of the alternative pathway, CFH, a regulatory factor, and sC5b-9, a marker of activation

of terminal complement, were measured from individual stored sera. Cerebrospinal fluid test results (cell counts and proteins) and clinical information were collected retrospectively from medical charts. For healthy controls, the reference values for healthy subjects indicated by the Japanese Society for Complement Research were used. The study was approved by the ethics committee of the institution.
Results: The sC5b-9 and sC5b-9/CFH correlated with the number of recurrences after 1 year (r=0.586 and r=0.571). Comparing the group of patients who had a next relapse one year after relapse (14 patients) with the group of patients who did not (21 patients), there were no significant differences in single complement factors, but there were significant differences in Ba/CFH values (23.9 ± 47.3 with relapse and 5.3 ± 2.5 without relapse, p=0.05) and sC5b-9/CFH values (18.1 ± 38.8 with relapse and 1.7 ± 1.7±1.7, P-0.02). When examining the risk of recurrence within one year in individual cases, 72.2% relapsed if CFH was below the reference value, and 100% relapsed if Ba was above the reference value. On the other hand, 78.9% did not relapse when sC5b-9 was below the threshold, and 86.7% did not relapse when CFH was high.
Conclusion: The biomarkers we have demonstrated in this study are useful for selecting therapeutic agents for relapse prevention. The limitation of this study is the small number of cases. Further accumulation of cases is needed.
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, Novartis Pharmaceutical Corporation, UCB Japan Co. Ltd., Sanofi, Chugai Pharmaceutical Co. Ltd. and Japan Blood Products Organization and research support from Alexion Pharmaceuticals, Inc.

Neuropathology

O-5

Clinical characteristics and diagnosis delay in NMOSD: A retrospective study at University Medical Center Ho Chi Minh City.

Huong Dinh[1,21], Hieu Dinh[2]
[1]*Neurology Department, University Medical Center HCMC, Vietnam*
[2]*Neurology Department, University of Medicine and Pharmacy HCMC, Vietnam*
Background: Neuromyelitis optica spectrum disorder (NMOSD) is a severe inflammatory demyelinating disease of the central nervous system with many relapses. Attacks of NMOSD are often severe, with only minor recovery, and accompanied by long-term disability. However, data related to the clinical and treatment of NMOSD in Vietnam is limited.
Objective: The objective of our study was to describe the clinical characteristics and diagnosis delay of NMOSD.
Methods: This is a retrospective cross-sectional descriptive study on 74 NMOSD patients treated at Ho Chi Minh City University of Medicine and Pharmacy Hospital from January 2018 to October 2022. The patients were diagnosed according to the NMOSD diagnostic criteria published by the 2015 International Panel for Neuromyelitis Optica Spectrum Disorders diagnosis (IPND) criteria.
Results: Our study has a female: male ratio of 10:1. The age of onset is 37.5 years [30.2;46.8], minimum 15, maximum 78. 78.4% of patients had an attack before diagnosis of NMOSD. The three common initial diagnoses before the diagnosis of NMOSD are MS 20.7%, myelitis 31%, and optic neuritis 15.5%. Time from first clinical symptoms to diagnosis: 18 months [2;39]. Two common clinical manifestations of the

first attack are acute myelitis (60,8%) and optic neuritis (14,9%). 89.2% of patients had AQP4 seropositivity. 85.1% of patients received preventive treatment: AZA (58.7%), MMF (33.3%), and corticosteroid (7.9%). 20.6% of patients discontinued preventive treatment due to side effects, all of whom were treated with AZA. Side effect includes Leukopenia 21.6%, increased liver enzymes 10.8%, and leukopenia combined with increased liver enzymes 2.7%.
Conclusion: The time from first clinical symptoms to diagnosis NMOSD in Vietnam is delayed, which prevents patients from receiving preventive treatment. The majority of our patients previously had at least one attack before being diagnosed.

PLENARY ORAL PRESENTATION - 2
Disease modifying therapies

O-6
Immunomodulatory Glycolipid OCH Reduces Relapses In Multiple Sclerosis (Phase II Clinical Trial)
Ben Raveney[1], Tomoko Okamoto[2], Atsuko Kimura[1], Youwei Lin[2], Yukio Kimura[3], Noriko Sato[3], Yuko Shimizu[4], Yoichiro Nishida[4], Takanori Yokota[5], Masanori Taketsuna[6], Yu Okada[6], Takami Ishizuka[7], Harumasa Nakamura[7], Sachiko Miyake[8], Yuji Takahashi[2], Wakiro Sato[1], Takashi Yamamura[1]
[1]Deparment of Immunology, National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan
[2]Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan
[3]Department of Radiology, National Center Hospital, National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan
[4]Department of Neurology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan
[5]Department of Neurology and Neurological Science, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan
[6]Translational Research Center for Medical Innovation, Foundation for Biomedical Research and Innovation at Kobe, Hyogo, Japan
[7]Department of Clinical Research Support, Clinical Research & Education Promotion Division, National Center Hospital, NCNP, Tokyo, Japan
[8]Department of Immunology, Juntendo University Graduate School of Medicine, Tokyo, Japan
Background: In RRMS and SPMS, different types of pathogenic T cells and cytokines seem to be involved. Previously, we reported therapeutic effects of OCH, a NKT cell-targeting glycolipid, in a mouse model of MS, EAE. However, the effects of OCH on pathogenic T cells have not been investigated for years after the role of IL-17 and GM-CSF in EAE was recognized.
Objective: This translational research aims to investigate the effects of OCH-NCNP1 (OCH) on pathogenic Th cells in mice and assess the efficacy and safety of OCH in patients with relapsing MS (RRMS or SPMS) in a Phase II clinical trial.
Methods: Mouse studies: Oral OCH treatment was tested in animal models of MS – acute EAE model mimicking RRMS (MOG35-55-immunised C57BL/6 mice) and a new model of chronic late EAE (Raveney et al. 2015) that mimics SPMS regarding the dominance of pathogenic T helper cells expressing Eomes (Raveney et al., PNAS 2021). Effects of OCH on specific pathogenic Th cell function were measured by flow

cytometry in each model.
Human phase II trial: A randomised, placebo-controlled, double-blind study was conducted in 30 MS patients (placebo group, n=15; OCH group, n=15). Both RRMS (n=18) and SPMS (n=12) patients with a recent history of clinical relapse were included in this study. OCH (3.0 mg) or the placebo were orally administered weekly for 24 weeks. The primary outcomes were based on disease activity and new relapses based on changes in magnetic resonance imaging results. Secondary outcomes were clinical observations, safety profiles, and exploratory biomarkers. Biomarkers included hallmark features of pathogenic Th cell activity.
Results: Oral OCH treatment reduced clinical signs in the acute EAE model, which coincided with reductions in pathogenic Th17 cells and GM-CSF production by T cells. OCH also reduced disease in the late, chronic EAE model, with a reduction of pathogenic Eomes+ Th cells.
In the human trial, the safety profile was similar between OCH and placebo groups. During the 6-months treatment of relapsing MS (RRMS and relapsing SPMS), fewer lesions were observed in the OCH group with more cases with no evidence of disease activity (NEDA; 10/15 OCH, 5/15 placebo) and lower cumulative relapses (4 relapses OCH; 8 relapses placebo). A striking difference was noted between OCH- and placebo-treated SPMS patients in the NEDA proportion (NEDA with OCH 5/6 cases vs NEDA with placebo 0/6 cases; p=0.015). Increased IL-4-producing Th cells were observed in OCH group (p=0.010) with decreases in the pathogenic Th17 cell-linked cytokine GM-CSF (p=0.0056), particularly in OCH-treated SPMS patients.
Conclusion: OCH treatment modulated immune cell profiles similarly in MS and EAE, reducing pathogenic Th cells and decreasing disease. OCH appeared strikingly effective for preventing relapses in SPMS. OCH is a promising treatment for MS, particularly for SPMS.
Disclosures: The authors have received research funding and royalties from EA Pharma Co. Ltd concerning the use of OCH as a treatment for MS.

Epidemiology, Genetics, and Epigenetics

O-7
Clinical and treatment comparison of MOG-associated disease and AQP4 positive neuromyelitis optica spectrum disorder: A multicenter cohort study in Taiwan
Yu-Ning Huang[1], Chao-Wen Lin[2], Wen-Chin Weng[2], Hsueh-Wen Hsueh[2], Ta-Ching Chen[2], Jen-Jen Su[2], Chih-Chao Yang[2]
[1]*Shuang Ho Hospital, Ministry of Health and Welfare*
[2]*National Taiwan University Hospital*
Background: CNS demyelinating disorders are important disabling diseases. In Asian communities, NMOSD can represent around 50% of CNS demyelination, with the majority being associated with AQP4 Ab and MOG Ab. Detailed comparisons in Southeast Asian populations are less described. Herein, we present a multicentre cohort study on AQP4-positive NMOSD and MOGAD.
Objective: To compare clinical features and treatment responses in patients presenting with NMOSD, who tested positive for AQP4 antibody, and in patients with MOGAD.
Methods: Clinical and neuroimaging data from patients diagnosed with either AQP4-positive NMOSD or MOGAD between 1997 and 2024 were analyzed.
Results: 76 patients diagnosed with AQP4+ NMOSD and 26 with MOGAD were documented, with 265 recorded events (211 in AQP4+, 54 in MOGAD). The AQP4+ group exhibited a female predominance and is associated with other detectable autoantibodies. In contrast, the MOGAD cohort manifested two distinct

phenotypes: young-onset encephalitis and adult-onset optic neuritis. AQP4+ patients presented with a significantly lower incidence of bilateral optic neuritis compared to MOGAD (4.2% vs. 18.5%, p = 0.001), but higher rates of myelitis (50.3% vs. 5.6%, p < 0.001) and area postrema syndromes (9.0% vs. 0%, p = 0.022). The AQP4+ group demonstrated poorer outcomes in ambulatory functions. Regarding treatment responses, MOGAD patients were more frequently medication-free (61.5%, p < 0.001). Univariate Cox analysis indicated that double filtration plasmapheresis (DFPP) during the acute phase significantly reduced the risk of recurrence in AQP4+ patients (hazard ratio: 0.387, p = 0.015).
Conclusion: MOGAD and AQP4+ NMOSD exhibit distinct phenotypes and treatment responses, with heterogeneity within the MOGAD cohort. MOGAD has better outcomes and remission rates. In AQP4+ patients, the use of DFPP correlates with prolonged periods of remission.
Disclosures: None

Neuroimaging and Neurophysiology

O-8
Association Between Volumetric Magnetic Resonance Imaging, and Neuroperformance Measures in Patients with Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease
Tatchaporn Ongphichetmetha[1], Mengke Du[1], Moein Amin[1], Justin Abbatemarco[1], Jeffery Cohen[1], Daniel Ontaneda[1], Amy Kunchok[1], Kunio Nakamura[2], Stephen Jone[2]
[1]*Mellen Multiple Sclerosis Center, Cleveland Clinic Foundation*
[2]*Cleveland Clinic Department of Radiology*
Background: Brain volumes and spinal cord area are associated with disability in multiple sclerosis (MS). The association of brain and spinal cord volumes with disability in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is not well studied.
Objective: To examine MRI derived brain volume and spinal cord area between MOGAD and associations with neuroperformance measures.
Methods: Participants were identified from the Cleveland Clinic MOGAD registries. All met diagnostic criteria1 and were MOG-IgG+ by fixed cell-based assay. Standardized volumetric MRI, using a deep learning-based method, measured fractional volumes of whole brain, total grey matter, deep grey matter (caudate, putamen, hippocampus, thalamus), and T2-weighted and T1-weighted lesion volumes (T2LV, T1LV). An atlas-based segmentation technique was used to determine the upper cervical cord area (UCCA, C1-C2). Neuroperformance measures were obtained within ±1 year from the MRI in MOGAD patients, including neuroperformance tests (contrast sensitivity test), manual dexterity test, walking speed test, processing speed test, and patient-determined disease steps (PDDS). Spearman's rank correlation was used to examine correlations between imaging and Z-scores of each neuroperformance measure and disability P values.
Results: 32 MOGAD were included with a mean age of 34 years. 75% were female. The majority had prior attacks of optic neuritis (19/32 patients, 59%), followed by myelitis (16/32 patients, 50%). The mean number of prior attacks was 1.72 (SD 1.4). Sixty-six percent were receiving maintenance treatment during the MRI, and the median PDDS was 1 (0-3).
Several associations between quantitative brain and spine MRI measures were observed. UCCA and whole brain volume were associated with PDDS (-0.72 and -0.66, both p=.004). Lateral ventricle volume was associated with PDDS (0.78, p=.0009). Whole brain volume was correlated with processing speed (0.52, p=.02). Whole brain volume and UCCA were associated with contrast sensitivity (0.65, p=.007, and 0.60,

p=.015).
Conclusion: Whole brain volume loss was associated with several disability measures including PDDS, processing speed and contrast sensitivity, suggesting that there may be a neurodegenerative component of MOGAD that impacts multiple disability measures.
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RB has served as a consultant for Astra Zeneca, Biogen, EMD Serono/Merck, Genzyme/Sanofi, Genentech/Roche, LabCorp, Lilly, Novartis, TG Therapeutics, and VielaBio/Horizon. He receives research support from Biogen, Genentech, and Novartis, and shares rights to intellectual property underlying the Multiple Sclerosis Performance Test, currently licensed to Qr8 Health and Biogen.
JRA has served on scientific advisory boards for of TG Therapeutics, EMD Serono, Genentech, Amgen; has received research support from Amgen.
SJ receives research support from NIH and Siemens and is a consultant to Monteris.
JAC has received personal compensation for consulting for Astoria, Atara, Biogen, Bristol-Myers Squibb, Convelo, and Viatris.
DO has received research support from the National Institutes of Health, National Multiple Sclerosis Society, Patient Centered Outcomes Research Institute, Race to Erase MS Foundation, Genentech, Genzyme, and Novartis. DO has received consulting fees from Biogen Idec, Genentech/Roche, Genzyme, Novartis, Merck, and Contineum Therapeutics.
KN has received personal licensing fee from Biogen and research funding from Department of Défense, National Institutes of Health, Patient Centered Outcomes Research Institute, Genzyme, and Biogen.

Neuropathology

O-9
Characteristics of Complement Deposition Pattern in MOGAD, Comparison with NMOSD
Yoshiki Takai[1]
[1]*Tohoku University Hospital*
Background: The involvement of the complement system is crucial in the pathogenesis of NMOSD with AQP4-IgG. This is supported by the drastic relapse-preventive effect of complement inhibitors on NMOSD. However, there is no clear consensus on the role of complements in MOGAD.
Objective: To compare the complement deposition patterns in NMOSD and MOGAD histopathologically.
Methods: We examined CNS tissues from patients with NMOSD (14 autopsies) and MOGAD (5 autopsies and 14 biopsies). Using immunohistochemistry, we evaluated the deposition of three complement pathway products (C3d, C4d, and C9neo) in relation to demyelination and astrocyte damage.
Results: The median (range) of age (years) at the time of tissue acquisition was 52(20-78) in NMOSD and 34.5(4-67) in MOGAD, and the sex ratio (F/M) was 12/2 in NMOSD and 11/8 in MOGAD. Both NMOSD and MOGAD showed perivascular complement deposition, with a typical rim/rosette pattern for all three complement products in the acute phase of NMOSD. On the other hand, MOGAD showed perivascular complement deposits consistent with perivenous demyelination at the white matter to corticomedullary junction but were not prominent within the cortical demyelinating lesions. In addition, C4d deposition was identified in almost all perivenous demyelinating lesions, while C9neo deposition was found in two

distinct patterns, one with weak (Pattern A) and one with strong (Pattern B) stainability. The frequency was 12 of 14 patients with confirmed perivascular complement deposition presented with Pattern A (86%) and only 2 with Pattern B (14%).
Conclusion: This study suggests that the formation of membrane attack complexes via the classical pathway may be weaker in MOGAD compared to NMOSD in general, although there were remarkable inter-individual differences in MOGAD.

Patient Reported Outcomes and Programs that Support Quality of Life

O-10
Enhancing Quality of Care for Patient Requiring Intravenous Rituximab: Reducing Door-to-Infusion Time at a Single Tertiary Centre
Wai Hian Ho[1], Si Yan Leo[1], Chen Yu[1], Mei Lian Goh[1], Su Rong Fam[1], Xuejuan Peng[1], Janis Siew Noi Tye[1], PeiPei Shen[2], Mai Moh Moh Thu[2], Anne Hui Ting Neo[2], Freddy Huang Mook Tang[2], Kevin Tan[1], Jeanne May May Tan[1], Josiah Yui Huei Chai[1], Tianrong Yeo[1]
[1]*National Neuroscience Institute*
[2]*Tan Tock Seng Hospital*
Background: Patients with Neuroimmunological conditions such as Multiple Sclerosis require Rituximab Infusion. This often takes a full day in our tertiary centre, resulting in patients being away from family and work. We identified factors that contribute to prolonged hospital stay and introduced measures to reduce the time patients spend in the hospital.
Objective: To improve the door-to-infusion time for IV Rituximab in a single tertiary centre, based on existing benchmarks and best practices.
Methods: We reviewed all patients with Neuroimmunological diseases who received Rituximab at the Medical Ambulatory Centre (MAC) of Tan Tock Seng Hospital (TTSH), Singapore, from October 2022 to June 2023. Gradual changes were implemented to improve the efficiency of the infusion process using various quality improvement tools, including comprehensive root cause analysis, Plan-Do-Study-Act (PDSA) cycles, and Pareto charts. Interventions included:
1. Assigning a designated healthcare assistant to collect reconstituted IV Rituximab from the pharmacy.
2. Developing standardized order sets with streamlined workflows.
3. Enhancing pharmacist efficiency by reducing verification checks.
Results: After implementing the new interventions, the average door-to-infusion time was reduced by 90 minutes, from 5 hours to 3.5 hours. Positive qualitative feedback was received from both patients and nurses regarding the new workflow, highlighting improved efficiency and reduced stress.
Conclusion: The implementation of a new protocol for Rituximab infusion significantly improved healthcare efficiency, reducing the time patients spend in the hospital and improve patient satisfaction during infusion visits.
Disclosures: No conflict of interest

POSTER SESSION - 1
Advances in Technology in Diagnosis and Care

P-1
Investigation of the Effects of IL-13 and IL-22 Cytokine Levels on Disease Activity, Prognosis, and

Treatment Response in Multiple Sclerosis Patients Treated with Fingolimod and Glatiramer Acetate

Mehmet Ufuk Aluclu[1], Fidel Demir[1], Deniz Evrim Kavak[2], Fırat Karaaslan[1], Sevgi Kandemir[3]
[1]*Department of Neurology, Faculty of Medicine, Dicle University*
[2]*Department of Medical Biology, Faculty of Medicine, Dokuz Eylul University, İzmir, Turkey*
[3]*Department of Medical Biology, Faculty of Medicine. Dicle University*

Background: Multiple Sclerosis (MS) is an inflammatory, demyelinating and neurodegenerative disease. In this study, we investigated serum protein levels of Interleukin-13 (IL-13) and Interleukin-22 (IL-22) cytokines.
Objective: These cytokines play an important role in the generation and regulation of the inflammatory response, which is the pathogenesis of MS, and are potential biomarkers for monitoring therapeutic response. Cytokines may play a role in the development of MS.
Methods: The study included 66 MS patients and 22 healthy individuals. IL-13 and IL-22 cytokine protein levels were measured by ELISA from peripheral blood serum samples collected from the participants. Patient demographics and treatment history data were also collected.
Results: IL-13 and IL-22 parameters were lower in MS patients compared to the control group. There was a significant difference between the patient and control groups in terms of IL-13 ($p<0.001$). Although the mean IL-22 level of the control group was higher than the patient group, the difference did not reach a significant level (p: 0.257).
Conclusion: The results of the study suggest that IL-13 and IL-22 cytokines play an important role in the pathogenesis of MS and are affected by fingolimod and glatiramer acetate treatment.
Disclosures: Nothing to disclose

P-2

Improving biomarker insights in neuromyelitis optica spectrum disorder: Temporal dynamics of neurofilament light chain and glial fibrillary acidic protein

Ho Jin Kim[1], Su-Hyun Kim[1], Ana Beatriz Ayroza Galvão Ribeiro Gomes[2], Patrick Schindler[3], Jae-Won Hyun[1], Ki Hoon Kim[1], Jasmine Lerner[4], Pascal Benkert[5], Jens Kuhle[5], Klemens Ruprecht[3], Friedemann Paul[3], Anne-Katrin Pröbstel[2]
[1]*Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Korea.*
[2]*Department of Neurology, University Hospital Basel and University of Basel, Basel, Switzerland*
[3]*Department of Neurology, Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany.*
[4]*Departments of Biomedicine and Clinical Research, University Hospital Basel and University of Basel, Basel, Switzerland*
[5]*Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel and University of Basel, Basel, Switzerland*

Background: Previous research has identified serum glial fibrillary acidic protein (sGFAP) and serum neurofilament light chain (sNfL) as biomarkers of disease activity for neuromyelitis optica spectrum disorder (NMOSD) but has not fully explored the significance of their temporal dynamics and demographic influences.
Objective: This study aimed to determine optimal timing for assessing sGFAP and sNfL during the attack and remission phases of NMOSD and to establish cutoff values that differentiate attacks from remission.
Methods: A multicenter, retrospective, longitudinal study analyzed 366 samples from 78 Korean patients

with aquaporin-4 antibody-positive NMOSD. External validation included 69 samples from 69 Brazilian patients and 199 samples from 34 German patients. sNfL and sGFAP concentrations were measured using a single molecule array assay. Z-scores for sNfL and sGFAP were adjusted for age, body mass index (BMI), and sex (sGFAP) utilizing a normative healthy control database. The temporal dynamics of sNfL and sGFAP post-attack were analyzed using generalized additive mixed models. ROC curve analysis was employed to establish the optimal Z-score cutoff for distinguishing between attack and remission phases.
Results: sGFAP levels peaked within the first week after attack onset, while sNfL levels gradually increased, peaking at 5 weeks. We established that the optimal period for evaluating attacks using sGFAP is within the first week following attack onset, and for sNfL, it ranges from 1 to 8 weeks post-attacks. For remission assessment, we measured sGFAP and sNfL levels at least six months after the attacks. Z-score cutoffs of 3.0 (99.9th percentile) for sGFAP and 2.1 (98.3rd percentile) for sNfL effectively distinguished between attack and remission phases, as indicated by area under the curve (AUC) values of 0.95 (95% CI:0.88-1.02) and 0.87 (95% CI 0.82-0.91), respectively. External validation cohorts supported these findings, showing 71% sensitivity and 96% specificity for sNfL. In the attack phase, one sample had an sGFAP Z-score above 3.0, while all 196 remission phase samples were below this cutoff.
Conclusion: This study identifies the optimal timing and demographic-adjusted thresholds for assessing sGFAP and sNfL during NMOSD attacks and remission. Understanding their temporal dynamics, it enhances their clinical utility in NMOSD management.
Disclosures: SHK has lectured, consulted, and received honoraria from Bayer Schering Pharma, Biogen, Genzyme, Merck Serono, and UCB and received a grant from the National Cancer Center of Korea. A.B.A.G.R.G. has received a research grant from Roche, paid to the University of São Paulo. PS received travel support by UCB and received speaker's honoraria by Roche and Alexion and served on advisory boards by Alexion. KR received research support from Novartis, Merck Serono, German Ministry of Education and Research, European Union (8212832-2), Stiftung Charité, Guthy-Jackson Charitable Foundation, and Arthur Arnstein Foundation; received speaker's honoraria from Virion Serion and Novartis. A-K.P. received financial compensation for participation in advisory boards, and consultations from Biogen, Roche, and Novartis, all used for research support. HJK 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, 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. All other authors report no potential conflicts of interest related to this study.

P-3
Withdrawn

P-4
Serum Proteomics Distinguish Subtypes of NMO Spectrum Disorder and MOG Antibody-Associated Disease and Highlight Effects of B-Cell Depletion
Yang Mao-Draayer[1]
[1]*Oklahoma Medical Research Foundation*
Refer to O-1 in Plenary Oral Presentation – 1

P-5

Diagnostic Delay In MOGAD: Prevalence and Impact On Relapse In A Korean Nationwide Cohort

Seung Ho Choo[1], Hyunjin Ju[2], Ki Hoon Kim[3], Ho Jin Kim[3], Su-Hyun Kim[3], Ju-Hong Min[4]

[1]Samsung Medical Center

[2]Department of Neurology, Soonchunhyang University Seoul Hospital

[3]Department of Neurology, Research Institute and Hospital of National Cancer Center

[4]Department of Neurology, Samsung Medical Center

Refer to O-2 in Plenary Oral Presentation – 1

P-6

Peripapillary Vessel Density and Visual Outcomes After Unilateral Optic Neuritis: An Optical Coherence Tomography Angiography Study

Natthapon Rattanathamsakul[1], Deena A. Tajifirouz[2], Kevin D. Chodnicki[3], Sean J. Pittock[4], Eoin P. Flanagan[4], John J. Chen[5]

[1]Department of Ophthalmology, Mayo Clinic, Rochester, MN; Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok Thailand

[2]Department of Ophthalmology, Mayo Clinic, Rochester, MN; Department of Neurology, Mayo Clinic, Rochester, MN

[3]Department of Ophthalmology, Mayo Clinic, Rochester, MN

[4]Department of Neurology, Mayo Clinic, Rochester, MN; Center for MS and Autoimmune Neurology, Mayo Clinic, Rochester, MN; Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN

[5]Department of Ophthalmology, Mayo Clinic, Rochester, MN; Department of Neurology, Mayo Clinic, Rochester, MN; Center for MS and Autoimmune Neurology, Mayo Clinic, Rochester, MN

Refer to O-3 in Plenary Oral Presentation - 1

POSTER SESSION - 2

Basic Science

P-7

Neutrophil extracellular traps citrullinate myelin to promote inflammatory demyelination in multiple sclerosis

Shishi Shen[1], Shilin Wu[1], Wenxuan Sun[1], Wei Cai[1], Wei Qiu[1]

[1]The Third Affiliated Hospital of Sun Yat-sen University

Background: Myelin citrullination is considered as a prodromal event upstream of autoimmune attack in multiple sclerosis (MS). Previous report demonstrated that neutrophil extracellular traps (NETs) contained peptidyl-arginine deiminases (PADs) to citrullinate endogenous antigen and enhance the immunogenicity.

Objective: To study the roles of NETs on myelin citrullination and the subsequent T cell mediated inflammatory demyelination in MS.

Methods: Immunofluorescent staining and ELISA were performed to detect NETs formation within CNS in MS patients and EAE model. Stereotaxic injection and cerebellum organic slice culture (OSC) were performed to study the impact of NETs on myelin citrullination and demyelination. Flow cytometry was performed to examine T cell activation in draining lymph nodes of spinal cord after NETs injection. LC-MS and Co-IP were performed to identify myelin citrullinome after NETs treatment.

Results: NETs was identified in brain biopsy sample from a MS patient and in spinal cords of EAE mice (N=8,

P<0.05). MPO-DNA was elevated in CSF of MS patients (N=10, P<0.05) and positively correlated with EDSS score (R2=0.32, P=0.04) or MRI lesion numbers (R2=0.36, P=0.03). In vitro experiments revealed that myelin debris efficiently induced NETs formation (N=3, P<0.05), which caused pronounced myelin citrullination and inflammatory demyelination when injected to healthy spinal cord (N=8, P<0.05). Unexpectedly, we found that citrullinated myelin was drained into vertebral lymph nodes and activated T cells after intraspinal NETs injection (N=6, P<0.05). Moreover, T cells in the draining lymph nodes promoted demyelination when injected back to healthy spinal cord (N=6, P<0.05).
Conclusion: Neutrophils in EAE lesions release NETs to catalyze myelin citrullination. Citrullinated myelin was drained into peripheral lymph nodes to active T cells and thus promoting inflammatory demyelination in MS.

P-8
Predicting Relapse of Neuromyelitis Optica by Complement Factors
Katsuichi Miyamoto[1], Norimitsu Inoue[2]
Refer to O-4 in Plenary Oral Presentation – 1

P-9
Neutrophil Extracellular Traps-Mediated Meningeal Inflammation Promotes Demyelination in Multiple Sclerosis
Wenxuan Sun[1], Shishi Shen[1]
[1]*The Third Affiliated Hospital of Sun Yat-Sen University*
Background: Multiple sclerosis (MS) is an autoimmune demyelinating disease of central nervous system (CNS). Neutrophils infiltrate into dura early in experimental autoimmune encephalitis (EAE) model and blocking it alleviates disease severity. Lymphatic vessels (LVs), a route for immune cells to enter or exit CNS, influence the development and pathogenicity.
Objective: To study the roles of meningeal neutrophil extracellular traps (NETs) formation in MS and the underlying mechanism, and thus providing promising therapeutic targets.
Methods: Single cell RNA sequencing analysis (scRNA-seq) and immunofluorescent staining were performed to detect the presence of NETs within LVs in EAE. Luxol fast blue (LFB) staining and flow cytometry were performed to evaluate inflammation and demyelination of EAE after intrathecally NETs inhibition. Real Time PCR and EILSA were used to detect the cytokines and chemokines expression of lymphatic endothelial cells (LEC).
Results: NETs formation pathway was enriched in the dural neutrophils according to scRNA-seq data. NETs were evident in the LVs which drains myelin debris on the meninges in EAE (N=6, p<0.05). Inhibition of NETs in the LVs ameliorated disease severity of EAE (N=5, p < 0.05). In vitro, myelin-pretreated human lymphatic endothelial cells (LEC) induced NETs formation, meanwhile NETs treated LEC upregulated expression level of chemokines and cytokines such as CXCL2 (N=3, p < 0.05).
Conclusion: LVs drain myelin debris and induce NETs formation on meningeal. NETs induce the inflammation phenotype of LEC and promote the inflammatory demyelination. Intrathecal inhibition of NETs can alleviate the disease severity and may be new therapy for MS.

P-10
Withdrawn

P-11
Withdrawn

P-12

The Investigation of Dectin-1 in Experimental Autoimmune Encephalomyelitis via CD8+ Regulatory T Cell

Chengkai Yan[1], Jian Zhang[2], Wei Qiu[1]

[1]*The Third Affiliated Hospital, Sun Yat-Sen University*

[2]*University of Iowa*

Background: A regulatory type of CD8+T cell has been discovered and showing its potential activities in multiple sclerosis. However, the regulatory mechanism of these cells are still missing. Dectin-1 is a critical pattern recognition receptor and plays a vital role in antifungal progression. We showed the possible connection between CD8+Treg and Dectin-1.

Objective: This study aims to investigate the potential mechanism of Dectin-1 and CD8+ Treg in the EAE model based on the in vivo/in vitro experiment and provide new ideas for studying multiple sclerosis.

Methods: 1. Immunize the Dectin-1 KO/WT mice(C57BL/6) with Myelin Oligodendrocyte Glycoprotein 35-55(MOG33-35) for the EAE model, and EAE clinical score has been applied to analyze the severity.

2. Analyze the subgroup of the immune cells harvested from the spleen and draining lymph nodes in EAE mice. Find out the cells responsible for the difference between the Dectin-1 KO and WT groups.

3. Figure out the cells directly influenced by dectin-1 during the EAE onset via adoptive cell transfer.

4. Investigate the effect of Dectin-1 on CD8+Treg via molecular and cellular techniques.

Results: 1. The EAE model has been successfully established. A higher EAE clinical score is shown in Dectin-1 KO mice, which means a worse status.

2. Dectin-1 KO mice show an increasing amount and higher percentage of CD4+T cells, and this difference may be due to a higher amount of Th17 cells. Meanwhile, CD8+Treg (CD44+CD122+Ly49+) shows a continuous decreasing trend in Dectin-1 KO mice. However, the difference between Th17 and CD8+Treg (CD44+CD122+Ly49+) does not exist in draining lymph nodes. Microglia has no difference between the groups.

3. The transferred CD4+T cells from Dectin-1 KO and WT mice do not change the severity of EAE. Moreover, the difference of Th17 cells has no significance between the two groups.

4. Dectin-1 constant expressed on CD8+T cells. The expression of Dectin-1 on dendritic cells may influence the number of CD8+Treg. Furthermore, the most significant amount of CD8+Treg only shows that both CD8+Treg and dendritic cells express Dectin-1.

Conclusion: 1. Dectin-1 plays a protective role during the onset of EAE

2. Dectin-1 changes the amount of CD8+Treg via the expression on both dendritic cells and CD8+Treg. Thus inhibit the Th17 to exhibit its protective function.

Disclosures: No

P-13

Cross-Reactive Antibodies to Butyrophilins in Myelin Oligodendrocyte Glycoprotein Antibody Disease.

Shuhei Nishiyama[1], Takahisa Mikami[2], Philippe Bilodeau[2], Monique Anderson[2], Natasha Bobrowski-Khoury[2], Natalia Drosu[2], Masahi Aoki[3], Michael Levy[2]

[1]*Tohoku University*

[2]*Massachusetts General Hospital*

[3]*Tohoku University Graduate school of Medicine*

Background: Myelin oligodendrocyte glycoprotein (MOG) antibody disease is an autoimmune condition

associated with antibodies against MOG. MOG belongs to the butyrophilin (BTN) family and shares significant homology with human and bovine BTNs.
Objective: To screen antibodies against human BTN1A1, BTN2A1, BTN3A1, CD80, CD86, PD-L1 (programmed death ligand 1), and bovine BTN1A1 in MOGAD patient sera using novel cell-based assays.
Methods: Sera from 14 MOG-IgG-positive MOGAD patients were tested by cell-based assay for binding to the BTN molecules BTN1A1, BTN2A1, BTN3A1, CD80, CD86, PD-L1, and bovine BTN1A1. Sera from ten AQP4-IgG seropositive NMOSD and ten healthy individuals were used as controls.
Results: Reactivity against BTN1A1, BTN2A1, BTN3A1, CD86, and PD-L1 was present in 78.6% (11/14), 7.1% (1/14), 64.3% (9/14), 14.3% (2/14), and 7.1% (1/14) of MOGAD patients, respectively; no serum reactivity against the BTN family was detected in the NMOSD or the healthy control groups. All 14 MOGAD cases showed similar bovine BTN1A1-IgG and MOG-IgG titers (correlation analysis $R2=0.9826$, $P<0.0001$).
Conclusion: We found that MOG-IgG could bind to the other BTNs. Despite its low affinity, MOG-IgG's cross-reactivity to BTNs could modulate the genesis of autoreactivity and the characteristic pathophysiology of MOGAD.

P-14

Novel Cytokine Candidate, p40-EBI3 Complex Ameliorates Experimental Autoimmune Encephalomyelitis with Inflammation and Demyelination via Targeting STAT3/Th17 Immune Activation

Woojun Kim[1], A Ram Lee[2], Mi-La Cho[2]
[1]*Dept. of Neurology, Seoul St. Mary's Hospital, The Catholic University of Korea*
[2]*The Catholic University of Korea*

Background: The IL-12 cytokine family is closely related to the development of Th cells, which are responsible for autoimmune disease enhancement or suppression. IL-12 family members share three α-subunits (p35, p19, and p28) and two β-subunits (p40 and EBI3). However, a β-sheet p40 homodimer has been shown to exist and antagonize IL-12 and IL-23 signaling.
Objective: We assumed the existence of a p40-EBI3 heterodimer in nature and sought to investigate its role in immune regulation. In this study, the therapeutic effect of p40-EBI3 in the mouse experimental autoimmune encephalomyelitis (EAE) model were evaluated.
Methods: EAE model was induced with MOG peptide, IFA mixture, and pertussis toxin. The presence of the p40-EBI3 heterodimer was confirmed by ELISA, immunoprecipitation, and western blotting. A p40-EBI3 vector and p40-EBI3-Fc protein were synthesized to confirm the immunological role of this protein in EAE mice. Clinical and histological scores and immune cell regulatory functions were evaluated in vivo and in vitro in the EAE model injected with synthesized p40-EBI3 vectors and p40-EBI3 transgenic mice, respectively.
Results: The clinical and histological scores were reduced in the EAE model of p40-EBI3 vector-treated mice and p40-EBI3 transgenic mice. p40-EBI3 vector significantly inhibited the differentiation of Th17 cells and promoted Treg in vivo and in vitro. The expression levels of proinflammatory cytokines, such as TNF-alpha, IL-1β, IL-6, IL-17, were significantly reduced by suppressing signal transducer and activator of transcription (STAT) 3 expression and increasing STAT5 expression.
Conclusion: p40-EBI3, a novel anti-inflammatory cytokine, ameliorated proinflammatory conditions in EAE mice both in vivo and in vitro. It was involved in suppressing the immune response through the expansion of Treg cells and suppression of Th17 cells.

P-15

Neurofascin 155, 186 and 140 Antibodies in a Cohort of Indian Multiple Sclerosis Patients

Thomas Mathew[1], Pritam Majumdar[1], Surabhi Garg[1], Shagun Bhardwaj[1], Sudheeran Kannoth[2], Annamma Mathai[2], Uday Murgod[3], Vikram Kamath[4], Subhash Kaul[5], Sindhu Nambiar[1], Akshata Huddar[1], Sonia Shivde[1], Sagar Badachi[1], Raghunandan Nadig[1], Sharath Kumar GG[1], Sai Kanth Deepalam[1], GRK Sarma[1]

[1]St. John's National Academy of Health Sciences

[2]Amrita Institute of Medical Sciences

[3]Manipal Hospital

[4]Trustwell Hospitals

[5]KIMS Hospital

Background: Anti-neurofascin antibodies (ANFA) are thought to be involved in the pathogenesis of multiple sclerosis (MS). ANFA can cause conduction block and axonal injury. Here we have analyzed antibodies to neurofascin (NF) 155, 186, and 140 in a large cohort of MS patients.

Objective: To analyze antibodies to neurofascin (NF) 155, 186, and 140 in a cohort of pure MS patients.

Methods: Consecutive MS patients from a neuroimmunological clinic underwent testing for a pan neurofascin assay using the ELISA technique. All MS patients satisfied the McDonald 2017 criteria and peripheral demyelination was ruled out by nerve conduction studies. Descriptive Statistics were performed using Microsoft Excel.

Results: During a 7-month period, we tested ANFA in 67 MS patients in which 54/67 (80.6%) were positive for at least one antibody and 13/67 (19.4%) tested negative for all antibodies. Isolated ANFA155 was positive in 1/67 (1.5%), isolated ANFA186 was positive in 11/67 (16.4%), and isolated ANFA140 was positive in 25/67 (37.3%). Combined positivity of ANFA 186/140 was seen in 16/67 patients (23.9%) and combined ANFA 155/140 was seen in 1/67 patients (1.5%). The ANFA155 patient had relapsing-remitting MS (RRMS). In the isolated ANFA186 patients, 8/11 (72.7%) had RRMS, 1/11 (9.1%) had radiologically isolated syndrome (RIS), 1/11 (9.1%) had clinically isolated syndrome (CIS) and 1/11 (9.1%) had secondary progressive MS (SPMS). In the isolated ANFA140 patients, 17/25 (68%) had RRMS, 6/25 (24%) had SPMS, and 2/25 (8%) had primary progressive MS (PPMS). In patients with ANFA 186/140 positivity, 12/16 (75%) had RRMS, 2/16 (12.5%) had SPMS, 1/16 (6.3%) had RIS, and 1/16 (6.3%) had CIS.

Conclusion: ANFA positivity to NF186 and NF140 appears to be higher in Indian MS patients. Further studies have to be done to understand the implications of these findings.

P-16

Withdrawn

P-17

Mitochondrial Transplantation Ameliorates Experimental Autoimmune Encephalomyelitis by Targeting of Mitochondrial Function and T cell Regulation

Woojun Kim[1], A Ram Lee[2], Mi-La Cho[2]

[1]Department of Neurology, Seoul St. Mary's Hospital, The Catholic University of Korea

[2]Department of Medical Life Sciences, The Catholic University of Korea

Background: The sustained inflammatory phase of multiple sclerosis (MS) leads to ion channel changes and chronic oxidative stress. Several studies have demonstrated mitochondrial respiratory chain deficiency in MS, as well as abnormalities in mitochondrial transport. These processes create an energy imbalance and contribute to a progressive neurodegeneration.

Objective: We investigated the role of mitochondrial dysfunction in the pathogenesis of mice experimental autoimmune encephalomyelitis (EAE) models in the spinal cord and analyzed the therapeutic effects of mitochondrial transplantation in EAE mice.
Methods: The EAE model was induced using MOG peptide, IFA mixture, and pertussis toxin. For mitochondrial transplantation, fresh mitochondria from mouse gastrocnemius muscle were delivered intravenously into the EAE mice. The clinical and histological scores, as well as spinal cord fibrosis, were assessed. Markers for immune cells and T helper/regulatory cell conversions were also investigated.
Results: EAE mice treated with mitochondrial transplantation had considerably lower clinical and histological scores than the control group. Th17 cell differentiation, Treg cell promotion, and mitochondrial reactive oxygen species were all considerably suppressed. The improvement in mitochondrial function in immune cells was confirmed. Fibrosis in the spinal cord was dramatically reduced by the mitochondria transplanting group. Furthermore, mitochondrial transplantation reduced the number of Enterobacteriaceae and Bacteroides species bacteria in the guts of the EAE mice.
Conclusion: Our findings suggested that mitochondrial dysfunction in the EAE mouse model is important to the pathogenesis of EAE, and mitochondrial transplantation has therapeutic potentials for onset and progression of multiple sclerosis.
Disclosures: Nothing to disclose.

P-18
Withdrawn

POSTER SESSION – 3
Disease modifying therapies

P-19
Improvement of Vision Through a Multimodal Treatment Approach in Patients with Optic Neuritis
Nimasha Ekanayaka[1], Shadia Hisham[1], Dileepa Ediriweera[2], Bimsara Senanayake[1]
[1]*Institute of Neurology, National Hospital of Sri Lanka*
[2]*Department of Health Data Science, Faculty of Medicine, University of Kelaniya, Sri Lanka*
Background: Visual loss due to optic neuritis (ON) can be reversed with early aggressive treatment. The primary treatment modality is high-dose intravenous corticosteroids (IV-Methylprednisolone (IV-MPP)). For patients exhibiting sub-optimal responses, therapeutic plasma-exchange (PLEX) and biologics (Rituximab/ Tocilizumab) have exhibited promising outcomes.
Objective: To describe visual outcomes after treatment with IV-MPP, PLEX, and biologic agents (Rituximab/ Tocilizumab) in patients with acute/ sub-acute presentations of first episode of ON and to evaluate predictors of final visual outcome.
Methods: All patients presenting with first episode ON to the multiple sclerosis and related disorders clinic between January 2022 and April 2024 were recruited and classified as definite/probable-ON (ICON-2022 criteria). Visual acuity (VA) was assessed using a Snellen chart and converted into base-10 logarithm of the minimum angle of resolution (logMAR) for statistical analysis. Severe visual impairment was defined as having a Best Corrected Visual Acuity (BCVA) (Snellen) worse than 20/200 at onset. Good visual outcome was defined as final Snellen VA better than 20/40. The average visual acuity in each studied eye was analysed throughout the treatment period. Fisher's exact test and Chi-square test was used to compare the categorical variables of clinical characteristics. The differences in the VA (logMAR) and the numbers of

patients in each category at each time (the onset, after IV MPP, following 5 PLEX cycles, after initial dose of IV Rituximab/ Tocilizumab, VA in 1, 3 & 6 months, and VA at 1 year) was evaluated by the Friedmann test along with post hoc Wilcoxon signed rank test (adjusted by Bonferroni corrections). Logistic regression was used to identify critical factors associated with final visual outcome.
Results: A total of 51 patients (56.8% females, median (IQR) age 38 (24-44) years) with 65 affected eyes were recruited. At presentation 76% eyes had severe visual impairment. Immunotherapy was initiated within 3-weeks in 79%. All received first line IV-MPP with a considerable visual recovery (P<0.001). Of those with sub-optimal response, 40% underwent PLEX, but did not show significant recovery by 5th PLEX (P=0.126). Biologics were administered to 34/65 (53%).
Good visual outcome was achieved in 84%. At 1-year, significant visual improvement was observed (Friedman test P<0.001), with the most significant improvement noted within the first-month post-treatment (P<0.001). Final visual outcome was strongly associated with VA at onset (P=0.010) and time from symptom onset-to- immunotherapy (P=0.001), but was not associated with demographics, laterality, treatment category or final diagnosis (45% single-isolated ON, 22%-Multiple-sclerosis, 17% Bilateral-sequential ON, MOGAD-13%, NMOSD-4%).
Conclusion: In patients with acute/sub-acute first-episode ON, rescue therapy with PLEX and/or biologics following pulsed steroids led to good visual outcomes regardless of the final aetiology. The earlier the treatment, the better the visual outcome.
Disclosures: No conflicts of interest to declare.

P-20
Relapse after negative seroconversion for 3 years in a patient with MOGAD
Jung Im Seok[1], Min Su Park[2], Jong Seok Bae[3]
[1]Catholic University of Daegu, School of Medicine
[2]Parkminsu Neurology Clinic
[3]College of Medicine, Hallym University
Background: While many patients with myelin oligodendrocyte glycoprotein antibody-mediated disease (MOGAD) will have a monophasic course, 30-80% of patients will relapse after the initial attack. MOG-antibody negative seroconversion was associated with a lower risk of relapse and may help inform treatment decisions and duration.
Objective: However, it is not conclusive whether negative seroconversion of antibody predict relapse.
Methods: We described a patient who experienced a relapse after seroconversion to MOG-IgG-negative.
Results: In 2016, a 31-year-old man was presented with a symptom of blurred vision. In 2019, he was presented with headache and fever. Cerebrospinal fluid analysis revealed lymphocyte-dominant pleocytosis and brain MRI showed bilateral asymmetric T2 hyperintense lesions. Then, he was diagnosed as MOGAD based on positive serum MOG-antibody and recurrent clinical symptoms including optic neuritis and meningitis. In 2021, his serum MOG-antibody levels became negative, and we discontinued steroids and immunosuppressant. Repeat serum MOG-antibody test for three times was negative until January 2024. In April 2024, he was presented with a fever and headache and his serum MOG-antibody showed positive.
Conclusion: It is difficult to predict which patients with MOGAD will relapse based on antibody status. Research is needed to determine the optimal timing and duration of treatment.
Disclosures: None

P-21
Time-to-treat the first acute attack of MOGAD: Association with relapse and MOG-IgG seroconversion

Young Nam Kwon[1], Boram Kim[2], Jun-Soon Kim[3], Kyung Seok Park[3], Da-Young Seo[4], Hyunjin Kim[4], Eun-Jae Lee[4], Young-Min Lim[4], Hyunjin Ju[5], Yeon Hak Chung[6], Ju-Hong Min[7], Tai-Seung Nam[8], Sooyoung Kim[9], Eunhee Sohn[9], Kyong Jin Shin[10], Jin Myoung Seok[11], Sunyoung Kim[12], Jong Seok Bae[13], Sukyoon Lee[14], Seong-il Oh[15], Yu Jin Jung[16], Jinseok Park[17], Seung Hyun Kim[17], Ki Hoon Kim[18], Ho Jin Kim[19], Jae Ho Jung[20], Seong-Joon Kim[20], Seung Woo Kim[21], Myoung-jin Jang[22], Jung-Joon Sung[23], Patrick Waters[24], Ha Young Shin[21], Sung-Min Kim[25]

[1]*Department of Neurology, Severance Hospital*
[2]*Seoul National University Hospital*
[3]*Seoul National University Bundang*
[4]*Asan Medical Center*
[5]*Soonchunhyang University Seoul Hospital*
[6]*Korea University Guro Hospital*
[7]*Samsung Medical Center*
[8]*Chonnam National University Medical School*
[9]*Chungnam National University College of Medicine*
[19]*Inje University College of Medicine*
[11]*Soonchunhyang University Cheonan Hospital*
[12]*University of Ulsan College of Medicine*
[13]*Kangdong Sacred Heart Hospital*
[14]*Busan Paik Hospital*
[15]*Kyung Hee University Hospital*
[16]*Daejeon St. Mary's Hospital*
[17]*College of Medicine, Hanyang University*
[18]*Inje University Sanggye Paik Hospital*
[19]*Research Institute and Hospital of National Cancer Center*
[20]*Department of Ophthalmology, Seoul National University College of Medicine*
[21]*Severance Hospital*
[22]*Medical Research Collaborating Center, Seoul National University Hospital*
[23]*Seoul National University College of Medicine*
[24]*Oxford Autoimmune Neurology Group, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital*
[25]*Seoul National University Hospital, Seoul National University College of Medicine*

Background: A proportion of people with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) have a relapsing disease course and persistent MOG-IgG seropositivity. Few studies have investigated whether the treatment of the first MOGAD attack can impact the long-term disease course and/or MOG-IgG seronegative conversion.

Objective: To investigate the impact of time-to-treat first acute MOGAD attack on relapse risk and MOG-IgG serostatus.

Methods: This is a retrospective, nationwide, multicenter cohort study, involving 14 secondary or tertiary hospitals in South Korea between November 2009 and August 2023. People with adult-onset MOGAD, who either had a relapse or were followed for more than 12 months after disease onset and had a detailed medical record of their first attack, were included. Among 315 individuals screened, 75 were excluded due to adolescent-onset, or short disease duration. Two-hundred and forty patients were categorized based on time-to-treat first acute MOGAD attack: 'early' (< 5 days), 'intermediate' (5 to 14 days), and 'late' (not treated within 14 days). A multivariable analysis for clinical and treatment factors associated with relapsing

disease course and/or MOG-IgG seronegative conversion was performed. Further subgroup analyses were conducted among those without long-term non-steroidal immunosuppressant (nsIS) maintenance treatment.
Results: A total of 240 patients (48.7% female) with median disease duration of 3.14 years (IQR, 2.00-6.15) were included. The median onset age was 40.4 years (IQR, 28.8-56.1), 46.7% relapsed after a median of 0.45 years (IQR, 0.18-1.68) and 29/116 (25.0%) converted to MOG-IgG seronegative. Both time-to-treat first MOGAD attack (aHR, 2.635, 'late' vs 'early'; 95% CI, 1.434-4.843; p=0.002; aHR, 2.024, 'intermediate' vs 'early'; 95% CI, 1.095-3.740; p=0.024) and nsIS maintenance treatment (aHR, 0.241; 95% CI, 0.139-0.415; p<0.001) were independently associated with the risk of relapse. In a subgroup without nsIS maintenance, the time-to-treat first MOGAD attack was still associated with higher risk of relapse (aHR, 3.506, 'late' vs 'early'; 95% CI, 1.639-7.501; p=0.001; aHR, 2.683, 'intermediate' vs 'early'; 95% CI, 1.232-5.845; p=0.013). Lastly, the time-to-treat first MOGAD attack was also associated with MOG-IgG seronegative conversion (aOR, 7.044, 'early' vs 'late'; 95%CI, 1.579-31.410; p=0.0
Conclusion: Early treatment of the first acute MOGAD attack reduces the proportion of relapsing disease course and increases the likelihood of MOG-IgG seronegative conversion, and results in better long-term prognosis.
Disclosures: Kwon received a grant from the National Research Foundation of Korea, Eisai, and Korean Neurological Association; lectured, consulted, and received honoraria from Celltrion, Eisai, GC Pharma, Merck Serono, Roche, Sanofi Genzyme and CorestemChemon. Min is funded by and has received research support from the National Research Foundation of Korea (MIST and KHIDI) and SMC Research and Development Grant. She has lectured, consulted and received honoraria from Bayer Healthcare, Merk, Biogen Idec, Sanofi, UCB, Samsung Bioepis, Mitsubishi Tanabe, Celltrion, Roche, Janssen, and AstraZeneca. Waters is a named inventor on patents for antibody assays and has received royalties. He has received honoraria from Biogen Idec, Mereo Biopharma, Retrogenix, UBC, Euroimmun AG, UCB, F. Hoffmann La-Roche and Alexion; travel grants from the Guthy-Jackson Charitable Foundation; and research funding from Euroimmun AG. He Work in the Autoimmune Neurology Diagnostic Laboratory is supported by the NHS Commissioning service for NMOSD. S-M. Kim has lectured, consulted, and received honoraria from Bayer Schering Pharma, Genzyme, Merck Serono, and UCB; received a grant from the National Research Foundation of Korea and the Korea Health Industry Development Institute Research; is an Associate Editor of the Journal of Clinical Neurology. S-M. Kim and Seoul National University Hospital has transferred the technology of flow cytometric autoantibody assay to EONE Laboratory, Korea.

P-22
Early Effects of Cladribine Tablets on Immune and Inflammatory Markers in Central and Peripheral Compartments in Relapsing Multiple Sclerosis
Anne H. Cross[1], Claudia Cantoni[2], Amber Salter[3], Samantha Lancia[3], Kenneth Lee[1], Rea Agnihotri[1], Dana C. Perantie[1], Robert C. Axtell[4], Julie Korich[5], Emily Evans[5], Gabriel Pardo[4], Olaf Stuve[3], Ahmed Z. Obeidat[6], Amit Bar-Or[7], Gregory F. Wu[1]
[1]Washington University in St. Louis School of Medicine, St. Louis, MO, USA
[2]Barrow Neurological Institute, Phoenix, AZ, USA
[3]University of Texas Southwestern Medical Center, Dallas, TX, USA
[4]Oklahoma Medical Research Foundation, Oklahoma City, OK, USA
[5]EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA
[6]Medical College of Wisconsin, Milwaukee, WI, USA

[7]*University of Pennsylvania School of Medicine, Philadelphia, PA, USA*

Background: Cladribine tablets (CladT) therapy is efficacious for relapsing multiple sclerosis (RMS). However, the mechanisms facilitating CladT effect on inflammation within the cerebrospinal fluid (CSF) in RMS remain unclear. CLOCK-MS is an open-label, randomised, multicenter phase 4 study exploring the mechanism of action of CladT in RMS (NCT03963375).

Objective: To investigate changes in CSF and blood levels of lymphocytes and markers of neuronal injury during treatment with CladT in patients (pts) with RMS.

Methods: 47 pts were recruited across 5 sites and randomised 1:2:2:1 to a lumbar puncture (LP) at baseline (BL) and a second LP at either 5 weeks (weeks), 10 weeks, 1 year, or 2 years post-CladT initiation. Primary endpoints are changes in CSF levels of CD3+ T lymphocytes, CD19+ B lymphocytes, and neurofilament-light (NfL) chain from BL to second LP. Secondary endpoints include changes in CSF lymphoid and myeloid immune cell subsets. CSF from pts completing testing at weeks 5 (n=7) and 10 (n=10) post-treatment and blood samples at weeks 5 and 10 from all pts (n=47) were analysed.

Results: Pts were 42.9±12.3 (mean±SD) years old, 59.6% female, 83% White/Caucasian, and had a median (25th, 75th percentile) Expanded Disability Status Scale score at BL of 2 (1.5, 4.0). While CD19+ B cells in the blood were reduced in proportion and number at weeks 5 and 10 vs BL post-CladT therapy ($p<0.0001$), significant reductions in CSF CD19+ B cells were observed only at week 10 ($p=0.002$). At week 5, the number of CD3+ T cells was reduced in the blood ($p=0.0024$) and CSF ($p=0.03$) vs BL. At week 10, the percentage ($p=0.0003$ and $p=0.047$) and number ($p=0.001$ and $p=0.004$) of CD3+ T cells were significantly reduced in both blood and CSF, vs BL. No significant changes in CSF NfL were observed at 5 or 10 weeks post CladT therapy vs BL. Additional immune cell changes observed in the CSF at week 10 were a reduction in CD4+ T cell numbers ($p=0.004$), an increase in proportion ($p=0.049$) and number ($p=0.01$) of CD4+ T cells with a regulatory phenotype, and a reduction in the number of monocytes ($p=0.004$).

Conclusion: Overall, CladT exerts early effects in the central nervous system compartment and in the periphery, including reductions in B and T cells, which may contribute to its therapeutic benefit in RMS.

Disclosures: AHC has consulted for Biogen, Bristol Myers Squibb, Horizon, Janssen, Merck, EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Roche/Genentech, Novartis, Octave, TG Therapeutics.

CC, SL, KL, RA, and DCP have nothing to disclose.

AS receives research funding from CMSC, Multiple Sclerosis Society of Canada, NMSS, and the US DOD and is a member of editorial board for Neurology. She serves as a consultant for Gryphon Bio, LLC and Abata Therapeutics. She has equity in Owl Therapeutics. She is a member of the DSMB for PREMOD2, CAVS-MS, and CELLO.

RCA has consulted for EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Biogen Idec, and Roche and is on the advisory board for Progentec Diagnostics Inc.

JK and EA are employees of EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA.

GP has received speaker honoraria and/or consulting fees from Alexion, Biogen Idec, Celgene/BMS, EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Horizon/ Amgen, Novartis, Roche/Genentech,

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P-23

Comparative Analysis of Five-Year Clinical Outcomes of Autologous Hematopoietic Stem Cell Transplantation and Alemtuzumab in Multiple Sclerosis Patients

Murat Kürtüncü[1], Hazal Ceren Manazoğlu[2], Gülce İşkan[1], Tuncay Gündüz[1], Ahmed Serkan Emekli[1], Gülşen Akman[1], Burcu Altunrende[3], Gülsan Sucak[4], Mutlu Arat[5], Tülay Özçelik[5], Sevda Öztürk Erden[1]
[1]Department of Neurology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey
[2]Neurology Clinic, Umraniye Training and Research Hospital, Istanbul, Turkey
[4]Department of Neurology, Health Sciences University, Istanbul Taksim Training and Research Hospital, Istanbul, Turkey
[4]Hematology Department, Medical Park Bahçelievler Hospital, Istanbul, Turkey
[5]Hematology Department, Florence Nightingale Hospital, Istanbul, Turkey

Background: Autologous hematopoietic stem cell transplantation (aHSCT) and alemtuzumab (ALZ) therapy have been successfully used in multiple sclerosis (MS) patients with high disease activity for a long time. However, the number of studies comparing these two treatment methods is insufficient.
Objective: This study aims to compare the five-year efficacy data of aHSCT and ALZ treatments in MS patients with high disease activity.
Methods: This multicenter observational study was conducted on MS patients who received aHSCT and ALZ treatments. Annual relapse rates (ARR), Expanded Disability Status Scale scores (EDSS), and annual cumulative disease activities (NEDA-3) were compared between patients before treatment and at five-year

follow-up. Additionally, subgroup analyses of treatments were performed based on baseline EDSS scores.
Results: The study included 39 patients who received ALZ treatment and 18 patients who underwent aHSCT. It was observed that three patients received both treatments. The median ages at treatment initiation for patients receiving ALZ and aHSCT were calculated as 38 (IQR: 13.0) and 40 (12.5) years, respectively, and the median baseline EDSS scores were 6.5 (1.5) and 6.5 (1.0), respectively. The median follow-up durations for patients were 1 (3) and 4.5 (5.8) years, respectively. In the total analysis, no significant differences were observed in the time to first relapse, worsening of EDSS, and time to NEDA loss in patients at five-year follow-up.
Conclusion: This study is the first to compare the effectiveness of aHSCT and ALZ treatments in MS patients in our country. Our study suggests that both treatments are at least equally effective, particularly in the early stages.
Disclosures: M.K. has received honoraria, travel support, and research funds from Merck, Novartis, Sanofi, Roche, Teva, Gen İlaç, Abdi İbrahim, and ARIS, served on advisory boards for these companies, received research funds from The Scientific and Research Council of Turkey and Neuroimmunological Society, TG has received honoraria, and travel support from Merck, Novartis, Sanofi, Teva, Gen İlaç, Roche, Abdi İbrahim, and ARIS, served on advisory boards for these companies, Other authors have nothing to disclose.

P-24

Incidence of Relapses After Meningococcal Vaccination in Clinical Trials and Real-World Evidence of Eculizumab and Ravulizumab in Anti-Aquaporin-4 Antibody-Positive (AQP4-Ab+) Neuromyelitis Optica Spectrum Disorder (NMOSD)

Sami Fam[1], Becky Parks[1], Kerstin Allen[1]
[1]*Alexion, AstraZeneca Rare Disease, Boston, MA, USA*

Background: Ravulizumab and eculizumab are complement component 5 inhibitor therapies (C5ITs) approved for AQP4-Ab+ NMOSD. Vaccination against Neisseria meningitidis (Nm) is generally advised ≥2 weeks prior to C5IT initiation; however, any vaccination may further activate the complement pathway and lead to increased signs and symptoms of underlying disease.
Objective: To report relapses occurring ≤4 weeks of Nm vaccination before initiating C5IT or placebo in patients with AQP4-Ab+ NMOSD screened in CHAMPION-NMOSD, enrolled in PREVENT, and included in a regulatory mandated postmarketing surveillance (PMS) study.
Methods: This retrospective analysis of both clinical trial and real-world data included patients with vaccination data in (1) those screened in CHAMPION-NMOSD (NCT04201262), irrespective of screening outcome, (2) those randomised to placebo or eculizumab in PREVENT (NCT01892345), and (3) those included in the Japanese PMS study from approval (Nov 2019) to data cutoff (Oct 2023). Outcomes were physician-reported relapses occurring within 4 weeks of last meningococcal vaccination and before ravulizumab, eculizumab, or placebo initiation.
Results: This analysis included 70 patients from CHAMPION-NMOSD (57 enrolled; 13 screen failures), 2.9% (2/70) of whom experienced a relapse per analysis criteria; both patients were screen failures. In PREVENT, 3.1% (3/96) of eculizumab-treated and 10.6% (5/47) of placebo-treated patients had a relapse. In the Japanese PMS study, 0.7% (1/151) of patients experienced a relapse.
Conclusion: This analysis indicates a low relapse incidence within 4 weeks of meningococcal vaccination before C5IT initiation in patients with AQP4-Ab+ NMOSD. Based on available data, whether relapses are due to vaccination or inherent relapse risk is unknown.

Disclosures: SF, BP, and KA are employees of Alexion, AstraZeneca Rare Disease, and hold stock or stock options in AstraZeneca.

P-25

Efficacy and Safety of Ravulizumab in Adults With Anti-Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder: Interim Analysis From the Ongoing Phase 3 CHAMPION-NMOSD Trial

Ichiro Nakashima[1], Sean J Pittock[2], Michael Barnett[3], Jeffrey L Bennett[4], Achim Berthele[5], Jérôme de Sèze[6], Michael Levy[7], Celia Oreja-Guevara[8], Jacqueline Palace[9], Friedemann Paul[10], Carlo Pozzilli[11], Yasmin Mashhoon[12], Kerstin Allen[13], Becky Parks[13], Ho Jin Kim[14]

[1]Tohoku Medical and Pharmaceutical University, Sendai, Japan
[2]Mayo Clinic, Rochester, MN, USA
[3]University of Sydney, Sydney, NSW, Australia
[4]University of Colorado, Aurora, CO, USA
[5]Technical University of Munich, Munich, Germany
[6]CHU de Strasbourg, Strasbourg, France
[7]Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
[8]San Carlos Clinical Hospital and Complutense University of Madrid, Madrid, Spain
[9]John Radcliffe Hospital, Oxford, UK
[10]Charité-Universitätsmedizin Berlin and Max Delbrück Center for Molecular Medicine, Berlin, Germany
[11]Sapienza University, Rome, Italy
[12]FORMERLY Alexion, AstraZeneca Rare Disease, Boston, MA, USA
[13]Alexion, AstraZeneca Rare Disease, Boston, MA, USA
[14]National Cancer Center, Goyang, Republic of Korea

Background: CHAMPION-NMOSD (NCT04201262) is an ongoing global, open-label, phase 3 study evaluating ravulizumab in anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD).

Objective: To report the interim efficacy and safety of ravulizumab in AQP4-Ab+ NMOSD.

Methods: Adult patients received an intravenous, weight-based loading dose of ravulizumab on day 1 and a maintenance dose on day 15 and every 8 weeks thereafter. Following a primary treatment period (PTP; up to 2.5 years), patients could enter a long-term extension (LTE). PTP primary endpoints were time to first adjudicated on-trial relapse and relapse risk reduction. Secondary endpoints included adjudicated on-trial relapse rate, change from baseline in Hauser Ambulation Index (HAI) and Expanded Disability Status Scale (EDSS) scores, and safety.

Results: 58 patients enrolled in the PTP; 56/2 entered/completed the LTE. As of 16 June 2023, median (range) follow-up was 138.4 (11.0-183.1) weeks for ravulizumab (n=58), with 153.9 patient-years. Across the PTP and LTE, no patients had an adjudicated on-trial relapse during ravulizumab treatment. 91.4% (53/58 patients) had stable or improved HAI score. 91.4% (53/58 patients) had no clinically important worsening in EDSS score. Treatment-emergent adverse event (TEAE) and serious adverse event incidences were 94.8% and 25.9%, respectively. Most TEAEs were mild to moderate in severity and unrelated to ravulizumab. TEAEs leading to withdrawal from study drug occurred in 1 patient. Two cases of meningococcal infection occurred during the PTP, none in the extension period. One death occurred (cardiovascular) during the LTE and was unrelated to ravulizumab.

Conclusion: These findings are consistent with outcomes during the PTP and demonstrate the long-term

clinical benefit of ravulizumab in the prevention of relapses in AQP4-Ab+ NMOSD.

Disclosures: IN has received honoraria for serving on the scientific advisory board of Alexion and by serving as speaker at a lecture meeting held by Alexion. CO-G has received honoraria for speaking and serving on advisory boards from Biogen Idec, Bristol Myers Squibb, F. Hoffmann-La Roche Ltd, Janssen, Merck, Novartis, Sanofi Genzyme, and Teva. SJP has received personal compensation for serving as a consultant for Astellas, Genentech, and Sage Therapeutics and for serving on scientific advisory boards or data safety monitoring boards for F. Hoffmann-La Roche AG, Genentech, and UCB; institution has received compensation for his serving as a consultant for Alexion, Astellas, and Viela Bio/MedImmune; has received research support from Alexion, Roche/Genentech, and Viela Bio/MedImmune; has Patent #8,889,102 (Application# 12-678350) and Patent #9,891,219B2 (Application# 12-573942) issued and patents for Kelch11, LUZP4, septin, and MAP1b antibodies pending. MB has received institutional support for research or speaking from Alexion, Biogen, Bristol Myers Squibb, Merck, Roche, and Sanofi Genzyme; and is Research Director, Sydney Neuroimaging Analysis Centre, and Research Consultant, RxMx. JLB has received personal fees from AbbVie, Alexion, BeiGene, Clene Nanomedicine, F. Hoffmann-La Roche Ltd, Genentech, Mitsubishi Tanabe, Reistone Biopharma, and Viela Bio; has received grants from Alexion, Mallinckrodt, Novartis, and the US National Institutes of Health; has a patent, 'Compositions and methods for the treatment of neuromyelitis optica,' issued. AB has received consulting and/or speaker fees from Alexion, Bayer Healthcare, Biogen, Celgene, Novartis, Roche, and Sandoz/Hexal; institution has received compensation for clinical trials from Alexion, Biogen, Merck, Novartis, Roche, and Sanofi Genzyme. JdS has served on the scientific advisory board and as a consultant for Alexion. ML has received research support from Alexion, Genentech, and Horizon Therapeutics; and has received consulting fees from Alexion, Genentech, Horizon Therapeutics, Sanofi, and UCB.JP has received support for scientific meetings and honoraria for advisory work from Alexion, Amplo, Argenx, Chugai, Janssen, MedImmune, Merck Serono, Mitsubishi, Novartis, Roche, Sanofi, and UCB; has received grants from Alexion, Amplo Biotechnology, MedImmune, Roche, and UCB; holds patent ref P37347WO and license agreement Numares multimarker MS diagnostics; holds shares in AstraZeneca; and acknowledges partial funding by Highly Specialised Services of National Health Service England. FP has received honoraria and research support from Alexion; has received research grant support from Almirall, Bayer, Biogen, Deutsche Forschungsgemeinschaft (DFG), the Einstein Foundation, the EU FP7 Framework Programme, Genzyme, the German Ministry for Education and Research (BMBF), the Guthy-Jackson Charitable Foundation, Merck Serono, Novartis, Parexel, and Roche; has received honoraria for lectures, presentations, and speakers bureaus and support for attending meetings from Alexion, Bayer, Biogen, Celgene, the Guthy-Jackson Foundation, Merck Serono, Mitsubishi Tanabe, Novartis, Roche, Sanofi Genzyme, UCB, and Viela Bio; has served as an advisory board member for Celgene, Merck, Roche, and UCB; and has served as an editor for PLOS One and as an associate editor for Neurology Neuroimmunology & Neuroinflammation. CP has served as a speaker and consultant and has received advisor fees, research support, and travel grants from Alexion, Almirall, Biogen, Bristol Myers Squibb, F. Hoffmann-La Roche Ltd, Janssen, Merck, and Novartis. YM was an employee at Alexion, AstraZeneca Rare Disease, and held stock or stock options in AstraZeneca at the time of the study. KA is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca. BP is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca. HJK has received a grant from the National Research Foundation of Korea and research support from AprilBio and Eisai; has received consultancy/speaker fees from Alexion, Altos Biologics, AprilBio, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll BioPharma, Handok, Horizon Therapeutics (formerly Viela Bio),

MDimune, Mitsubishi Tanabe Pharma, Merck Serono, Novartis, Roche, Sanofi Genzyme, Teva-Handok, and UCB; and is a co-editor for the Multiple Sclerosis Journal and an associate editor for the Journal of Clinical Neurology.

P-26

Rituximab in Secondary Progressive Multiple Sclerosis: A Systematic Review and Meta-analysis

Tatchaporn Ongphichetmetha[1], Pasin Intarakhao[1], Taksaporn Laipasu[1], Jiraporn Jitprapaikulsan[1], Sasitorn Siritho[1]

[1]Mahidol University Siriraj Hospital

Background: Multiple sclerosis (MS) is a CNS demyelinating disease where most patients initially have relapsing-remitting MS (RRMS), with 60% to 90% progressing to secondary progressive MS (SPMS). Rituximab (RTX) has been proven effective in preventing relapses and is used off-label for RRMS. However, its efficacy in treating SPMS remains uncertain.

Objective: To evaluate the efficacy of RTX in stabilizing disability progression in SPMS.

Methods: A systematic review was conducted, encompassing studies from inception to April 2023, utilizing the MEDLINE and EMBASE databases. Inclusion criteria comprised studies with a minimum of 3 SPMS patients receiving intravenous RTX in at least one infusion, with a follow-up duration of at least 6 months. Primary outcome measures included changes in Expanded Disability Status Scale (EDSS) scores. Mean differences in pre- and post-RTX EDSS scores were analyzed using a random-effects model. Meta-regression examined age at RTX initiation, pre-RTX EDSS scores, disease duration, and outcome reported time as variables. Secondary outcomes assessed changes in the annualized relapse rate (ARR).

Results: Thirteen studies, involving 604 SPMS patients, met the inclusion criteria. Following a mean follow-up of two years, the mean difference in EDSS scores (ΔEDSS=EDSS pre-RTX − EDSS post-RTX) was -0.21 (95% CI -0.51 to 0.08, p=0.16), indicating no significant variation. Multivariable meta-regression identified significant associations between EDSS score mean difference and pre-RTX EDSS scores, disease duration at RTX initiation, and outcome reported time. However, age at RTX initiation showed no significant association. Pre- and post-RTX ARR data were available for 245 out of 604 SPMS patients across 7 studies, revealing a mean difference in ARR (ΔARR=ARR pre-RTX − ARR post-RTX) of 0.74 (95% CI 0.19 to 1.29, p=0.008).

Conclusion: RTX demonstrates efficacy in reducing relapse frequency and exhibits potential in stabilizing disability progression over a 2-year follow-up, particularly among individuals with shorter disease duration.

P-27

Long-Term Safety, Effectiveness, and Corticosteroid-Sparing Effects of Eculizumab in Patients With AQP4-Ab+ Neuromyelitis Optica Spectrum Disorder: Real-World Data From Japan

Noriko Isobe[1], Jin Nakahara[2], Ichiro Nakashima[3], Hiroaki Yokote[4], Kou Hasegawa[5], Kazuo Fujihara[6]

[1]Kyushu University, Fukuoka, Japan

[2]Keio University School of Medicine, Tokyo, Japan

[3]Tohoku Medical and Pharmaceutical University, Sendai, Japan

[4]Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan

[5]Alexion Pharma GK, Tokyo, Japan

[6]Department of Multiple Sclerosis Therapeutics, Fukushima Medical University School of Medicine, Fukushima, Japan and Multiple Sclerosis and Neuromyelitis Optica Center, Southern TOHOKU Research

Institute for Neuroscience, Koriyama, Japan

Background: Eculizumab (ECU) has been commercially available in Japan for >4 yrs for the prevention of relapses in adults with anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD). Regulatory-mandated postmarketing surveillance (PMS) of its real-world use is ongoing from approval (Nov 2019).

Objective: To assess real-world long-term safety and effectiveness of ECU in patients (pts) with AQP4-Ab+ NMOSD and evaluate changes in concomitant oral corticosteroid (OCS) use.

Methods: This PMS interim analysis assessed the safety and effectiveness of ECU and OCS use in pts with AQP4-Ab+ NMOSD and ≥1 case report form locked in Japan from approval (Nov 2019) to data cutoff (Oct 2023).

Results: In the effectiveness set (n=155), 93.4% of pts were female, mean disease duration was 5.4 yrs (SD±6.0), and mean age was 50.3 yrs (SD±13.8); values were similar for the safety set (n=151). Median treatment duration was 52.1 wks (range, 0.1-174.3). In the safety set, adverse drug reactions (ADRs) were reported in 31 pts (20.0%); 14 pts (9.0%) reported serious ADRs. No meningococcal infections were observed. In the 2 yrs before ECU, 173 relapses were reported (annual relapse rate [ARR] 0.57/patient-year [PY]) in 95 pts. During ECU treatment (184.1 PY), 11 physician-determined relapses from 7 pts were reported (ARR 0.06/PY). The proportion of pts taking prednisolone (PSL) ≥10 mg/day decreased from 60.3% at baseline (0-4 wks after ECU) to 12.2% at 100-104 wks after ECU. PSL ≤5 mg/day use increased from 17.9% to 68.2%. PSL average daily dose decreased from 16.0 mg/day (SD±10.7) before ECU initiation to 7.7 mg/day (SD±5.9) at 100-104 wks after ECU.

Conclusion: This is the longest observational, real-world safety/effectiveness study among biologics in pts with AQP4-Ab+ NMOSD. ECU was associated with robust relapse prevention and decreased concomitant OCS use over time, suggesting a steroid-sparing effect.

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P-28

Post-marketing Surveillance of Inebilizumab for Neuromyelitis Optica Spectrum Disorder in Japan (Third interim analysis): Safety and Effectiveness

Kazuo Fujihara[1], Yoshito Nagano[2], Yoshikazu Naito[3], Hideaki Hida[3], Muneyoshi Kudo[3], Satoshi Yuki[3], Shinya Hirota[3], Kyoko Kato[3]

[1]*Department of Multiple Sclerosis Therapeutics, Fukushima Medical University*
[2]*Shion Daini Clinic*
[3]*Mitsubishi Tanabe Pharma Corporation*
Background: Inebilizumab (INE) was approved as a drug for preventing recurrence of neuromyelitis optica spectrum disorder (NMOSD) in Japan. A post-marketing surveillance (all-case surveillance, UMIN000044431) has been conducted in Japan since June 2021 to collect information on the long-term safety and effectiveness of INE.
Objective: We report the safety and effectiveness of INE in real-world clinical practice in Japan based on the third interim analysis of this surveillance.
Methods: Among patients (pts) with NMOSD who have received INE in this surveillance, the interim analysis was conducted for 142 pts whose data were locked as of December 2023 and who consented to publication. Of them, all 142 pts were included in the safety analysis set and 138 pts were included in the effectiveness analysis set in this presentation.
Results: The median observation period in the safety analysis set was 50.5 (range: 14–773) days. Adverse drug reactions (ADRs) occurred in 26 pts (18.3%), of which serious ADRs occurred in eight pts (5.6%) and one pt, as previously reported, died due to interstitial lung disease. Among ADRs listed in the safety specification of the risk management plan for this surveillance, those observed were infusion reaction (n=9) and infections (n=6 [urinary tract infection, n=2; COVID-19, n=4]). Among 138 pts in the effectiveness analysis set, four pts experienced a single optic neuritis attack each. Three of the four pts experienced the optic neuritis attack between 1 and 1.5 years after the last attack before INE treatment. Also, of the four pts who relapsed, two pts each experienced a relapse while tapering oral glucocorticoids (GCs), and one pt experienced a relapse after discontinuing both oral GCs and immunosuppressants.
Conclusion: "We presented the safety and effectiveness of INE in the interim analysis of ongoing surveillance, with final results reported in the future.
The data were presented at 65th Annual Meeting of the Japanese Society of Neurology (May 29-June 1, 2024)."
Disclosures: Kazuo Fujihara has received lecture fees for attending meetings/making presentations from Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, Novartis Pharma, and Biogen Japan; also belongs to Southern TOHOKU Research Institute for Neuroscience. Yoshito Nagano is a physician of Shion Daini Clinic. Yoshikazu Naito, Hideaki Hida, Muneyoshi Kudo, Satoshi Yuki, Shinya Hirota, Kyoko Kato are employees of Mitsubishi Tanabe Pharma Corporation.

P-29

Insights into rituximab failure rates in neuromyelitis optica spectrum disorder : real-world data from a multicenter study

Ho Jin Kim[1], Su-Hyun Kim[1], Ju-Hong Min[2], Yeon Hak Chung[2], Woohee Ju[3], Sung-Min Kim[3], Eun-Jae Lee[4], Young-Min Lim[4], Ha Young Shin[5], Young Nam Kwon[5], Eunhee Sohn[6], Sooyoung Kim[6], Min Su Park[7], Tai-Seung Nam[8], Byeol-A Yoon[9], Jong Kuk Kim[9], Kyong Jin Shin[10], Yoo Hwan Kim[11], Jin Myoung Seok[12], Jeong Bin Bong[13], Sohyeon Kim[14], Hung Youl Seok[14], Sun-Young Oh[15], Ohyun Kwon[16], Sunyoung Kim[17], Suk Yoon Lee[18], Nam-Hee Kim[19], Eun Bin Cho[20], Sa-Yoon Kang[21], Seong-il Oh[22], Jong Seok Bae[23], Suk-Won Ahn[24], Ki Hoon Kim[25], You-Ri Kang[1], Seong Ho Choo[2], Jae-Won Hyun[1]
[1]*Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Korea.*
[2]*Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea*

[3]*Department of Neurology, Seoul National University College of Medicine, Seoul, Korea*
[4]*Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea*
[5]*Department of Neurology, Yonsei University College of Medicine, Seoul, Korea*
[6]*Department of Neurology, Chungnam National University of Hospital, Daejeon, Korea*
[7]*Parkminsu Neurology Clinic, Daegu, Korea*
[8]*Department of Neurology, Chonnam National University Hospital, Korea*
[9]*Department of Neurology, Dong-A University College of Medicine, Busan, Korea*
[10]*Department of Neurology, Haeundae-Paik Hospital, Inje University, College of Medicine, Busan, Korea*
[11]*Department of Neurology, Hallym University Sacred Heart Hospital, College of Medicine, Hallym University, Anyang, Republic of Korea*
[12]*Department of Neurology, Soonchunhyang University Hospital Cheonan, Soonchunhyang University College of Medicine, Cheonan, Korea*
[13]*Department of Neurology, Chosun University Hospital, Gwangju, Korea*
[14]*Department of Neurology, Dongsan Hospital, Keimyung University School of Medicine, Daegu, Korea.*
[15]*Department of Neurology, Jeonbuk National University Hospital, Jeonju-si, Korea*
[16]*Department of Neurology, Uijeonbu Eulji Medical Center, Eulji University School of Medicine, Uijeongbu, Korea*
[17]*Department of Neurology, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea*
[18]*Department of Neurology, Inje University Busan Paik Hospital, Inje University College of Medicine, Busan, Korea*
[19]*Department of Neurology, Dongguk University Ilsan Hospital, Goyang, Korea*
[20]*Department of Neurology, Gyeongsang National University Changwon Hospital, Changwon, Korea*
[21]*Department of Neurology, Jeju National University Hospital, Jeju National University School of Medicine, Jeju, Korea*
[22]*Department of Neurology, Kyung Hee University Medical Center, Seoul, Korea*
[23]*Department of Neurology, Kangdong Sacred Heart Hospital, Hallym University college of medicine, Seoul, Korea*
[24]*Department of Neurology, Chung-Ang University Hospital, Seoul, Korea*
[25]*Department of Neurology, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Korea*

Background: Recent treatments like eculizumab, ravulizumab, satralizumab, and inebilizumab have been approved to prevent relapses in neuromyelitis optica spectrum disorder (NMOSD). However, their high costs limit their use as first-line therapy. Rituximab, although off-label, is preferred due to its efficacy, safety, and lower cost.

Objective: We conducted a nationwide study in South Korea to assess the real-world failure rate of rituximab in NMOSD patients.

Methods: In February 2024, we retrospectively collected clinical data on seropositive NMOSD patients who started rituximab treatment from 22 centers in South Korea.

Results: Among 1218 seropositive NMOSD patients, 605 (49.6%) initiated rituximab treatment, with 75 (12.4%) using it as a first-line treatment. The total follow-up period for rituximab-treated patients was 3168 patient-years, with a median treatment duration of 47 months (IQR, 15,87). By February 2024, 525 (86.7%) of the patients were still on rituximab, 41 (6.7%) had switched to other treatments, 11 (1.8%) had died, and 28 (4.6%) were lost to follow-up. During rituximab treatment, 117 (19.3%) patients experienced at least one relapse. Severe relapse at least once occurred in 45 (7.4%) patients, and EDSS worsening was observed in 27 (4.4%) patients. Patients with two or more relapses or one severe relapse were 68 (11.2%). Of 41 patients who discontinued rituximab, 17 (2.8%) patients did due to relapse, 13 (2.1%) patients due to side

effects, and 11 (1.8%) due to other reasons, mainly cost.
Conclusion: Rituximab prevented relapses in NMOSD patients, with 81% of 610 relapse-free and 93% free from severe relapse over four years. However, 13% experienced failure, marked by relapses, a severe relapse, or discontinuation due to adverse events.

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Effectiveness of Satralizumab, an Interleukin-6 Receptor Inhibitor, for Neuromyelitis Optica Spectrum Disorder in a Real-world Clinical Setting in Japan: A Six-month Interim Analysis of a Multicentre Medical Chart Review

Kazuo Fujihara[1], Noriko Isobe[2], Katsuichi Miyamoto[3], Masaaki Niino[4], Jin Nakahara[5], Satoshi Hattori[6], Mamoru Yamamoto[7], Izumi Kawachi[8], Naoko Matsui[9], Chiyoko Nohara[10], Norito Kokubun[11], Norio Chihara[12], Tatsuro Misu[13], Kazumasa Okada[14], Katsuhisa Yamashita[15], Tadashi Nagatsuka[15], Hiroki Adachi[15], Ichiro Nakashima[16]

[1]Department of Multiple Sclerosis Therapeutics, Fukushima Medical University School of Medicine, Fukushima, Japan; Multiple Sclerosis and Neuromyelitis Optica Center, Southern TOHOKU Research
[2]Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[3]Department of Neurology, Wakayama Medical University, Wakayama, Japan
[4]Department of Clinical Research, National Hospital Organization Hokkaido Medical Center, Sapporo, Japan
[5]Department of Neurology, Keio University School of Medicine, Tokyo, Japan
[6]Department of Biomedical Statistics, Graduate School of Medicine and Integrated Frontier Research for Medical Science Division, Institute for Open and Transdisciplinary Research Initiatives (OTRI), Osaka University, Osaka, Japan
[7]Department of Neurology, Faculty of Medicine, University of Toyama, Toyama, Japan
[8]Medical Education Center, Niigata University School of Medicine, Niigata, Japan; Department of Neurology, Brain Research Institute, Niigata University, Niigata, Japan
[9]Department of Neurology, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan
[10]Department of Neurology, Tokyo Metropolitan Ebara Hospital, Tokyo, Japan
[11]Department of Neurology, Dokkyo Medical University, Tochigi, Japan
[12]Division of Neurology, Kobe University Graduate School of Medicine, Kobe, Japan
[13]Department of Neurology, Tohoku University, Sendai, Japan
[14]Department of Neurology, University of Occupational and Environmental Health, Kitakyushu, Japan
[15]Chugai Pharmaceutical Co., Ltd., Tokyo, Japan
[16]Division of Neurology, Tohoku Medical and Pharmaceutical University, Sendai, Japan

Background: Satralizumab, an interleukin-6 receptor inhibitor, has been approved for relapse prevention in anti–aquaporin-4 antibody–positive neuromyelitis optica spectrum disorder (AQP4[+] NMOSD) in Japan. However, limited real-world data are available on satralizumab in Japan.
Objective: SAkuraBeyond was designed to evaluate the effectiveness and safety of satralizumab in patients with AQP4[+] NMOSD for up to 2.5 years in a real-world clinical setting in Japan. Herein, we present the 26-week interim effectiveness analysis.
Methods: This observational study evaluated 124 of 125 enrolled satralizumab-treated patients with AQP4[+] NMOSD from 25 sites in Japan (1 patient met the exclusion criteria). Patients aged ≥7 years with a documented diagnosis of AQP4[+] NMOSD (including neuromyelitis optica [NMO]) before satralizumab

treatment, and who initiated satralizumab treatment on or after August 26, 2020, were enrolled in this study. Data for 52 weeks prior to and 26 weeks after initiating satralizumab were evaluated. The anticipated satralizumab exposure was based on the Japanese prescribing information (subcutaneous dose: initial [120 mg at weeks 0, 2, and 4] and maintenance dose [120 mg at 4-weekly intervals thereafter]). The primary endpoints included annualized relapse rate (ARR, 95% confidence interval [CI]), and relapse-free rate (Kaplan-Meier method) at Week 26. Secondary endpoints included changes in oral glucocorticoid (GC) and immunosuppressant therapy (IST: azathioprine [AZA], tacrolimus [TAC]) doses over 26 weeks among relapse-free patients. Per protocol, safety will be evaluated at the final analysis.

Results: Baseline (BL) mean±SD age was 51.1±14.0 years (females, 93.5%), disease duration (n=113) was 7.0±6.0 years, and number of relapses (past 52 weeks) was 0.4±0.7. At BL 73.4% used oral GC, 16.9% used AZA, and 35.5% used TAC with satralizumab. ARR [95% CI] decreased from within 52 weeks prior to 26 weeks after satralizumab initiation (0.445 [0.342–0.580] to 0.069 [0.026–0.183]); relapse-free rate was 96.6% at Week 26. Relapse symptoms were not severe and 1 of 4 relapse patients was treated with hospitalization. Among relapse-free patients (n=120), the oral GC dose decreased from 10.5±10.4 mg/day at BL to 7.2±8.9 mg/day (0 mg/day, 30.8%; >0–≤5 mg/day, 18.7%; >5–≤10 mg/day, 28%) at Week 26. The oral GC dose decreased from 14.3±9.6 mg/day (n=87) to 9.5±9.3 mg/day (n=78: 0 mg/day, 9%; >0–≤5 mg/day, 24.4%; >5–≤10 mg/day, 37.2%) at Week 26 in patients with oral GC dose >0 mg/day at BL. Of those receiving AZA (n=20) and TAC (n=44) at BL, 35.3% and 26.2% discontinued the IST, respectively, at Week 26.

Conclusion: The real-world relapse-free rate at Week 26 in satralizumab-treated patients with AQP4[+] NMOSD was 96.6% and the relapse symptoms were not severe. These results support the relapse-preventive effect of satralizumab shown in the Phase 3 study.

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Real-World Treatment Adherence and Persistence with Eculizumab (C5 Inhibitor) or Satralizumab in Patients With Neuromyelitis Optica Spectrum Disorder in Japan

Norio Chihara[1], Justin Lee[2], Jeffrey C Yu[2], Tatsuro Misu[3]
[1]*Kobe University Graduate School of Medicine, Kobe, Japan*
[2]*Alexion, AstraZeneca Rare Disease, Boston, MA, USA*
[3]*Tohoku University Hospital, Sendai, Japan*

Background: Eculizumab (ECU) (complement component 5 inhibitor) and satralizumab (SAT) (interleukin-6 receptor inhibitor) are approved treatments for neuromyelitis optica spectrum disorder (NMOSD) in Japan.
Objective: To compare real-world treatment adherence and persistence with ECU vs SAT in patients (pts) with NMOSD in Japan.
Methods: Retrospective observational study used data from Japan Medical Data Vision database, covering ~45 million pts in Japanese hospitals. Evaluated treatment adherence (number of treated days, proportion of days covered [PDC], continuous multiple-interval measure of gaps [CMG], observed vs expected doses ratio [OvEDR]) and treatment persistence (proportion of pts without treatment discontinuation) in adult pts with NMOSD treated with ECU or SAT. Primary treatment persistence analysis used a maximum gap of 3 times normal dosing interval (ECU, 6 weeks; SAT, 12 weeks); a sensitivity analysis used maximum gap of 2 months. Study period: 01/01/2016 to 30/06/2023, with 1-year follow-up since treatment initiation.
Results: 132 pts met study criteria: 31 (23%) received ECU, 101 (77%) received SAT. ECU pts were younger (50.2 years [SD 11.2]) vs SAT pts (55.2 years [SD 13.7]; P=0.046). Comedication rates were similar at baseline and over time. Mean number (SD) of treated days: 344.3 (16.4) for ECU and 314.4 (68.1) for SAT. Mean (SD) treatment adherence was slightly higher in ECU vs SAT: 94.3% (4.5%) vs 86.1% (18.7%) for PDC, 5.7% (4.5%) vs 13.9% (18.7%) for CMG, and 94.1% (5.1%) vs 81.9% (17.7%) for OvEDR, respectively; P<0.001 for all. Treatment persistence per primary analysis was 100% for ECU and 91.1% for SAT (P=0.09)

and per sensitivity analysis was 100% for ECU and 90.1% for SAT (P=0.073).
Conclusion: Treatment adherence and persistence were slightly higher in pts with NMOSD receiving ECU vs SAT in Japan. Future larger scale studies of adherence and persistence in NMOSD treatment are desirable.
Disclosures: NC has received funding for travel and/or speaker honoraria from AbbVie, Alexion, Biogen, Chugai, Mitsubishi Tanabe, Novartis, and Takeda. JL is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca. JCY is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca. TM has received speaker honoraria from Alexion, Biogen Idec Japan, Mitsubishi Tanabe, Novartis, Teijin, Viela Bio; research support from Cosmic Corporation and Medical and Biological Laboratories Co.; and Grant-in-Aid for scientific research from Ministry of Education, Culture, Sports, Science, and Technology.

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Relationship between glucocorticoids and vertebral fractures in MS and NMOSD
Yuu-ichi Kira[1], Yurino Yamazaki[2], Mitsuru Watanabe[1], Katsuhisa Masaki[1], Kazunori Iwao[1], Eizo Tanaka[1], Koji Shinoda[1], Ryo Yamasaki[1], Noriko Isobe[1]
[1] Department of Neurology, Graduate School of Medical Sciences, Kyushu University
[2]Department of Medicine, School of Medicine, Kyushu University
Background: Vertebral fracture is one of the well-known complications of glucocorticoids. However, the relationship between glucocorticoids and vertebral fractures is not well studied in patients with multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD).
Objective: To assess the relationship between glucocorticoid usage and vertebral fractures than in MS and NMOSD using sequential whole spine MRI images.
Methods: We retrospectively investigated 125 patients with MS and 49 with NMOSD who had at least two whole spine MRIs by 2020. Patients with a vertebral fracture at the time of later MRI was defined as having a new fracture. We compared the frequency of vertebral fractures between MS and NMOSD and performed a multivariate regression analysis for new vertebral fractures.
Results: New vertebral fractures occurred in 14/49 (28.6%) NMOSD and 4/125 (3.2%) MS patients, demonstrating significantly higher incidence of vertebral fractures in NMOSD than MS ($P < 0.05$). The median observation period was 109 months for NMOSD and 79 months for MS, with no significant differences. Multivariate regression analysis revealed that, irrespective of MS or NMOSD, receiving daily prednisolone ≥ 5 mg/day (compared to < 5 mg/day) (OR 19.14 [95%CI 1.10-332.34]), older age (OR 1.12 [1.04-1.20]), and longer observation period (OR 1.04 [1.01-1.07]) were independent risk factors for novel vertebral fractures.
Conclusion: Glucocorticoid ≥ 5 mg/day is a strong risk factor for vertebral fractures, irrespective of MS or NMOSD. Treatment strategies should be carefully considered to prevent of both relapses and vertebral fractures.

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Deciphering Immune Heterogeneity in Response to First-Line Therapy in Patients with Multiple Sclerosis
Sungmin Cheong[1], Hyo Jae Kim[1], Young Nam Kwon[2], Hyun Je Kim[3], Jong-Eun Park[1], Sung-Min Kim[4]
[1] Korea Advanced Institute of Science and Technology (KAIST)
[2]Severance Hospital, Yonsei University College of Medicine
[3]Seoul National University College of Medicine

[4]*Seoul National University Hospital, Seoul National University College of Medicine*
Background: Multiple sclerosis (MS) is a central nervous system (CNS) inflammatory demyelinating disease, and it exhibits various symptoms with differing severity or courses. Since current disease modifying therapies for MS (DMTs) have diverse safety and efficacy profiles, predicting the treatment response to DMT is crucial for optimizing the prognosis.
Objective: This study aims to reveal immune heterogeneity in PwMS regarding treatment response to intermediate efficacy DMTs, postulating that immunopathological variances underlie observed heterogeneities in therapeutic responsiveness.
Methods: In total, 13 PwMS who were treatment-naïve and met the international panel criteria for MS, were enrolled. Longitudinal blood samples were taken from patients both prior to and consequent to the administration of DMT. All patients were categorized into intermediate efficacy DMT responder and non-responder groups. The intermediate efficacy DMT included interferon-beta, dimethyl fumarate, and teriflunomide. The responder group was defined as a patient who satisfied NEDA-3 without changing DMT. Peripheral blood mononuclear cells were isolated from blood samples and then were cryopreserved. Single-cell cDNA synthesis was generated using the Single Cell 5' and V(D)J Reagent Kits (10X Genomics) and sequencing was carried out on an NovaSeq (Illumina). The Scanpy and Scirpy Python packages with custom Python codes were used for analyzing sequencing data. Cell proportions, gene expression features, and T cell clonality were analyzed. For differentially expressed gene (DEG) analysis, generalized linear model provided by pyDESeq2 were used.
Results: Longitudinal blood samples were taken from 13 patients (5 responders and 8 non-responders) both prior to and consequent to the administration of DMT, yielding a total of 104,432 PBMCs. We investigated immune phenotypes distinguishing responders from non-responders, discovering that the most variable transcriptomic markers originated from T cell populations. Correspondingly, the responder group had a significantly higher proportion of CD8+ T cells. Within the T cell subset, the responder group showed an elevated proportion of effector memory CD8+ T cells, terminally differentiated effector memory CD8+ T cells, and cytotoxic CD4+ T cells. Also, the TCR clonality of cytotoxic T cell subsets was significantly higher in the responder group. Conversely, monocytes, cDCs, and B cells in the non-responder group demonstrated an increase in the type 1 IFN signatures. Following DMT, the augmented T cell subsets in the responder group regressed to levels observed in the non-responder group.
Conclusion: PwMS with higher cytotoxic T cells might be crucial in disease pathogenesis. This finding highlights immunological heterogeneity, aids in predicting therapeutic responses, and helps identify candidates for early initiation of high-efficacy DMTs.

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The Behaviour Of Serum CH50 In AQP4-NMOSD Patients Treated With Complement C5-inhibitory Therapies.

Satoshi Kitagawa[1], Jin Nakahara[1], Koji Sekiguchi[1], Haruhiko Motegi[1], Kenji Kufukihara[1], Tatshuo Iwashita[2]
[1] *Keio University Hospital*
[2]*Inagi Municipal Hospital*
Background: The classical complement pathway is responsible for astrocytic lysis by anti-aquaporin 4 (AQP4) antibodies in neuromyelitis optica-spectrum disorders (NMOSD). Eculizumab (ECU) and ravulizumab (RAV) are complement C5 inhibitory therapies (C5ITs) approved for AQP4-NMOSD, however direct measurements of C5 activities are unavailable in clinics.

Objective: CH50 (50% hemolytic complement activity) is a biomarker to measure the activity of classical complement pathway in general, thus we evaluated its utility to monitor the efficacy of C5ITs in AQP4-NMOSD patients.
Methods: We collected 16 longitudinal CH50 datasets from 15 AQP4-NMOSD patients treated with C5ITs at Keio University Hospital and subclassified into five groups: continuous ECU group (n=1), ECU-to-RAV switch group (n=11), continuous RAV group (n=1), RAV-to-other (non-C5ITs) switch group due to C5 genetic polymorphism (n=1), and RAV-to-other (non-C5ITs) switch group due to other reasons (n=2). This study was approved by the Ethics Committee of Keio University School of Medicine.
Results: In the continuous ECU and RAV groups, CH50 rapidly decreased and became undetectable (<10U/ml) within weeks. In the ECU-to-RAV switch group, eight cases maintained undetectable CH50 levels before and after the switch, whereas three cases showed slight increase and maintained 10-13U/ml CH50 levels after the switch. In the RAV-to-other switch group due to C5 genetic polymorphism, CH50 remained within normal range (30-45U/ml) even under RAV, suggestive of inefficacious blockade of the classical complement pathway. In the RAV-to-other switch group due to other reasons, one case experiencing relapse shortly after the switch showed rapid elevation of CH50, while the other case without relapse maintained very low CH50 level (12.9U/ml) even at 16 weeks after the switch (to satralizumab). Of note, certain discordance between the actual C5 activity and CH50 levels under RAV in atypical hemolytic uremic syndrome has previously been reported (Cataland et al, Blood 134:1099 (2019)).
Conclusion: CH50 may be useful in monitoring the efficacy of C5ITs in AQP4-NMOSD. Minimal and uneventful increase in CH50 may occur by the ECU-to-RAV switch. A possible association of the increased CH50 and relapse after the switch should be studied further.

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The Effects of Anti-CD40 Blockade on B cell Differentiation and T cell Activation in a Marmoset EAE model: Preliminary results
Ohn Dong Seok[1], Chung-Gyu Park[2], Jae Won Jung[3], Geon Woo Park[4], Seong-Jun Kang[2], Yong-Hee Kim[2], Hyun Je Kim[2], Sung Min Kim[1]
[1]*Department of Neurology, Seoul National University, College of Medicine*
[2]*PB Immune Therapeutics*
[3]*Department of Interdisciplinary Program of Cancer Biology, Seoul National University Graduate School*
[4]*Department of Biomedical Sciences, Seoul National University Graduate School, Seol, Korea*
Background: Costimulation by CD40 and its ligand CD40L (CD154) is pivotal for the functional differentiation of T cells, playing a critical role in immune responses. Preclinical studies have highlighted the therapeutic potential of inhibiting the CD40-CD40L pathway in experimental models of multiple sclerosis (MS).
Objective: This study investigates the mode of action of Chi-PB101, an anti-CD40 monoclonal antibody, in modulating immune cell populations and influencing disease progression in a marmoset model of MS.
Methods: The experimental autoimmune encephalomyelitis (EAE) model was induced in marmosets via MOG peptide administration. Two groups were established: MOG+saline (n=2) and MOG+Chi-PB101 treated (n=3). Marmosets were treated weekly with either Chi-PB101 or a placebo from the day of induction (day 0) until the day of sacrifice. Peripheral blood mononuclear cells (PBMCs) were analyzed using single-cell RNA sequencing (scRNA-seq) at pre-induction (day 0), 2 weeks after induction, and various times post-symptom onset.

Results: "Chi-PB101 treated marmosets reached an EDSS score of 20-25 at a median of 12 weeks post-induction, compared to 4 weeks for controls, indicating reduced EAE severity.
Two weeks after EAE induction, compared to the healthy state, the control group showed a significant increase in B cell populations (25.7% to 51%, p-value 0.02), whereas the Chi-PB101 treatment group showed a decrease (25.7% to 9.8%, p-value 0.036). Specifically, plasmablasts increased in the control group (2.8% to 5.3%, p-value 0.048), while the Chi-PB101 treatment group showed a decrease (2.8% to 0.9%, p-value 0.018), implying that Chi-PB101 inhibits plasmablast differentiation through the CD40/CD40L axis. Additionally, an increase in activated CD8+ T cells (marker CD8A) was observed in the control group (10.3% to 27.1%, p-value 0.048), whereas the Chi-PB101 treatment group showed no significant difference (10.3% to 11.7%, p-value 0.5). This reduction is likely due to reduced antigen presentation by B cells."
Conclusion: The anti-CD40 antibody Chi-PB101 alleviates marmoset EAE symptoms by inhibiting plasmablast differentiation and altering the number of activated CD8+ T cells. This study elucidates Chi-PB101's mode of action and its potential as an MS therapeutic.
Disclosures: Funded by PB Immune Therapeutics

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Post-marketing Surveillance of Inebilizumab for Neuromyelitis Optica Spectrum Disorder in Japan (Third interim analysis): Real-world Use of Glucocorticoids

Shinya Hirota[1], Kyoko Kato[1], Yoshikazu Naito[1], Yoshito Nagano[2], Hideaki Hida[1], Muneyoshi Kudo[1], Satoshi Yuki[1], Kazuo Fujihara[3]
[1]*Mitsubishi Tanabe Pharma Corporation*
[2]*Shion Daini Clinic*
[3]*Department of Multiple Sclerosis Therapeutics, Fukushima Medical University*

Background: Inebilizumab (INE) was approved as a drug for preventing recurrence of neuromyelitis optica spectrum disorder in Japan. In N-MOmentum trial, all participants received oral glucocorticoids (GCs) 20 mg/day on day 1-14, tapered to day 21, and no use of immunosuppressants (IMs) was permitted. However, many patients receive oral GCs with INE in Japan.
Objective: We report on the use of oral GCs in real-world clinical practice in Japan based on the latest interim analysis results of the post-marketing surveillance (all-case surveillance, UMIN000044431) that has been conducted since June 2021.
Methods: Among 142 patients whose data were locked as of December 2023 and who consented to publication, we analyzed the doses of oral GCs in 138 patients in the effectiveness analysis set in this presentation after the start of INE treatment.
Results: " The median observation period (min–max) of 142 patients was 50.5 (14–773) days. Among 138 patients in the effectiveness analysis set, the mean daily dose of oral GCs (prednisolone equivalent) was 10.9 [standard deviation (SD): 7.6] mg/day at the start of INE treatment (n=138), 6.0 (SD: 6.1) mg/day at week 26 (n=54), and 5.1 (SD: 5.4) mg/day at week 52 (n=35). The percentage of patients who received no oral GCs was 11.6% (16/138) at the start of INE treatment, 33.3% (18/54) at week 26, and 31.4% (11/35) at week 52. While one patient experienced an attack after discontinuing oral GCs, 12 patients discontinued oral GCs without a relapse until the data cut-off date (Patients without a history of IM use during INE treatment, n=7; patients with a history of IM use during INE treatment, n=5).
Conclusion: "Here, we presented the real-world use of oral GCs during INE administration in the interim analysis of ongoing surveillance.

The data were presented at 65th Annual Meeting of the Japanese Society of Neurology (May 29 - June 1, 2024)."

Disclosures: Shinya Hirota, Kyoko Kato, Yoshikazu Naito, Hideaki Hida, Muneyoshi Kudo, Satoshi Yuki are employees of Mitsubishi Tanabe Pharma Corporation. Yoshito Nagano is a physician of Shion Daini Clinic. Kazuo Fujihara has received lecture fees for attending meetings/making presentations from Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, Novartis Pharma, and Biogen Japan; also belongs to Southern TOHOKU Research Institute for Neuroscience.

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Efficacy And Safety Of Tolebrutinib Versus Teriflunomide In Relapsing Multiple Sclerosis: Results From The Phase 3 GEMINI 1 and 2 Trials

Ho Jin Kim[1], Jiwon Oh[2], Douglas L. Arnold[3], Bruce A.C. Cree[4], Carolina Ionete[5], Maria Pia Sormani[6], Sana Syed[7], Yixin Chen[7], Christina R. Maxwell[7], Patrick Benoit[8], Timothy J. Turner[7], Erik Wallstroem[7], Heinz Wiendl[9]

[1]Department of Neurology, National Cancer Center, Goyang, South Korea
[2]St. Michael's Hospital, University of Toronto, Toronto, Canada
[3]McGill University, Montréal, Canada; NeuroRx Research, Montréal, Canada
[4]Department of Neurology, UCSF Weill Institute for Neurosciences, University of California San Francisco, San Francisco, USA
[5]Neuroimmunology/MS Division and Multiple Sclerosis Center, UMass Chan Medical School, Worcester, USA
[6]Department of Health Sciences, University of Genoa, Genoa, Italy; Department of Health Sciences, IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[7]Sanofi, Cambridge, USA
[8]Sanofi, Chilly-Mazarin, France
[9]Department of Neurology with Institute of Translational Neurology, University Hospital Münster, Münster, Germany

Background: Tolebrutinib is a potent, brain-penetrant, and bioactive bruton's tyrosine kinase inhibitor that targets multiple cellular processes thought to be relevant to the disease biology of multiple sclerosis (MS). Tolebrutinib acts rapidly on peripheral B cells and modulates the CNS immune microenvironment thought to be driven by microglia.

Objective: To report the results of the phase 3 GEMINI 1 and 2 trials, which evaluated the efficacy and safety of tolebrutinib compared with teriflunomide in participants with relapsing MS.

Methods: GEMINI 1 (NCT04410978) and GEMINI 2 (NCT04410991) were phase 3, multicentre, randomised, double-blind, double-dummy, active-controlled, parallel-group, event-driven trials. The trials included participants aged 18–55 years with a diagnosis of relapsing MS, Expanded Disability Status Scale (EDSS) score ≤5.5, and either ≥1 relapse within the previous year, ≥2 relapses within the previous 2 years or ≥1 Gd-enhancing T1 brain lesion on magnetic resonance imaging (MRI) within the previous year. Participants were randomised 1:1 to receive oral tolebrutinib (60 mg once daily) or oral teriflunomide (14 mg once daily), each with matching placebo. Stratification factors were EDSS score at screening (<4 vs ≥4) and region (US vs non-US). The primary endpoint was the annualised relapse rate. Secondary endpoints included measures of disability, MRI outcomes, and safety.

Results: These trials enrolled 1873 participants (974 in GEMINI 1 and 899 in GEMINI 2) across 42 countries between June 25, 2020 and August 8, 2022. In the combined trial cohort, baseline mean age was 36.5 years and mean time since diagnosis was 4.3 years. Most participants were female (67%), more than half were

treatment-naïve (63%) and the mean number of relapses in the year prior to enrolment was 1.2. Mean EDSS score was 2.38 (median 2.0; interquartile range 1.5–3.0) and 34.4% of participants had Gd-enhancing T1 lesions at baseline. The last participant visit is expected to occur in July 2024. Efficacy and safety results will be presented at PACTRIMS.
Conclusion: The presented phase 3 GEMINI 1 and 2 trial results will provide a comprehensive assessment of tolebrutinib efficacy and safety in participants with relapsing MS.
Disclosures: HJK: Grant (National Research Foundation of Korea); research (Aprilbio, Eisai); consulting (Alexion, Aprilbio, Altos, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll, Handok, Horizon Therapeutics, MDimune, Mitsubishi Tanabe Pharma, Merck, Novartis, Roche, Sanofi, Teva, UCB); Mult Scler J coeditor; J Clin Neurol associate editor. JO: Consulting and/or speaking (Amgen, Biogen, Eli Lilly and Company, EMD Serono, Novartis, Roche, Sanofi); research (Biogen, Roche). DLA: Personal compensation for serving as a consultant (Alexion, Biogen, Celgene, Eli Lilly and Company, EMD Serono, Frequency Therapeutics, Genentech, Merck, Novartis, Roche, Sanofi, Shionogi); equity interest (NeuroRx). BACC: Consulting (Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Horizon, Immunic, Neuron23, Novartis, Sandoz, Sanofi, Siemens, TG Therapeutics, Therini); research (Genentech). CI: Grants (Genentech); scientific advisor (Sanofi). MPS: Fees (Biogen, Merck, Roche, Sanofi, Novartis, Geneuro, GSK); grants (Italian Multiple Sclerosis Foundation). SS, YC, CRM, PB, TJT, and EW: Employees of Sanofi (may hold shares and/or stock options in the company). HW: Honoraria (AbbVie, Alexion, Argenx, Biogen, BMS, F Hoffmann-La Roche, Janssen, Merck, Neurodiem, Novartis, Roche, Sanofi, Teva, WebMD); consulting (AbbVie, Actelion, Argenx, Biogen, BMS, EMD Serono, Fondazione Cariplo, Gossamer Bio, Idorsia, Immunic, Immunovant, Janssen, Lundbeck, Merck, NexGen, Novartis, PSI, Roche, Sanofi, Swiss Multiple Sclerosis Society, UCB, Worldwide Clinical Trials); research funding (German Ministry for Education & Research, Deutsche Forschungsgesellschaft, Deutsche Myasthenie Gesellschaft, Alexion, Amicus, Argenx, Biogen, CSL, F Hoffmann-La Roche, Merck, Novartis, Roche, Sanofi, UCB).

P-38
Dosages of Rituximab and Treatment Outcomes in a Cohort of Patients with Neuromyelitis Optica Spectrum Disorders: A Real-World Registry Based Data Study from South India
Pritam Majumdar[1], Thomas Mathew[1], Shagun Bhardwaj[1], Surabhi Garg[1], Akshata Huddar[1], Sonia Shivde[1], Sagar Badachi[1], Raghunandan Nadig[1], Sharath Kumar GG[1], Sai Kanth[1], Sindhu V Nambiar[1], Gosala Raja Kukkuta Sarma[1]
[1]*St Johns National Academy of Health Sciences Bengaluru*
Background: Rituximab is the most widely used drug for preventing relapses in neuromyelitis optica spectrum disorder (NMOSD) in India. The usual dosages used and their treatment outcomes are presented in this paper.
Objective: To investigate the treatment outcomes and safety of rituximab with different dosages in NMOSD patients.
Methods: In this retrospective study, medical records were reviewed, and telephonic interviews were conducted for 40 NMOSD patients who had completed at least one year of follow-up after receiving at least one dose of rituximab. Diagnoses of NMOSD were made using the 2015 International Consensus Criteria for NMOSD.
Rituximab dosages were categorized into induction and maintenance doses. Induction was further divided into three regimens: high-dose (2 grams divided over two weeks), medium-dose (single 1-gram infusion),

and low-dose (single 500-milligram dose). Maintenance therapy consisted of either low-dose (500 milligrams every six months) or high-dose (1 gram every six months) regimens.
Results: The median age of patients in our study was 39.5 years (range 14-64), with the majority being female [n=32 (80%)]. 72.5% of patients tested positive for the anti-aquaporin-4 antibody. The median duration of rituximab treatment was 48 months (range 12-120). After initiating rituximab, 90% of patients either stabilized or improved. The annualized relapse rate (ARR) decreased significantly [median ARR pre-treatment 0.05 vs post-treatment 0 (p=0.01)]. Significant improvements were also seen in the mRS (p=0.01) & EDSS vision scale (p=0.01). Of all patients, 42.5% received high-dose induction, 30% received medium-dose induction, and 27.5% received low-dose induction. For maintenance, 60% were on the low-dose regimen, 30% were on the high-dose regimen & 10% received only an induction dose. 10% relapsed after a low-maintenance regimen due to B cell repopulation & 10% relapsed due to non-adherence. 10% of patients had pneumonia & 5% had urinary tract infections, all on the high-dose regimen.
Conclusion: RTX is well-tolerated, lowers the frequency of relapses, and improves disability outcomes in the majority of patients with NMO. High dose maintenance regimens though more effective are associated with more infections.
Disclosures: Nothing to disclose.

P-39

Efficacy And Safety of Tolebrutinib Versus Placebo In Non-Relapsing Secondary Progressive Multiple Sclerosis: Results From The Phase 3 HERCULES Trial

Ho Jin Kim[1], Robert J. Fox[2], Amit Bar-Or[3], Anthony Traboulsee[4], Celia Oreja-Guevara[5], Gavin Giovannoni[6], Patrick Vermersch[7], Sana Syed[8], Ye Li[9], Wendy S. Vargas[8], Timothy J. Turner[8], Erik Wallstroem[8], Daniel S. Reich[10]
[1]*Department of Neurology, National Cancer Center, Goyang, South Korea*
[2]*Mellen Center for Multiple Sclerosis, Cleveland Clinic, Cleveland, USA*
[3]*Center for Neuroinflammation and Experimental Therapeutics and Department of Neurology, University of Pennsylvania, Philadelphia, USA*
[4]*Division of Neurology, The University of British Columbia, Vancouver, Canada*
[5]*Department of Neurology, University Hospital San Carlos, Madrid, Spain*
[6]*Queen Mary University London, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK*
[7]*University of Lille, Inserm U1172, CHU Lille, FHU Precise, Lille, France*
[8]*Sanofi, Cambridge, USA*
[9]*Sanofi, Bridgewater, USA*
[10]*Translational Neuroradiology Section, National Institutes of Health, Bethesda, USA*

Background: Tolebrutinib is a potent, brain-penetrant, and bioactive BTKi that targets B cells and microglia, and has the potential to modulate MS related pathological processes leading to disability. It is being investigated in four phase 3 trials for MS, including non-relapsing secondary progressive MS (nrSPMS), for which there are no approved treatments.
Objective: To report the results of the phase 3 HERCULES trial, which evaluated the efficacy and safety of tolebrutinib in participants with nrSPMS.
Methods: HERCULES (NCT04411641) was a phase 3, multicentre, randomised, double-blind, placebo-controlled, parallel-group, event-driven trial. Participants were 18–60 years of age with SPMS and had an Expanded Disability Status Scale (EDSS) score of 3.0–6.5, inclusive, documented evidence of disability

progression during the prior 12 months, and no clinical relapses during the prior 24 months before screening. Participants were randomised 2:1 to receive oral tolebrutinib (60 mg once daily) or matching placebo. Stratification factors were age (<40 vs ≥40 years) and region (US vs non-US). The primary endpoint was time to onset of 6-month confirmed disability progression as measured by EDSS. Secondary endpoints included additional measures of disability, magnetic resonance imaging outcomes and safety.
Results: A total of 1131 participants were randomised across 31 countries between October 23, 2020, and January 12, 2023. At baseline, the overall mean age was 48.9 years, and 62% were female. Mean time since relapsing-remitting MS symptom onset was 17.3 years, and mean time since most recent relapse was 7.5 years. Most participants (77%) had previously received ≥1 disease-modifying therapies. At baseline, mean EDSS score was 5.53 (median 6.0; interquartile range 5.0–6.3), 12.8% of participants had gadolinium-enhancing T1 lesions, and mean (standard deviation) T2 lesion volume was 18.9 (14.6) cm3. The last participant visit is expected to occur in July 2024. Efficacy and safety results will be presented at PACTRIMS.
Conclusion: The presented HERCULES trial results will provide a comprehensive assessment of tolebrutinib efficacy and safety in participants with nrSPMS.
Disclosures: HJK: Grant (National Research Foundation of Korea); research (Aprilbio, Eisai); consulting (Alexion, Aprilbio, Altos, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll, Handok, Horizon Therapeutics, MDimune, Mitsubishi Tanabe Pharma, Merck, Novartis, Roche, Sanofi, Teva, UCB); Mult Scler J coeditor; J Clin Neurol associate editor. RJF: Consulting (AB Science, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Greenwich Biosciences, Immunic, INmune Bio, Eli Lilly and Company, Janssen, Novartis, Sanofi, Siemens, TG Therapeutics) and research support (Biogen, Novartis, Sanofi). AB-O: Grant support to the University of Pennsylvania (Biogen Idec, EMD Serono, Novartis, Roche Genentech); speaking and/or consulting (Accure, Atara Biotherapeutics, Biogen, Bristol-Myers Squibb, EMD Serono, GlaxoSmithKline, Gossamer, Janssen, Medimmune, Novartis, Roche Genentech, Sanofi). AT: Consulting and/or speaking and grant/research support (Biogen, EMD Serono, Roche, Sanofi). CO-G: Speaking and/or consultancy (Bayer, Biogen, Merck Serono, Novartis, Roche, Sanofi, Teva). GG: Consulting/speaking and/or research support (Astoria Biologica, Aurinia Pharmaceuticals, Biogen, BMS-Celgene, GSK, Janssen/J&J, Japanese Tobacco, Merck KGaA/EMD Serono, Moderna, Novartis, Roche/Genentech, Sandoz, Sanofi, Vir Biotechnology, Viracta). PV: Honoraria or consulting (AB Science, Ad Scientiam, Biogen, Celgene-BMS, Imcyse, Merck, Novartis, Roche, Sanofi); research support (Biogen, F. Hoffmann-La Roche, Merck, Novartis, Sanofi). SS, YL, WSV, TT, and EW: Employees of Sanofi (may hold shares and/or stock options in the company). DSR: Grant/research support (Abata, Sanofi).

P-40

A report of long-term rituximab use in patients with multiple sclerosis: (Is it safe and effective ?)

Nahid Beladi Moghadam[1], Marzieh Khazaei[1], Mehran Ghaffari[1], Sadra Habibi Moini[2]
[1]Shahid Beheshti University of Medical Sciences
[2]Neurology Research Center at IKHC Hospital

Background: Before 2017 when FDA approved Ocrelizumab for relapsing-remitting and primary-progressive multiple sclerosis (PPMS) , Rituximab (RTX) the first anti-CD20 therapy to be used in multiple sclerosis (MS), was a popular option for neurologists to prescribe.
Objective: Rituximab still is used despite of availability of further approved disease modifying drugs (DMDs) in recent years. Since it has been continued for a long time in some patients, it is important to consider its long-term safety and efficacy.
Methods: In a single-center retrospective observational study of patients receiving rituximab for the

treatment of multiple sclerosis with minimum 3 consecutive years duration, we collected demographic characteristics such as age and gender, as well as clinical information including the duration of RTX drug use, illness duration, type of MS, previous DMD, reason for change to RTX, annual attack rate, MRI findings, and side effects. All information were collected from the Hospital Information System (HIS) and patient medical records at the MS clinic of a university Hospital. We included 95 patients.
Results: The average duration of the disease among the patients was 11.45 years. 51% of the patients had been receiving RTX therapy for a duration of 3 to 4 years and 17.9 % more than 5 years. Focusing on changes in the EDSS, 66 cases (69%) had an unchanged EDSS score, whereas 29 cases (30%) showed an increase in their EDSS score. Regarding MRI findings, 75 cases 79%) had stable MRI results, 7 cases (7%) showed new T2-weighted MRI lesions, and 3 cases (3%) had gadolinium-enhanced (GAD+) MRI changes indicative of active inflammation. In terms of relapse, 90 cases (95%) did not report any relapses, whereas 5 cases (5%) experienced relapses . Injection-related side effects were experienced by only 8 out of 95 patients (8.4%). Infectious complications were absent in 58% of the patients, and while 24% were diagnosed with COVID-19. Notably, one case had a malignancy (cervical cancer).
Conclusion: It seems that the long-term use of RTX has a good effect and is well tolerated.

P-41
Efficacy and Safety of Glatiramer Acetate
Akihito Hao[1], Yoko Warabi[1], Kazushi Takahashi[1]
[1]*Tokyo Metropolitan Neurological Hospital*
Background: Glatiramer acetate (GA) has been used as a disease-modifying drug (DMD) for relapsing-remitting multiple sclerosis (RRMS) since its launch in Japan (2015). However, a limited number of real-world data in our country has been reported.
Objective: We aimed to evaluate the efficacy and safety of GA in the Japanese population in a real clinical setting.
Methods: We conducted a single-center retrospective study of the patients with RRMS who were admitted to our department between November 2015 and April 2024 and have been treated with GA.
Results: Twenty-two patients with RRMS (16 females and 6 males) were included in this study. The mean age at disease onset was 33.8 ± 10.6 years. In addition, the mean follow-up period and duration of GA administration were 6.0 ± 3.1 and 2.8 ± 2.3 years, respectively. Under the administration of GA, the mean annualized relapse rate was reduced from 0.6 to 0.1, and the number of new T2 lesions per year was also reduced from 1.8 to 0.9. During the follow-up period, 9 patients (40.9 %) could continue the treatment for its effectiveness, but 13 patients (59.1 %) switched to different DMD. The reasons for the switch were as follows: ineffectiveness in 9 patients, ineffectiveness and infusion site reaction in 2 patients, abnormal blood test results (The causal relationship was unclear.) in 1 patient, and transition from RRMS to secondary progressive MS (SPMS) in 1 patient. In addition, 3 female patients have delivered their babies safely (2 patients continued GA and the other discontinued it).
Conclusion: GA was well tolerated with few severe side effects and safe in pregnancy. In addition, the escalation of DMD was needed in approximately 60 % of the RRMS patients, but the others were stable on GA.

P-42
Outcomes of immunosuppressive therapy discontinuation in patients with myelin oligodendrocyte glycoprotein antibody disease

You-Ri Kang[1], Hyunjin Ju[2], Ki Hoon Kim[3], Sung-Min Kim[4], Woohee Ju[4], Sooyoung Kim[5], Eunhee Sohn[5], Sun-Young Oh[6], Byeol-A Yoon[7], Jong Kuk Kim[7], Tai Seung Nam[8], Hyunjin Kim[9], Eun Jee Lee[9], Young-Min Lim[9], Youna Min Kwon[10], Seung Woo Kim[10], Ha Young Shin[10], Jee-Ein Kim[11], In Su Joo[12], Minsu Park[13], Hyung-Soo Lee[14], Byung-Jo Kim[14], Jin-Woo Park[14], Suk Yoon Lee[15], Woo Joon Kim[16], Jae-Woon Hyun[1], Su-Hyun Kim[1], Ho Jin Kim[1]

[1]Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Korea.

[2]Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

[3]Department of Neurology, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Korea

[4]Department of Neurology, Seoul National University College of Medicine, Seoul Korea

[5]Department of Neurology, Chungnam National University Hospital, Chungnam National University College of Medicine, Daejeon, Korea

[6]Department of Neurology, Jeonbuk National University Hospital, Jeonju-si

[7]Department of Neurology, Dong-A University College of Medicine, Busan, Korea

[8]Department of Neurology, Chonnam National University Medical School and Hospital, Gwangju, Korea

[9]Department of Neurology, Asan Medical Center, University of Ulsan, Seoul, Korea

[10]Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

[11]Department of Neurology, College of Medicine, Ewha Womans University, Seoul, Korea

[12]Department of Neurology, Ajou University School of Medicine, Suwon, Korea

[13]Parkminsu Neurology Clinic, Daegu, Korea

[14]Department of Neurology, Korea University Ansan Hospital, Korea University College of Medicine, Seoul, Korea

[15]Department of Neurology, Busan Paik Hospital, Inje University College of Medicine, Busan, Korea

[16]Department of Neurology, Seoul St. Mary's Hospital, The Catholic University of Korea, College of Medicine, Seoul, Korea

Background: Approximately 40% of patients diagnosed with myelin oligodendrocyte glycoprotein antibody disease (MOGAD) exhibit a relapsing course, warranting immunosuppressive therapy (IST) to prevent relapses. However, there is limited evidence regarding the optimal duration of IST and the outcomes upon its discontinuation.

Objective: This study aims to evaluate the outcomes following the discontinuation of IST in individuals with MOGAD.

Methods: Data were retrospectively collected from MOGAD patients who met the diagnostic criteria across 28 hospitals in Korea. Among 333 with disease duration over 6 months, 273 patients received IST. Of these, the outcomes for 41 patients who subsequently discontinued IST were investigated.

Results: IST was discontinued after a median relapse-free period of 21 months (interquartile range [IQR], 7-44). The mean age at disease onset was 38 years (IQR, 28-53), with 3 patients having pediatric onset (7%). Negative seroconversion of anti-MOG antibody was observed in 51% (19/37) of patients during the disease course. Prior to IST withdrawal, the median number of attacks was 2 (IQR, 1-3), and 21 (51%) patients exhibited a relapsing course. Over a median follow-up period of 24 months (IQR, 2 – 40) after discontinuation, 10 (24%) of the 41 patients experienced relapses, occurring at a median interval of 8 months (IQR, 6 – 31). None of the 20 patients with prior monophasic disease relapsed, whereas 10 (48%) of 21 patients with relapsing courses experienced subsequent relapses after IST cessation. Among those with relapsing courses prior to IST withdrawal, the duration on IST was shorter for those with post-discontinuation relapses than those without (median, 9 months vs 51 months, p=0.036).

Conclusion: Patients with a history of a relapsing course prior to the cessation of IST are at a higher risk of post-discontinuation relapse, particularly those who had shorter duration of treatment.

P-43

Safety and Effectiveness of B cell Therapy in Older People with Multiple Sclerosis: Real World Evidence

Turlough Montague[1], Yuuki Kang[1], Katherine Zeme[1], Spencer Ferrier[1], Emily Cheung[1], Sophie Chatterton[1], John Parratt[1]

[1]Royal North Shore Hospital

Background: People with multiple sclerosis (MS) over 55 years old were excluded from pivotal phase III clinical trials for ocrelizumab and ofatumumab. Older people with MS are at higher risk of infection and may be more vulnerable to the immunosuppressive effects of B cell therapy. They are also at higher risk of progressive disease.

Objective: 1. To determine the rate of adverse events and treatment discontinuation amongst older people with MS on B cell therapy. 2. To determine the impact of B cell therapy on disability accumulation amongst older people with MS.

Methods: People with MS over 55 years of age attending a tertiary MS referral centre and treated with ofatumumab or ocrelizumab were identified. A retrospective review of medical records, MRI and pathology results was undertaken to determine disability progression and adverse event rates. A sub-analysis of people over 65 years was also performed.

Results: 138 patients were included. 67.4% were female and median age was 62 (interquartile range (IQR) 58-67) years. Median disease duration was 16 (IQR 11-26) years and median duration of B cell therapy was 45 (26-77.5) months. 89% had been treated with a different disease modifying therapy (DMT) before. EDSS was stable during the study period (mean 3.38 (± 2.27) to 3.44 (±2.35), p=0.67). 29% recorded an adverse event and in 11 (8%), B cell treatment was stopped as a result. 18.8% reported infections. A significant decrease in IgM was observed (p<0.001), whereas IgG and IgA remained stable. A significant increase in total lymphocyte count (p<0.001), CD8 (p=0.03) and CD4 (p<0.001) cells occurred.

A sub-analysis of 43 people over the age of 65 years (mean 70.1± 4.1) found similar adverse event rates (total=28.3%, infections=16.3%). Over a median interval of 28 (IQR 8-62) months, a significant decrease in mean EDSS occurred (4.47 (±2.32) to 4.02 (±2.35), p=0.02).

Conclusion: In this real-world retrospective analysis, B cell therapy in people over 55 years old was generally safe and well tolerated. In the over 65 population, a significant decrease in disability was observed over median follow up of 28 months.

Disclosures: Not applicable

P-44

Efficacy and Safety of Cladribine Tablets in Korean Patients with Relapsing-Remitting Multiple Sclerosis: Prospective, Real-World Evidence Study

Ho Jin Kim[1], Su-Hyun Kim[1], Sung Min Kim[2], Ha Young Shin[3], Young Nam Kwon[3], Tai-Seung Nam[4], Ju-Hong Min[5], Jun Soon Kim[6], Min Su Park[7], Nam-Hee Kim[8], Jin-Hong Shin[9], Young Eun Park[10], Eun-Jae Lee[11], Woojun Kim[12], Eun Hee Shon[13], Tae-Kyeong Lee[14], Karim Taha[15], Sungjin Ahn[16], Beom Jun Seo[16]

[1]National Cancer Center

[2]Seoul National University Hospital

[3]Yonsei University Severance Hospital

[4]Chonnam National University Hospital

[5]Samsung Medical Center

[6]Seoul National University Bundang Hospital

[7]ParkMinSu Neurology Clinic

[8]Dongguk University Ilsan Hospital

[9]*Pusan National University Yangsan Hospital*
[10]*Pusan National University Hospital*
[11]*Asan Medical Center*
[12]*Seoul St. Mary's Hospital*
[13]*Chungnam National University Hospital*
[14]*Soon Chun Hyang University Hospital Bu-Cheon*
[15]*Merck Serono, Global Medical of N&I, Merck KGaA*
[16]*Merck Ltd., Korea, an affiliate of Merck KGaA*
Background: Cladribine tablets are used for relapsing-remitting multiple sclerosis (RRMS), but real-world evidence (RWE) regarding their efficacy and safety in Asian patients remains insufficient.
Objective: To assess the real-world efficacy and safety of cladribine tablets in Korean patients with RRMS.
Methods: This study is a prospective, observational, real-world evidence study that monitored Korean patients with RRMS who were treated with cladribine tablets as part of their standard regimen from March 2021 to June 2024. A total of 142 patients from 17 sites were enrolled, with 69.7% being female and a median age of 34 years (interquartile range [IQR], 28-42). Enrolled patients were monitored for adverse events, incidence of adverse drug reactions, EDSS progression, and MRI activity.
Results: The median duration of cladribine tablet treatment was 20.4 months (IQR, 14.1-24.4), with 93 patients completing two years and 49 patients completing one year. During treatment, 119 patients (83.8%) remained relapse-free. Among the 23 patients (16.1%) who relapsed, the median time to the first relapse was 2.3 months (IQR, 1.3-6.8), and 4 patients (2.8%) discontinued cladribine due to relapses.
EDSS progression occurred in 8 patients (7.4%) after one year and in 4 patients (3.7%) after two years of treatment. MRI activity was lower in the second year (14.8 %) compared to the first year (24.1%).
Additionally, six patients (4.2%) experienced serious adverse events, with 2 (1.4%) being drug-related, including cases of COVID-19 and upper respiratory tract infection. No cases of Grade 4 lymphopenia were reported. Only 1 patient (0.7%) discontinued due to a subarachnoid haemorrhage, which was evaluated by the investigator as not related to cladribine.
Conclusion: This report represents the largest patient number of interim real-world evidence on the efficacy and safety of cladribine tablets in Asian patients from Korea, with findings that align with global studies.
Disclosures: This research is supported by Merck KGaA. Karim Taha is an employee of Merck Serono Middle East FZ-Ltd., Dubai, UAE, an affiliate of Merck KGaA. Sungjin Ahn and Beom Jun Seo are employees of Merck Ltd., Korea, an affiliate of Merck KGaA. The other authors have no conflicts of interest.

P-45

Immunomodulatory Glycolipid OCH Reduces Relapses In Multiple Sclerosis (Phase II Clinical Trial)

Ben Raveney[1], Tomoko Okamoto[2], Atsuko Kimura[1], Youwei Lin[2], Yukio Kimura[3], Noriko Sato[3], Yuko Shimizu[4], Yoichiro Nishida[4], Takanori Yokota[5], Masanori Taketsuna[6], Yu Okada[6], Takami Ishizuka[7], Harumasa Nakamura[7], Sachiko Miyake[8], Yuji Takahashi[2], Wakiro Sato[1], Takashi Yamamura[1]
[1]*Deparment of Immunology, National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan*
[2]*Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan*
[3]*Department of Radiology, National Center Hospital, National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan*
[4]*Department of Neurology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan*
[5]*Department of Neurology and Neurological Science, Graduate School of Medical and Dental Sciences,*

Tokyo Medical and Dental University, Tokyo, Japan
[6]Translational Research Center for Medical Innovation, Foundation for Biomedical Research and Innovation at Kobe, Hyogo, Japan
[7]Department of Clinical Research Support, Clinical Research & Education Promotion Division, National Center Hospital, NCNP, Tokyo, Japan
[8]Department of Immunology, Juntendo University Graduate School of Medicine, Tokyo, Japan
Refer to O-6 in Plenary Oral Presentation - 2

P-46
Efficacy of Cladribine in RRMS patients in Singapore in a single center - Year 3 to 5
Jeanne MM Tan[1], Janis SN Tye[1], Amelia YY Aw[1], Rachel Wan En Siew[1], Sarah Hasnor[1], Si Yan Leo[1], Su Rong Fam[1], Xuejuan Peng[1], Kevin Tan[1], Tianrong Yeo[1]
[1]National Neuroscience Institute, Singapore
Background: Cladribine is currently an FDA approved disease modifying treatment (DMT) for highly active relapsing remitting multiple sclerosis (RRMS). We have previously described reduced annualized relapse rates at 2 years in our patient population. However, the efficacy of Cladribine beyond 3 years is yet to be fully elucidated.
Objective: To determine the efficacy of Cladribine in patients with RRMS in NNI, Singapore in Year 3 to 5 after Cladribine initiation.
Methods: Data from RRMS patients who are registered in the institutional database before 1 July 2024 were collected. Inclusion criteria are patients: 1) on active follow up in NNI in year 3 to 5 of Cladribine treatment and 2) have completed full course of Cladribine. Clinical efficacy was determined by (1) breakthrough disease activity, (2) ARR at 3 years before and after Cladribine initiation, and (3) disability accumulation measured by EDSS score at Cladribine initiation (baseline), 2 years after completion of Cladribine dose, and at clinical review at least on or more than 6 months after 2 years from Cladribine initiation. New disease activity was defined as the presence of clinical relapse and/or radiological activity (defined as the presence of ≥2 new lesions at least 6 months from completion of cladribine dose). Patients were grouped into those: (i) no new disease activity and no further immunotherapy; (ii) new disease activity and no further immunotherapy; (iii) new disease activity and received 3rd dose of Cladribine; (iv) new disease activity and switched to different immunotherapies.
Results: Twenty-six patients were included; 24 were analyzed (20 female [83.3%], median age 27.4 years; 2 patients transferred care). Twelve patients had prior DMT use. Nine patients (37.5%) had new disease activity; 6 (25%) of which had clinical relapse at year 3; 8 (33.3%, including 5 with clinical relapses) had radiological disease activity, 5 at year 3 and 3 at year 4. Five of 9 patients with new disease activity switched to anti-CD20 therapies while 1 was given a 3rd dose of cladribine. In addition, 1 patient was given 3rd dose of cladribine due to clinical relapse in year 3 and subsequently switched to B cell therapy in year 5 after new radiological activity at Year 4. Two patients opted for close surveillance. ARR 3 years after Cladribine initiation was significantly lower than ARR 3 years prior to treatment [0.125 (0.30), vs. 0.93(SD 0.58) p<0.001]. There is no significant change in pre and post-treatment EDSS at 2.5 years for these patients.
Conclusion: While Cladribine is an effective treatment for NNI RRMS patients evidenced by reduction in ARR and absence of disability worsening. New disease activity was observed in a quarter to a third of our patients in year 3 to 5 of Cladribine treatment.
Disclosures: NA

P-47

Longitudinal Quantification Of SARS-Cov2 Neutralising Antibodies, Pro-Inflammatory Cytokines, NfL and GFAP Before And After Breakthrough COVID-19 Infection In Patients With CNS Neuroimmunological Diseases

Hema Prashaad M.[1], Rachel Wan En Siew[2], Yaaseen S/O Gulam Mohamed Muhammad[2], Amelia Yun Yi Aw[2], Kalpana Prasad[2], Kevin Tan[2], Yinxia Chao[2], Ivy Ai-Wei Ho[2], Jens Kuhle[3], Tianrong Yeo[2]

[1]*Duke-NUS Medical School, Singapore*

[2]*National Neuroscience Institute, Singapore*

[3]*University Hospital Basel*

Background: COVID-19 has brought new challenges in managing patients with neuroimmunological diseases. Immunosuppressive medication used for disease control in these patients can attenuate SARS-CoV2 vaccine-induced humoral responses. Moreover, SARS-CoV2 has neuroinvasive potential and may induce a persistent pro-inflammatory milieu following infection.

Objective: To investigate if diminished post-vaccine humoral responses can be overcome with additional vaccine doses and/or breakthrough COVID-19 infections, and if COVID-19 infection can lead to intermediate-term neuroaxonal/neuroglial injury.

Methods: This is a prospective study conducted at the National Neuroscience Institute's Neuroimmunology Clinic. Demographic, clinical, immunotherapy, COVID-19 infection and vaccination information were obtained from the electronic medical records. The humoral immune responses generated by SARS-CoV2 mRNA vaccine dose 4 (V4) or symptomatic COVID-19 infection or both (after V3), and their temporal sequences were investigated through the measurement of serum SARS-CoV2 neutralising antibodies (NAbs) using the Genscript® cPass™ surrogate virus neutralisation test. Serum levels of pro-inflammatory cytokines interleukin 6 (IL-6) and tumour necrosis factor (TNF) were evaluated post-COVID-19 infection and post-V4, compared to baseline within individuals, using a two-plex cytokine assay (Milliplex®). Serum neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP), biomarkers of neuroaxonal and astroglial injury respectively, were measured pre- and post-COVID-19 infection within individuals using the Simoa® platform.

Results: Fifty-one patients with various CNS neuroimmunological diseases, including 21 with Multiple Sclerosis (MS) and 18 with Neuromyelitis Optica Spectrum Disorder (NMOSD), were recruited. All had received at least three doses of the SARS-CoV2 mRNA vaccine. Patients on anti-CD20/sphingosine-1-phosphate-receptor modulators (S1PRM) showed significantly reduced NAbs levels in both post-V4 and post-COVID-19 infection scenarios, compared to patients on other immunotherapies. COVID-19 infection was neither superior nor inferior to V4 in terms of producing a NAbs response within patients receiving anti-CD20/S1PRM.

No significant differences between pre- versus post-COVID-19 infection concentrations of IL-6 and TNF were observed. A similar finding was also noted for V4 with regards to the pro-inflammatory cytokines. Within MS and NMOSD patients, NfL and GFAP levels remained similar pre- and post-COVID-19 infection.

Conclusion: While anti-CD20/S1PRM are associated with persistently diminished humoral responses post-V4/infection, intermediate-term pro-inflammatory states and neural injury are unlikely in patients with CNS neuroimmunological diseases after COVID-19 infection.

P-48

Resolution of Magnetic Resonance Imaging (MRI) Lesions Following Immune Reconstitution Therapy in Multiple Sclerosis.

Nasheeda Saeed[1], Hui Jan Tan[1], Shahizon Azura Binti Mohamed[2], Rabani Remli[1]
[1]*Department of Medicine, Faculty of Medicine, University Kebangsaan Malaysia*
[2]*Department of Radiology, Faculty of Medicine, University Kebangsaan Malaysia*

Background: Immune reconstitution therapy (IRT) has been increasingly recognized for its ability to modify the course of multiple sclerosis (MS) by reducing inflammation during the most inflammatory phase of the disease.
Objective: To present two cases of MS treated with IRT.
Methods: Two female patients with relapsing-remitting multiple sclerosis (RRMS) were treated with different IRTs. Case 1 was treated with Cladribine and case 2 with Alemtuzumab. Both cases were monitored with regular clinical evaluations and MRI for assessments.
Results: Case 1: A 27-year-old female presented with a history of recurrent neurological symptoms, including optic neuritis and right-hand paresthesia. Cerebrospinal fluid oligoclonal bands was positive. MRI Brain was normal. Spine MRI showed focal intramedullary T2 hyperintense ovoid lesion at C6 level. She completed two cycles of Cladribine therapy. Follow-up MRI revealed no new lesions with resolution of the existing cervical cord lesion. She remained stable with no further relapses.
Case 2: A 23-year-old female with highly active RRMS experienced multiple relapses with sensory deficits. Examination showed right hemianesthesia. MRI brain and spine showed multiple periventricular and juxtacortical lesions with short segment intramedullary enhancing lesion at T6/T7. The patient received two cycles of Alemtuzumab therapy. Follow-up MRI showed a reduction in the size of periventricular lesions and resolution of the intramedullary lesion, with no new active lesions. She remained relapse free.
Conclusion: Early treatment with IRTs led to the resolution of MRI lesions and prevented further relapses. These cases highlight the effectiveness of early treatment with IRT in achieving radiological remission and relapse free state in MS patients.

P-49

The Use of Immunotherapies in a Country with Limited Availability of Disease Modifying Therapies for Multiple Sclerosis

Rocksy Fransisca Vidiaty Situmeang[1], Anyeliria Sutanto[1], Catherine Siany Kurniawan[1], Rosaria Oktafiani Darmawan[2], Billy Susanto[1]
[1]*Faculty of Medicine Pelita Harapan University*
[2]*Siloam Hospitals Lippo Village*

Background: Data from the Atlas of MS shows that 72% of countries cite barriers to access Disease Modifying Therapies (DMTs). Off-label medications may be prescribed due to limited treatment options available. From our previous study we found that governments, physicians and patients all had roles in the use of immunotherapies for MS in our country.
Objective: This study aims to portray the current state of immunotherapy utilization in Indonesia and identify the factors contributing to its limited application.
Methods: Data were collected from questionnaires distributed to neurologist and MS patients in Siloam Hospitals Lippo Village during June to July 2024. The immunotherapies assessed included DMT's available such as interferon-beta, fingolimod and cladribine, as well as off-label drugs rituximab, azathioprine, and mycophenolic acid. We investigated the reasons that influenced the use of those immunotherapies.

Results: A total of 69 subjects were included in this study. The mean age was 36.65 ± 12.02 years, with a mean age at diagnosis of 30.77 ± 11.19 years, and an average disease duration of 5.39 ± 4.23 years. Most patients were female (78.6%). The relapsing-remitting type was the most prevalent at 84%. Less than half of subjects are covered by insurance (24.6% by government insurance, and 23.2% by private insurance). Among the subjects, 17 (24.6%) never used any immunotherapy due to financial reasons, lack of experience and hesitancy in emphasizing the importance of immunotherapy among neurologists, and patients with milder symptoms consider the cost of DMD treatment is higher than its benefit. DMT's available in Indonesia are Interferon beta, fingolimod and cladribine (been used by 26, 5, and 2 subjects respectively). 2 subjects have used glatiramer acetate and natalizumab available abroad.
Conclusion: Despite the recognized efficacy, its implementation remains limited due to restricted availability and economic constraints.

P-50
Natalizumab İn Multiple Sclerosis: Long-Term Treatment Management
Mesrure Koseoglu[1], Mehmet Demir[1], Kursat Usalan[1], Keriman Oguz[1], Ayca Gul Gungordu[1], Tamer Yazar[1]
[1]*University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital*
Background: Natalizumab is an effective treatment option for RRMS patients. Numerous studies have been conducted to determine the optimal approach for minimizing the risk of rebound and clinical and radiological relapses associated with natalizumab. The administration of natalizumab during pregnancy is a new concern.
Objective: We aimed to present the clinical characteristics and treatment management data of patients receiving natalizumab treatment in our clinic.
Methods: The study included RRMS patients who were followed up in the Multiple Sclerosis Unit of the Neurology Department of Istanbul Kanuni Sultan Süleyman Training and Research Hospital and who received natalizumab. Data on demographic and clinical characteristics of the patients, disease activity before and after natalizumab, pregnancies followed during treatment, dose administration intervals, side effects observed and reasons for discontinuation were analyzed retrospectively.
Results: The mean age of 61 patients (45 females and 16 males) was 39.75 years (24 - 54 years) and the mean duration of disease onset was 11.9 years (2 - 30 years). It was found that 60.6% of the patients were switched from first-line preventive treatment to natalizumab treatment and the most common reason for drug change was new attacks. Duration of drug use ranged between 6 months and 9 years with a mean duration of 2.6 years and only 1 patient developed an attack in the 3rd month after discontinuation of natalizumab treatment due to drug supply problems. No serious side effects requiring treatment discontinuation were observed during follow-up. In 6 patients, treatment was terminated due to increased John Cunningham virus (JCV) levels. In 6 pregnancies that developed under treatment, healthy delivery was observed in 3 patients whose treatment was continued until the end of the second trimester, and 3 patients are still in the process of pregnancy.
Conclusion: Natalizumab treatment is an effective treatment option in patients with high disease activity with regular use. In pregnancies followed up under treatment, healthy deliveries were observed without new attacks and progression.
Disclosures: There is no conflict of interest

POSTER SESSION – 4
Epidemiology, Genetics, and Epigenetics

P-51

The Risk of Autoimmune Diseases in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder: A Nationwide Cohort Study in South Korea

Soonwook Kwon[1], Kyung-Do Han[2], Jin Hyung Jung[3], Eun Bin Cho[4], Junhee Park[5], Yeonghee Eun[6], Hyungjin Kim[5], Yeon Hak Chung[7], Dong Wook Shin[5], Ju-Hong Min[5]

[1]*Inha University Hospital*
[2]*Soongsil University*
[3]*Catholic University of Korea*
[4]*Gyeongsang National University Changwon Hospital*
[5]*Samsung Medical Center*
[6]*Kangbuk Samsung Hospital*
[7]*Korea University Guro Hospital*

Background: The co-occurrence of various autoimmune diseases (AIDs) is frequently reported in multiple sclerosis (MS) or neuromyelitis optica spectrum disorder (NMOSD) with patients. However, there are few nationwide epidemiologic studies of the risk of AIDs in MS and NMOSD and no studies have compared MS and NMOSD.

Objective: We aimed to investigate the risk of AIDs in MS and NMOSD compared with a control population using the Korean National Health Insurance Service (KNHIS) database.

Methods: MS/NMOSD cohorts were collected from the KNHIS between 1 January 2010 and 31 December 2017 using the International Classification of Diseases 10th diagnosis codes and information in the Rare Intractable Disease management program. The incidence rate and risk of AIDs that occurred after a 1-year lag period was calculated and compared with that of control cohorts matched for age, sex, hypertension, diabetes mellitus, and dyslipidemia in a 1:10 ratio.

Results: The incidence rates of AIDs in MS and NMOSD were 3.56 and 9.13 per 1,000 person-years, respectively. The hazard ratios (HRs) of AIDs in MS and NMOSD were 5.35 (95% confidence interval [CI] 3.50–8.19) and 9.13 (95% CI 5.83–14.28), respectively. The risk of Behçet's disease (HR 17.24, 95% CI 4.12–72.14), systemic lupus erythematosus (HR 12.25, 95% CI 4.12–36.44), Sjögren's syndrome (HR 6.16 95% CI 1.80–21.04), and seropositive rheumatoid arthritis (HR 3.32, 95% CI 1.78–6.19) was increased in MS. In NMOSD, the risk of polymyositis (HR 82.63, 95% CI 19.00–359.38), systemic lupus erythematosus (HR 30.85, 95% CI 6.23–152.80), antiphospholipid syndrome (HR 15.36, 95% CI 2.57–91.93), and Sjögren's syndrome (HR 3.86, 95% CI 1.80–8.31) was increased.

Conclusion: The risk of AIDs was increased in MS/NMOSD, and the risk of each AIDs differed between MS and NMOSD.

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P-52

Clinical and treatment comparison of MOG-associated disease and AQP4 positive neuromyelitis optica spectrum disorder: A multicenter cohort study in Taiwan

Yu-Ning Huang[1], Chao-Wen Lin[2], Wen-Chin Weng[2], Hsueh-Wen Hsueh[2], Ta-Ching Chen[2], Jen-Jen Su[2], Chih-Chao Yang[2]

[1]*Shuang Ho Hospital, Ministry of Health and Welfare*

[2]*National Taiwan University Hospital*

Refer to O-7 in Plenary Oral Presentation - 2

P-53

Hand-Grip Strength in Multiple Sclerosis Patients in Mongolia: A Cross-Sectional Study

Myadagmaa Jaalkhorol[1], Amarsaikhan Dashtseren[2], Gantuya Magnaibayar[3], Badrangui Bat-Orgil[4], Ganjargal Tsetseg[4]

[1]*Department of Health Research, Graduate School, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia*

[2]*Department of Preventive Medicine, School of Public Health, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia*

[3]*Department of Neurology, General Hospital for State Special Servants, Ulaanbaatar, Mongolia*

[4]*Mongolian Naran Multiple Sclerosis Society, Ulaanbaatar, Mongolia*

Background: Mongolia is located at 45° north latitude in the center of the Asian continent, and about 80% of the territory is at 1,000 m above sea level. Little is known about the frequency and severity of hand grip strength (HGS) in Mongolia's individuals with multiple sclerosis (MS).

Objective: We aimed to investigate the association between MS-related parameters and HGS levels.

Methods: This cross-sectional observational study was conducted at Ulaanbaatar city hospitals from January 2023 to July 2023. Participants completed a questionnaire on their lifestyles and clinical information. HGS was measured by a handheld dynamometer with maximum effort; two attempts were made with each hand. HGS was categorized into low (<26kg for males and <18 kg for females) or normal, defined according to the Asian Working Group for Sarcopenia (AWGS) criteria. Sunlight exposure is measured by asking whether or not from >30min/day goes up to the sun. Multivariate logistical regression analyses were used to identify low and normal hand grip strength predictors.

Results: Thirty-one patients were recruited, with a mean age of 45.9±11.1. Twenty-two (71%) had low hand grip strength and 9 (29%) had normal hand grip strength. Sex, relapse rate, and RRMS and PPMS of MS were univariately significantly associated with HGS, as was monthly income However, onset age, treatment duration, and 25(OH) D level were not associated with HGS. After adjusting for sex, odds ratios (OR) for low hand grip strength remained significantly associated with sunlight exposure in MS men and women (OR, 3,60; p=0.027; 95% Confidence Interval (Cl) (1,50-8,96).

Conclusion: Low hand-grip strength is associated with sunlight exposure in men and women amongst Mongolian MS patients. Prospective studies are needed to determine whether a causal association exists between MS-related parameters and HGS in MS patients.

Disclosures: The authors declare no conflicts of interest.

P-54

Assessment of Concurrent Neoplasms and a Paraneoplastic Association in MOGAD

Nanthaya Tisavipat[1], Young Nam Kwon[2], Yong Guo[1], Stephanie Syc-Mazurek[3], Ji Yeon Han[4], Jun-Soon Kim[5], Kyomin Choi[6], Seong-il Oh[7], Sung Hyuk Heo[7], Seok-Jin Choi[8], Eunhee Sohn[9], Jeeyoung Oh[10], Seung Woo Kim[2], Ha Young Shin[2], Byung Chan Lim[11], Hye Jung Lee[12], Byoung Joon Kim[12], Kyung Seok Park[5], Jung-Joon Sung[8], Se Hoon Kim[13], Moonhang Kim[14], Sung-Hye Park[15], Anastasia Zakeridou[16], Claudia Lucchinetti[1], Sean Pittock[1], John Chen[17], Sung-Min Kim[8], Eoin Flanagan[1]

[1]Department of Neurology and Center for MS and Autoimmune Neurology, Mayo Clinic, Rochester, MN, USA

[2]Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

[3]Department of Neurology, Mayo Clinic, Rochester, MN, United States

[4]Department of Pediatrics, Inha University Hospital, Incheon, Republic of Korea

[5]Department of Neurology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea

[6]Department of Neurology, Soonchunhyang University Cheonan Hospital, Cheonan, Republic of Korea

[7]Department of Neurology, Kyung Hee University Hospital, Kyung Hee University College of Medicine, Seoul, Republic of Korea

[8]Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea

[9]Department of Neurology, Chungnam National University College of Medicine, Chungnam National University Hospital, Daejeon, Republic of Korea

[10]Department of Neurology, Konkuk University School of Medicine, Konkuk University Medical Center, Seoul, Republic of Korea

[11]Department of Pediatrics, Seoul National University College of Medicine, Seoul National University Children's Hospital, Seoul, Republic of Korea

[12]Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

[13]Department of Pathology, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

[14]Biomedical Research Institute, Seoul National University Hospital, Seoul, Republic of Korea

[15]Department of Pathology, Seoul National University Hospital, Seoul National University, College of Medicine, Seoul, Republic of Korea

[16]Department of Neurology, Laboratory Medicine and Pathology, and Center for MS and Autoimmune Neurology, Mayo Clinic, Rochester, MN, United States

[17]Department of Neurology and Ophthalmology, Mayo Clinic, Rochester, MN, United States

Background: Myelin oligodendrocyte glycoprotein (MOG) antibody is classified as a low-risk antibody for paraneoplastic neurologic syndrome (PNS) in the 2021 Updated PNS Criteria. There have been some case reports of possible paraneoplastic MOGAD, but evidence of MOG expression in tumor tissue has been demonstrated only in two cases so far.

Objective: To investigate the frequency of concurrent neoplasm in MOG antibody-associated disease (MOGAD) in comparison to the general population and determine its clinical implications.

Methods: We performed an international, multicenter, retrospective cohort study of MOGAD from South Korea (multiple hospitals) and USA (Mayo Clinic) through April 2023. Patients fulfilling 2023 International

MOGAD Panel diagnostic criteria with ≥2 years of follow-up were included. Concurrent neoplasms were those diagnosed within 2 years of MOGAD onset. Standardized incidence ratio (SIR) for neoplasm was calculated based on expected incidence from country-specific national cancer databases. All tumors obtained were immunostained for MOG expression.
Results: In total, 445 MOGAD patients (median age, 28 years; 56% female) were included. Sixteen (3.6%) had concurrent neoplasm; all were adult-onset. Neoplasm diagnosis preceded MOGAD onset in 9/16 (56%) patients, and the types of neoplasm were heterogeneous without predominance of any specific types. The SIR of concurrent neoplasm in MOGAD was increased at 3.10 (95% confidence interval [CI] 1.77–4.81; p<0.001; normal, 1) compared to their age-matched general population, especially in the South Korean cohort (SIR 4.40; 95% CI 2.26–7.23; p<0.001) but not in the Mayo Clinic cohort (SIR 1.65; 95% CI 0.43–3.65; p=0.227). All 9 available tumors had negative MOG immunostaining.
Conclusion: Concurrent neoplasms were more frequent in MOGAD than the general population, but the absence of MOG immunostaining in tumors suggests that paraneoplastic MOGAD is very rare, and other factors may contribute to the increased detection of neoplasia.
Disclosures: The authors report no relevant disclosures.

P-55

Impact of the COVID-19 outbreak on the Incidence of Antibody-Positive Autoimmune Encephalitis and Paraneoplastic Neurological Syndromes in Singapore

Rui Ling Rena Lau[1], Karine Su Shan Tay[2], Seyed Ehsan Saffari[1], Patricia Yut Wan Wong[2], Mei Ting Lim[2], Angelia Swee Hoon Koe[2], Jeanne May May Tan[2], Kok Pin Yong[2], Kevin Tan[2], Josiah Yui Huei Chai[2], Tianrong Yeo[2]
[1]*Duke-NUS Medical School*
[2]*National Neuroscience Institute*

Background: While COVID-19 infection is primarily recognised for causing respiratory symptoms, emerging evidence suggests it may precipitate autoimmune neurological conditions, including autoimmune encephalitis (AE). The aetiology for this is unclear; proposed mechanisms include molecular mimicry and immune system dysregulation.
Objective: This study aims to evaluate the incidence of antibody (Ab)-positive autoimmune encephalitis (AE) and paraneoplastic neurological syndromes (PNS) in Singapore in relation to COVID-19.
Methods: A retrospective study was performed to determine the rate of Ab positive samples tested at the National Neuroscience Institute Singapore. Surface-exposed Ab associated with AE were tested using a multiplex cell-based assay, while intracellular Ab associated with PNS were detected by immunoblot and primate cerebellum / intestine (all kits from Euroimmun AG, Germany). Only the first sample from each individual was evaluated, i.e. no repeat counting. To increase the robustness of laboratory-based diagnosis – (1) for NMDAR Ab, only CSF positive samples; (2) for CASPR2 Ab, only titre ≥1:100; (3) for PNS, only positivity on both immunoblot and tissue assays, were considered positives.
Results: From 2017-2023, 4,347 samples were screened for AE Ab; 87 were positive (43 NMDAR, 29 LGI1, 13 GABAb, 1 CASPR2, 1 DPPX). From 2018-2023, 29 of 3,393 samples tested for PNS Ab were positive (9 GAD, 5 Yo, 4 Hu, 3 SOX1, 2 Zic4, 2 Ri, 1 Ma2, 1 Tr, 1 CV2, 1 Amphiphysin). A spike in AE incidence was observed in 2020 (4.92 [95%-CI 3.05-7.53] per 100,000), coinciding with the outbreak of the COVID-19 pandemic. From 2021 to 2023, the average incidence decreased to 2.74 per 100,000 despite more samples being tested, returning to levels seen in the pre-pandemic period (average incidence from 2017-2019 was 2.44 per 100,000) (p value for trend=0.767). PNS incidence remained largely unaffected by COVID-19, with

a gradual consecutive increase from 0.94 per 100,000 in 2019 to 1.8 per 100,000 in 2023 as more samples were tested (p value for trend=0.214).
Conclusion: The temporal association of Ab positive AE and COVID-19 outbreak suggests a potential causal link. Subsequent decline in cases may be due to SARS-CoV2 vaccination and new variants. PNS incidence remained stable, given its association with malignancy.

P-56
Observation of Vitamin D Levels in Newly Diagnosed Multiple Sclerosis Patients: A Case Series
Huynh Y[1], Luong Nguyen Ngoc[1]
[1]*Military Hospital 175*
Background: Many environmental factors have been reported to be associated with the risk of developing multiple sclerosis (MS), such as lack of exposure to sunlight, vitamin D deficiency, obesity, smoking, and infectious mononucleosis. Vitamin D deficiency has been shown to play a role in immune system function and may increase the risk of developing MS.
Objective: In this report, we evaluated vitamin D levels in newly diagnosed MS patients to determine the need for vitamin D supplementation.
Methods: We observed vitamin D levels in newly diagnosed MS patients who had not previously used corticosteroids and vitamin D. We measured serum 25-hydroxyvitamin D (25 OH vitamin D) levels when patients with suspected MS were hospitalized. All patients were evaluated for kidney function, and normal function was ensured.
Results: We recorded 6 patients (5 female, 1 male), aged from 17 to 66 years old, newly diagnosed with MS from January 2024 to July 2024, and 4 patients had positive oligoclonal bands. 25 OH vitamin D levels were low in 5 patients and normal in 1 patient. The patient with normal 25 OH vitamin D levels was the youngest with a serum level of 83.95 ng/ml. In the remaining patients, deficient 25 OH vitamin D levels were recorded in 1 patient (15.91 ng/ml) and insufficient levels in 4 patients (ranging from 20.46 to 28.4 ng/ml). Patients with low 25 OH vitamin D levels were then supplemented with vitamin D2 or D3.
Conclusion: Most MS patients have low 25 OH vitamin D levels, so vitamin D supplementation in MS treatment is necessary. However, further observations with larger sample sizes and comparisons with healthy individuals or non-MS patients are needed.

P-57
HLA association with AQP4 IgG positive neuromyelitis optica spectrum disorder in the Korean population
Jae-Won Hyun [1], Sinae Kim[1], Jangsup Moon[2], Na Young Park[1], You-Ri Kang[1], Ki Hoon Kim[3], Su-Hyun Kim[1], Ho Jin Kim[1]
[1]*National Cancer Center*
[2]*Seoul National University Hospital*
[3]*Sanggye Paik Hospital*
Background: Association of human leukocyte antigen (HLA) with anti-aquaporin-4 immunoglobulin-G-positive neuromyelitis optica spectrum disorder (AQP4-IgG NMOSD) has been reported. However, this association in the Korean population has not been previously investigated.
Objective: We aimed to evaluate whether specific HLA subtypes were associated with Korean patients with AQP4-IgG NMOSD and whether the HLA genotype is associated with specific clinical features.
Methods: We compared the HLA subtypes of 122 patients with AQP4-IgG NMOSD with those of 485

(HLA-A, B, C, DRB1, and DQB1) and 173 (HLA-DPB1) healthy controls. Additionally, we compared the clinical features of patients with and without specific HLA genotypes.
Results: The most significant risk allele for AQP4-IgG NMOSD was HLA-DRB1*03:01 (24 patients (19.67%), odds ratio [OR]:3.985, pc-value=0.0004). Susceptibility of AQP4-IgG NMOSD was significantly associated with the HLA-DRB1*03:01–DQB1*02:01 (23 patients (18.85%), OR:15.758, pc-value<0.0001) and DRB1*12:02–DQB1*03:01 haplotypes (23 patients (18.85%), OR:13.763, pc-value<0.0001). Patients with the DRB1*12:02–DQB1*03:01 haplotype showed more frequent spinal involvement, a higher expanded disability status scale at disease-onset nadir, and a shorter time to second attack than patients without this haplotype.
Conclusion: HLA-DRB1*12:02–DQB1*03:01 haplotype was associated with disease-onset severity in AQP4-IgG NMOSD. HLA-DRB1*03:01, widely reported as a susceptibility allele of NMOSD across diverse ethnic groups, showed a significant risk association in Korean. **Disclosures:** "This study was supported by National Cancer Center in Korea (Grant No. 2310300) & National Research Foundation of Korea (Grant No. NRF-2018R1A5A2023127).
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P-58

Analysis of Pregnancy Complications and Offspring Outcomes in Neuromyelitis Optica Spectrum Disorders Using National Health Care Data in Korea

Hye Lim Lee[1], Hyun Ji Lyou[2], Jin Myoung Seok[3], Geum Joon Cho[1]
[1]*Korea University Guro Hospital*
[2]*Eunpyeong St. Mary's Hospital*
[3]*Soonchunhyang University Cheonan Hospital*

Background: Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease that primarily affects the spinal cord and optic nerves. Pregnancies in patients with NMOSD are often considered high risk due to a higher incidence of obstetric complications and an increased likelihood of relapse.
Objective: We investigated pregnancy-related and fetal complications in patients with NMOSD using data from the National Health Insurance Service (NHIS) in Korea.
Methods: We analyzed NHIS claim data, including information from National Health Screening Examination and National Health Screening Program for Infants and Children in Korea. Our cohort consisted of pregnant women with NMOSD and matched controls, selected based on age and Charlson Comorbity Index. This study included women with singleton pregnancies with live births from 2011 to 2020 who had participated in the NHSE within 4 years prior to pregnancy. We assessed pregnancy complications (e.g., gestational hypertension, diabetes mellitus) and offspring outcomes (e.g., congenital malformations, respiratory issues). Propensity score matching and multivariable logistic regression were used to estimate the risk of maternal complications and fetal outcomes. All statistical analyses were performed using SPSS (version

23.0), and p value <0.05 was considered statistically significant.
Results: A total of 6,607,934 women who delivered between 2011 and 2020, 101 (0.002%) were diagnosed with NMOSD. NMOSD patients were more frequently primiparous (68.32% vs 46.83%, p<0.001) and had higher rates of hypertension (3.96% vs 0.5%, p=0.0002) and diabetes mellitus (7.92% vs 3.47%, p=0.0269). However, no significant differences were observed in obstetric complications, including gestational hypertension (p=0.17), gestational diabetes mellitus (p=0.45), preterm birth (p=0.14), cesarean section (p=0.14), placental abruption (p=0.40), placenta previa (p=0.11), and postpartum hemorrhage (p=0.72). Offspring of NMOSD patients had a higher incidence of congenital malformations of respiratory system (2.97% versus 0.2%, p<0.0001), but no significant differences were found for other neonatal complications such as respiratory distress syndrome (p=0.56), bronchopulmonary dysplasia (p=0.75) or hypoglycemia (p=0.32). In multivariable regression analysis, fetal outcomes did not significantly differ after adjusting for confounding factors.
Conclusion: Our study evaluated pregnancy-related complications and fetal outcomes in patients with NMOSD. Pregnancies in women with NMOSD did not show increased risks for most obstetric complications or adverse fetal outcomes compared to the general population. **Disclosures:** None

P-59
Real-World Evidence on the Status of Diagnosis, Treatment and Disease Characteristics in Japanese Patients with Multiple Sclerosis (2nd report of MSERJ)
Noriko Isobe[1], Yoichiro Nishida[2], Fumitaka Shimizu[3], Yusei Miyazaki[4], Yuki Fukami[5], Chieko Suzuki[6], Ichiro Nakashima[7], Izumi Kawachi[8], Ryo Tajiri[9], Michihiro Kanda[10], Yayoi Sato[10], Jun-Ichi Kira[11], MSERJ Study Group
[1]*Department of Neurology, Graduate School of Medical Sciences, Kyushu University*
[2]*Department of Neurology and Neurological Science, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University*
[3]*Department of Neurology and Clinical Neuroscience, Graduate School of Medicine, Yamaguchi University*
[4]*Department of Clinical Research, National Hospital Organization Hokkaido Medical Center*
[5]*Department of Neurology, Nagoya University Graduate School of Medicine*
[6]*Department of Neurology, Hirosaki University Graduate School of Medicine*
[7]*Division of Neurology, Tohoku Medical and Pharmaceutical University*
[8]*Department of Neurology, Brain Research Institute, Niigata University*
[9]*Mebix*
[10]*Biogen Japan Co., Ltd*
[11]*Translational Neuroscience Center, Graduate School of Medicine, and School of Pharmacy at Fukuoka, International University of Health and Welfare*
Background: Real-world evidence on the disease characteristics and treatment transitions of patients with multiple sclerosis (MS) in Japan is limited.
Objective: To investigate the status of diagnosis, treatment and disease characteristics in Japanese patients with MS in a multicentre retrospective observational study, MSERJ (UMIN000038060).
Methods: Patients diagnosed with radiologically isolated syndrome, clinically isolated syndrome and MS were enrolled between July 2022–May 2023. The date of diagnosis, all MS treatments from the first visit at the center until informed consent (IC), and demographic and clinical data at the first visit and for 2 years before IC were collected retrospectively.
Results: Of 842 patients from 20 centers across Japan, 81.4%, 9.1% and 7.4% had relapsing-remitting (RR), secondary progressive (SP) and primary progressive (PP) MS at final evaluation. Corresponding median

Expanded Disability Status Scale scores were 1.5, 6.0, 6.0, and mean age were 44.1 ± 10.8, 53.8 ± 10.6 and 48.9 ± 11.4 years. Over successive 3-year periods from 2011 to 2023, 52.1%, 66.1%, 77.2% and 89.2% used disease-modifying drugs (DMDs) (Cochran-Armitage Test: p<0.0001). The median time from MS diagnosis to 1st DMD were 3.7, 3.1, 3.0 and 1.2 months. At final evaluation, dimethyl fumarate (34.5%), siponimod (41.7%), and ofatumumab (38.8%) were most frequently used for RRMS, SPMS, and PPMS, respectively. Overall, the annualized relapse rate (ARR) was 0.12. Younger age at onset (HR: 1.03, 95% CI :1.01-1.05, P=0.0019) and shorter DMD treatment (HR: 1.08, 95% CI: 1.04-1.11, P<0.0001) were related with higher ARR on multivariate negative binomial regression analysis.
Conclusion: Treatment status has been changed over 10 years and most patients were treated with ≥1 DMD. ARR was relatively low; younger age at onset and shorter DMD treatment were risk factors for higher ARR.
Disclosures: This study is funded by Biogen Japan. MK and YS are employees of and hold stock in Biogen.

P-60
Clinical and Radiological Features of Multiple Sclerosis and Related Disorders: A Retrospective Study
Subarna Giri[1], Bikram Prasad Gajurel[1]
[1]*Tribhuvan University Teaching Hospital, Kathmandu*
Background: Primary central nervous system (CNS) demyelinating disorders can have identical radiological features but varies in terms of distribution, natural history, and prognosis. While advancements in diagnostics and treatment are still not available in developing countries, reliance remains on clinical findings.
Objective: To explore various clinical and radiological presentations of multiple sclerosis (MS), neuromyelitis optica spectrum disorders (NMOSD), and myelin oligodendrocyte glycoprotein antibody disease (MOGAD).
Methods: A retrospective study including all the new and old cases of MS, NMOSD, and MOGAD admitted in a tertiary center over the last one year was conducted. We used non-probability convenience sampling method. Data were collected from discharge summary and analyzed using SPSS statistics. Magnetic resonance imaging (MRI) reports were collected from patient using phone call when needed. Ethical clearance from institutional board was obtained.
Results: Of the 49 patients, NMOSD, MS and MOGAD were 25(51%), 18(36.73%), 6(12.24%) respectively. The mean age of patients was 39.91±11.37. In NMOSD, common clinical manifestations were sensory symptoms (68%), quadriparesis/paraparesis (52%), optic neuritis (44%), and bowel/bladder dysfunction (24%). 20% had area postrema syndrome and 52% were antibody positive. Sensory symptoms (50%), optic neuritis and brainstem manifestations (33.30% each), bowel/bladder dysfunction and quadriparesis/paraparesis (22.20% each) were common among MS. In MOGAD, optic neuritis (66.70%) was the most common feature. Distribution of lesion in MRI of MS patients were periventricular (72.22%), brainstem (44.44%) and cortical white matter (33.33%) whereas in NMOSD spinal cord (56%), and brainstem (24%) were the most common site. 48% of NMOSD had longitudinally extensive transverse myelitis. MRI showed features of optic neuritis in 24% of NMOSD and 50% of MOGAD patients.
Conclusion: Primary CNS demyelinating disorders display diverse clinical features with majority having sensory symptoms, quadriparesis/paraparesis and visual manifestations. On MRI, commonly involved sites were periventricular, spinal cord and brainstem.
Disclosures: There is no conflict of interests.

P-61

Demography, Clinical Patterns and Therapy of Multiple Sclerosis Over Two Decades – a Single-centre Experience from a Low-middle Income Country

Sruthi Sivaraman Nair[1], Avinash Kulkarni[1], Vaibhav Tandon[1], Soumya Sundaram[1]
[1]*Sree Chitra Tirunal Institute for Medical Sciences and Technology*

Background: The burden of multiple sclerosis (MS) has increased manifold in India over the last 50 years including recent changes in therapeutic preferences. These changes have not been well-quantified.
Objective: We aimed to study the changes in clinic-demographic profile, diagnosis and therapeutic choices over 20 years from a tertiary care centre in South India.
Methods: This retrospective observational study was done by review of case records of all patients diagnosed with multiple sclerosis in a single institute from 2001 to 2020. The patients were classified into 2 groups based on the year of presentation (Group D1: 2001-2010 and group D2: 2011-2020). Demographics, clinical profile, laboratory parameters, disease course, and use of disease modifying therapies (DMTs) were extracted from the records and compared between the two groups. A p value of 0.05 was assigned for significance.
Results: Of 306 patients, 72 and 234 belonged to groups D1 and D2, respectively, representing a 3.7-fold increase in the second decade. The age of onset, female-male ratio and urban-rural distribution did not vary significantly between the groups.
Relapse onset disease was noted in 290 (94.8%). Isolated optic neuritis presentation decreased significantly while cerebellar and opticospinal presentations increased from D1 to D2. Time from symptom onset to presentation and time to first MRI were similar. Oligoclonal band positivity was significantly higher in D2 ($p<0.01$).
Disease modifying therapies (DMTs) were more frequently initiated in D2 (85.5 vs 56.9%, $p<0.01$). Time to DMT initiation from onset (37.1 vs 64.5 months, $p<0.01$) was significantly shorter in D2. DMT was shifted in 36.6% in D1 and 42.5% in D2. The median expanded disability status scale (EDSS) at final visit was 3 (range 0-10) in D1 against 1.5 (0 – 8.5) in D2. Frequency of SPMS was higher in D1 (25%vs 11.1%, $p=0.007$).
Conclusion: The MS patient number markedly increased whereas time to initiation of therapy and disability reduced in the second decade compared to the first. The demographic constitution and distribution of MS subtype remained stable.
Disclosures: None of the authors have any conflicts of interest to declare.

P-62

Withdrawn

P-63

Human leukocyte antigen class II association in Korean patients with myelin oligodendrocyte glycoprotein antibody-associated disease

Jin Myoung Seok[1], Soonwook Kown[2], Mi Young Jeon[3], Hye Lim Lee[4], Yeon Hak Chung[4], Hyunjin Ju[5], Byoung Joon Kim[6]
[1]*Department of Neurology, Soonchunhyang University Hospital Cheonan*
[2]*Department of Neurology, Inha University Hospital*
[3]*Department of Neurology, Neuroscience Center, Samsung Medical Center*
[4]*Department of Neurology, Korea University Guro Hospital, Korea University College of Medicine*
[5]*Department of Neurology, Soonchunhyang University College of Medicine Seoul Hospital*

[6]*Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine*
Background: Understanding of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) has improved substantially with the discovery of autoantibody, leading to the proposal of international consensus diagnostic criteria. However, genetic factors predisposing to MOGAD remain unclear.
Objective: We aimed to analyze the association of Human Leukocyte Antigen (HLA) class II alleles with MOGAD in the Korean population.
Methods: Seropositive MOGAD patients who met the recent international MOGAD Panel proposed criteria were enrolled. HLA class II genotyping (HLA-DRB1, -DPB1, and DQB1) were performed using the sequence-specific oligonucleotide probe method with the Luminex system and the WAKFlow HLA typing kit. The results were compared with published HLA allele data from 173 genetically unrelated healthy Korean controls.
Results: A total of 13 patients were included, with 69.2% of females (9/13). The median age of onset was 34.0 years (range 15.0–59.3), and the median disease duration was 3.6 years (range 0–27.6). HLA-DRB1*04:06 and -DQB1*03:02 were found to be significantly associated with MOGAD (OR 5.42, 95%CI 1.59–16.40; and OR 3.92, 95%CI 1.44–10.04, respectively). In-silico predictions of MOG-deprived peptides binding with high affinity to HLA-DRB1*04:06 or HLA-DQA1*03:01-DQB1*03:02 were performed using NetMHCIIpan 4.1 server. Interestingly, the peptide with the strongest affinity for HLA-DRB1*04:06 was located in the transmembrane region (FVIVPVLGP, 181-195 in human MOG alpha1 isoform).
Conclusion: This study identified the HLA-DRB1*04:06 and -DQB1*03:02 as predisposing factors for MOGAD in Korean patients. Large-scale studies are needed to further elucidate the relationship between these genetic factors and clinical spectrum of MOGAD.

P-64

Clinical Profile and Therapeutic Response in Paediatric Inflammatory Demyelinating Diseases of the Central Nervous System -a single centre experience from India

Soumya Sundaram[1], Manuraj N[1], Sruthi S Nair[1]
[1]*Sree Chitra Tirunal Institute for Medical Sciences and Technology*
Background: The clinical presentation, therapeutic options, and outcomes of various acquired pediatric inflammatory demyelinating disorders (PIDDs) of the central nervous system (CNS) differ from those in adults. However, robust data is lacking, leading to this study's conceptualisation.
Objective: To compare the clinical, laboratory, and radiological profile and treatment of paediatric IDDs of CNS-multiple sclerosis (MS), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and neuromyelitis optica spectrum disorder (NMOSD).
Methods: The clinical, laboratory and radiological profile and treatment details in patients with PIDDs (age of onset ≤18 years) from 2012 to 2022 were collected retrospectively, and their subtypes were compared. The McDonald criteria, international consensus diagnostic criteria for NMOSD and Banwell et al. criteria for MOGAD were used to include cases. Secondary causes of demyelination due to systemic autoimmune disorders, mitochondrial disorders, CNS neoplasms and genetic white matter disorders were excluded. Patients with inadequate clinical, laboratory and imaging data were also excluded from the analysis.
Results: The mean age of onset of 87 patients was 12 ± 4.4 years; 63 (72.4%) were females. MS, NMOSD, and MOGAD were seen in 42 (48.3%), 20 (21%) and 9 (11.3%) patients, respectively, with a mean age of onset of 14.2±3, 11.3±4.6 and 7±3.2 years (MS vs MOGAD, $p<0.0001$). In MS and NMOSD, the most

frequent initial presentation was brainstem/cerebellum (20.9% vs 40%), followed by spinal cord and optic nerve, whereas in MOGAD, it was hemispheric (33.3%) and optic nerve (33.3%). Relapsing course was seen in 30 (71.4%), 15 (75%) and 6 (66.7%) patients with MS, NMOSD and MOGAD respectively. The most common maintenance therapy was rituximab (13/33, 31%) in MS and mycophenolate mofetil (MMF) in NMOSD (6/16, 37.5%) and MOGAD (5/9, 55.6%). Despite maintenance therapy, 16 (42%), 9 (45%), and 2 (22.2%) patients with MS, NMOSD and MOGAD respectively relapsed.
Conclusion: MS was more frequent in older children, whereas in younger children, it was MOGAD. Relapses were seen in all subgroups but more frequent in MS. Rituximab was the preferred agent for maintenance therapy in MS and MMF for non-MS (NMOSD and MOGAD).

P-65

Differences in susceptibility to multiple sclerosis by sex with a focus on the susceptibility regions on X chromosome and MHC region

Masaya Harada[1], Hajime Takeuchi[1], Keisuke Mizutani[1], Ayano Matsuyoshi[1], Kaitto Ogura[2], Siqi Song[1], Ezgi Ozdemir Takase[1], Megumi Kiyota[3], Yuu-ichi Kira[1], Kazunori Iwao[1], Koji Shinoda[1], Mitsuru Wtanabe[1], Katsuhisa Masaki[1], Ryo Yamasaki[1], Jun-ichi Kira[4], Noriko Isobe[1]
[1]Department of Neurology, Graduate School of Medical Sciences, Kyushu University
[2]Department of Biomedical Science, Kyushu University School of Medicine
[3]The Research Support Center, Research Center for Human Disease Modelling, Kyushu University Graduate School of Medical Sciences
[4]Translational Neuroscience Research Center, Graduate School of Medicine, and School of Pharmacy at Fukuoka International University of Health and Welfare
Background: A recent genome-wide association study of Northern Europeans identified T allele of rs2807267 on X chromosome was associated with increased risk of multiple sclerosis (MS). However, this association has not been verified in Asians. Additionally, it has been unclear whether sex difference exists on the impact of susceptibility HLA alleles in Asians.
Objective: To examine the association of rs2807267 and HLA-DRB1*15:01 on MS susceptibility and see whether there is any gender difference on their susceptibility impact.
Methods: Genotyping of rs2807267 was performed for DNA from 116 MS patients (male (M)/female (F) 37/79) and 178 healthy controls (HC) (M/F 84/94) by Taqman Assays. Association analysis was performed using previously measured HLA information and clinical information.
Results: The frequency of the T allele of rs2807267 was associated with MS susceptibility in men (MS 43.2% vs. HC 19.0%, unit OR = 1.80, p = 0.007), while it was not significantly associated in women (MS 25.3% vs. HC 19.7%, unit OR = 1.42, p = 0.191). Within 147 individuals with the data on the carrying status of HLA-DRB1*15:01 allele available, a multivariate logistic analysis with the number of carried HLA-DRB1*15:01 alleles and rs2807267 T allele dose as covariates demonstrated that MS susceptibility association was only found for HLA-DRB1*15:01 allele (unit OR = 3.47, p = 0.024) but not for rs2807267 in women, while it was only found for the number of T alleles in rs2807267 (unit OR = 1.95, p = 0.045) but not for HLA-DRB1*15:01 in men.
Conclusion: X chromosome SNP rs2807267 and HLA-DRB1*15:01 may be associated with MS susceptibility differently by sex. Further study is required to clarify the underlying susceptibility mechanisms.
Disclosures: Declarations of interest: none

P-66

Small extracellular vesicle-derived miRNAs to differentiate monophasic from relapsing MOGAD

Seung Ho Choo[1], Hyunjin Ju[2], Yongeun Cho[3], Eun-Seon Ju[4], Yeon Hak Chung[5], Dong-Gyu Jo[3], Ju-Hong Min[4]
[1]*Samsung Medical Center*
[2]*Department of Neurology, Soonchunhyang University Seoul Hospital*
[3]*School of Pharmacy, Sungkyunkwan University*
[4]*Department of Neurology, Samsung Medical Center*
[5]*Department of Neurology, Korea University Guro Hospital*

Background: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) exhibits a monophasic course in 40-50% of adult patients, distinguishing it from multiple sclerosis (MS) or neuromyelitis optica spectrum disorder (NMOSD). However, reliable biomarkers predicting relapse in MOGAD remain largely unknown.
Objective: This study aims to investigate serum-derived small extracellular vesicle (sEV) miRNAs as potential biomarkers for MOGAD to distinguish between relapsing and monophasic courses.
Methods: We conducted a comprehensive miRNA analysis on serum sEV, identifying differentially expressed miRNAs (DEmiRNAs) between monophasic and relapsing MOGAD groups. The discriminatory power of these miRNAs was evaluated using area under the curve (AUC) analysis in receiver operating characteristic (ROC) curves. We examined correlations between miRNA profiles and clinical parameters, such as disease severity by the expanded disability status scale (EDSS) score and disease activity by annualized relapse rate (ARR).
Results: Serum samples were obtained from 23 patients with MOGAD patients, with a median disease duration of 3.7 years; 10 patients were classified as monophasic while 13 patients were classified as relapsing MOGAD. We identified 34 DEmiRNAs (15 up-regulated, 19 down-regulated) in relapsing MOGAD compared to monophasic MOGAD. Notably, hsa-miR-1234-3p (AUC=0.846) and hsa-miR-654-3p (AUC=0.846) demonstrated the highest AUC values for distinguishing relapsing from monophasic MOGAD. Their combined use as a panel further improved discriminatory power (AUC=0.985). Additionally, hsa-miR-877-5p was negatively correlated with ARR, while hsa-miR-363-3p and miR-767-5p correlated negatively with EDSS scores. Furthermore, hsa-miR-671-3p, hsa-miR-767-5p, and hsa-miR-363-3p were negatively correlated with EDSS score changes from sampling to last follow-up.
Conclusion: Our study suggests that hsa-miR-1234-3p and hsa-miR-654-3p hold promise as biomarkers for distinguishing between monophasic and relapsing courses in MOGAD. Further validation of these miRNAs could enhance management and prognostication in MOGAD.

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Conflict of Interest:

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P-67

Neuromyelitis Optica Spectrum Disorder and Pregnancy: Insights from a Single-Center Study in Thailand

Nuttakarn Budtarad[1], Tatchaporn Ongphichetmehta[2], Sasitorn Siritho[1]
[1]*Faculty of Medicine Siriraj Hospital, Mahidol University*

[2]*Siriraj Neuroimmunology Center, Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University*

Background: There has never been a study focused on assessing disease and pregnancy outcomes in Thai patients with Neuromyelitis Optica Spectrum Disorder (NMOSD), a condition that disproportionately affects women of childbearing age and poses risks to both mother and fetus.

Objective: Our study aimed to assess disease and pregnancy outcomes in Thai patients with Neuromyelitis Optica Spectrum Disorder (NMOSD).

Methods: From our central nervous system inflammatory demyelinating diseases (CNS-IDDs) registry, we retrospectively identified and included patients with NMOSD who had a pregnancy history between December 2011 and November 2023 in our study. The study period encompassed the 12-month-before pregnancy (BP) to the 12-month-postpartum (PP) for each pregnancy.

Results: We found 8 NMOSD patients with sufficient data from 10 pregnancies. During the study period, we observed 13 relapses, with a notable 76.92% occurring PP. The mean annualised relapse rate (ARR) peaked at 1.2 (SD±1.93) during specific postpartum intervals (0-3 and 6-9 months PP), significantly increasing from 0.20 (SD±0.42) in the 12 months BP to 1.00 (SD±1.49) during the 12 months PP. Our study revealed a high incidence (75%) of maternal and/or fetal complications, even in patients who experienced no relapses during the 12 months before pregnancy. Disability, assessed using Expanded Disability Status Scale (EDSS) scores, worsened from 1.56 (SD±2.18) BP to 2.1 (SD±2.63) at 6 months PP. Increase in mean EDSS scores from the pre-pregnancy (BP) period to delivery (DP) and further to postpartum (PP), consistent with findings from meta-analyses. Maternal and fetal complications were prevalent, with six out of nine pregnancies experiencing adverse outcomes.

Conclusion: Similar to other studies, we found high relapse rate esp. at postpartum and high incidence of maternal and fetal complications in NMOSD patients with pregnancy. Our study highlights the critical need for comprehensive management strategies for NMOSD.

Disclosures: No authors have Conflict of Interests.

P-68

The Prevalence of Sleep Abnormalities in Patients with Neuromyelitis Optica Spectrum Disorder: An Actigraphy Study

Tatchaporn Ongphichetmetha[1], Jiraporn Jitprapaikulsan[1], Chawanont Pimolsri[2], Wattanachai Chotinaiwattarakul[2], Natthapon Rattanathamsakul[1], Naraporn Prayoonwiwat[1], Sasitorn Siritho[1]

[1]*Siriraj Neuroimmunlogy Center, Mahidol University Siriraj Hospital*

[2]*Siriraj Sleep Center, Mahidol University Siriraj Hospital*

Background: Sleep problems are common in neuromyelitis optica spectrum disorder (NMOSD) due to the preferential expression of AQP4 in periventricular organs, affecting the reticular activating system which is crucial for sleep generation and the control of the sleep-wake cycle. These sleep problems are often under detected and underreported in outpatient settings.

Objective: To examine sleep abnormalities in NMOSD patients using wearable actigraphy.

Methods: NMOSD patients from the Multiple Sclerosis and Related Disorders Clinic at Siriraj Hospital were included. A 7-day sleep diary and wrist-worn actigraphy for seven consecutive nights were used for data collection. Descriptive data were reported as mean ± SD or median (IQR) for continuous data, and frequency for categorical data.

Results: Twenty-four NMOSD patients were included in the study. The mean age was 50 ± 14 years, with 96% being female (23/24). The mean BMI was 24.02 ± 3.75 kg/m². The mean disease duration was 10 ±

7.58 years, with a median baseline EDSS of 3.0 (2-4.25). The mean time in bed, total sleep time, and sleep onset latency were 507.2 ± 63.16 minutes, 425 ± 54.06 minutes, and 23.25 ± 17.30 minutes, respectively. Among the 24 NMOSD patients, 6 (25%) had sleep efficiency < 80%. The mean wake after sleep onset (WASO) was 39.41 ± 19.92 minutes.
Conclusion: A significant proportion of NMOSD patients experienced decreased sleep efficiency as evaluated by wearable sleep actigraphy. Greater attention to sleep problems should be given to NMOSD patients.
Disclosures: None

P-69
Knowledge of Multiple Sclerosis and Neuromyelitis Optic among Undergraduate Health Students in Indonesia: A Preliminary Study
Gita Ambarsari[1], Riwanti Estiasari[2], David Pangeran[3]
[1]*Undergraduate Program Faculty of Medicine University of Indonesia*
[2]*Neurology Department Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo General Hospital Jakarta*
[3]*Neurology Department Faculty of Medicine Universitas Indonesia, Universitas Indonesia Hospital*
Background: Albeit rare, multiple sclerosis (MS) and neuromyelitis optic spectrum disorder (NMOSD) have been increasingly detected in recent years in Indonesia, typically affecting young adult females. Thus, it is essential to raise awareness beginning from primary healthcare services, which is the first line of detection.
Objective: This study aimed to assess the knowledge of undergraduate health students regarding MS and NMOSD in Indonesia.
Methods: A series of 13 and 11 binary questions of MS and NMOSD, respectively, was presented to 97 undergraduate students from Universitas Indonesia, including Faculty of Medicine, Dentistry, Pharmacy, Nursing, and Communities. Questionnaire was categorized to profile, risk factor, and prognosis. It demonstrated good validity based on Pearson's correlation but had low reliability.
Results: The majority of respondents were female (81 (83.5%) subjects) of 20 (18-23) years old. There were 49 (50.5%) and 22 (22.7%) subjects who had ever heard and 29 (29.9%) and 13 (13.4%) subjects who had ever studied about MS and NMOSD, respectively. Of 13 MS questions, respondents provided 10 (5-13) [76.9 (38.5-100)%] right answers. Three highest right answers were about whether MS is linked to morbidity (94.8%), MS as non-communicable disease (NCD) (92.8%), and MS as central nervous system (CNS) disease (90.7%) whereas three lowest right answers were MS is more common in woman (43.3%), MS drug was insured by the government (45.4%), and relapse of MS (47.4%). Of 11 NMOSD questions, respondents provided 9 (5-11) [81.8 (45.5-100)%] right answers. Three highest right answers were about aquaporin-4 diagnose test (94.8%), NMO as CNS disease (92.8%), and NMO as NCD (91.8%). Three lowest right answers were about its symptoms (44.3%), its smoke-related (50.5%), and the vitamin D role (61.9%).
Conclusion: Undergraduate health students mostly perceived MS and NMOSD as noncontagious CNS disease with high morbidity. However, awareness about the clinical symptoms of MS and NMOSD as well as its relapse prevention should be increased among this population.

P-70
From First Signs to Accurate Diagnosis: Correlating Initial Symptoms with Typical and Atypical Presentations of Multiple Sclerosis
Anyeliria Sutanto[1], Rocksy Fransisca Vidiaty Situmeang[1], Billy Susanto[2], Catherine Siany Kurniawan[2], Rosaria

Oktafiani Darmawan[1]
[1]*Siloam Hospitals Lippo Village, Tangerang, Indonesia*
[2]*Faculty of Medicine Pelita Harapan University, Tangerang, Indonesia & Siloam Hospitals Lippo Village, Tangerang, Indonesia*
Background: Employing McDonald criteria to diagnose multiple sclerosis (MS) requires a cautious approach to clinical characteristics, alongside CNS imaging and CSF analysis. MS exhibits a spectrum of clinical manifestations that overlap with other CNS demyelinating disorders. Proper differentiation is essential for initiating effective therapeutic intervention.
Objective: This descriptive study seeks to enhance the diagnostic value of early onset symptoms of typical versus atypical presentation in the diagnosis of MS relative to other demyelinating CNS disease.
Methods: The data was sourced from the medical record of individuals diagnosed with MS based on the McDonald Criteria at the MS Clinic of Siloam Hospitals Lippo Village in Tangerang, Indonesia. Data analysis was conducted to derive the percentage of early clinical manifestations reported by the patients.
Results: Out of 83 patients diagnosed MS patients, 90.4% exhibited with typical presentations and 9.6% with atypical presentations. Among patients with typical presentation, the most common manifestations were focal supratentorial syndromes (36.0%), followed by partial myelopathy (29.3%), focal brainstem/cerebellar syndromes (20.0%), and unilateral optic neuritis (14.7%). Bilateral optic neuritis (62.5%) and complete myelopathy (37.5%) were observed in patients with atypical presentations.
Conclusion: Patients predominantly exhibit typical clinical presentation according to the McDonald criteria. Thus, it is crucial to apply these criteria meticulously to accurately diagnose MS and to differentiate it from other CNS demyelinating conditions.

P-71

Eye Movement Disorders in Patients with Optic Neuritis Associated with Central Nervous System Demyelinating Diseases

Peerawat Thavonlun[1], Natthapon Rattanathamsakul[1]
[1]*The Faculty of Medicine, Siriraj Hospital, an Affiliated Institution of Mahidol University*
Background: CNS demyelinating diseases affect neuroaxonal structures in the brain parenchyma, and ocular motility abnormalities can occur as a consequence of optic neuropathies or lesions affecting ocular motor pathway.
Objective: To study the prevalence and clinical features of eye movement abnormalities in patients with optic neuritis (ON).
Methods: We conducted a prospective observational study among consecutive patients with the history of at least one episode of ON. Comprehensive neurological and ophthalmological examinations were performed, along with brain MRI and qualitative assessment of video ocular motor recording.
Results: Of all 53 patients, 42 (79.2%) were female, and median disease duration was 12 months (IQR [6, 16]). NMOSD was the most common cause (66.2%), followed by MS (26.4%) and MOGAD (11.4%). Abnormal spontaneous eye movements (ASEMs) were noted in 13 cases (24.5%), including gaze-evoked nystagmus (13.2%), Hiemann-Bielschowsky phenomena (HBP, 9.4%) and abducting nystagmus (7.5%). Square wave jerks were reported in 37.7% of cases. Those with ASEMs were likely to have poor visual acuity (p=0.007), more ON attacks (p=0.004). HBP was found in those having poor visual acuity (range 20/200 to NLP).
Conclusion: ASEMs are not uncommon in patients with ON. Their presence is associated with poorer visual functions.

Disclosures: All authors have no relevant financial disclosure.

POSTER SESSION - 5
Infection as Differential Diagnosis and Treatment-related Diseases

P-72
Multiple sclerosis-like attack following adalimumab treatment in ankylosing spondylitis
Seong-il Oh[1], Kyong Jin Shin[2]
[1]*Kyung Hee University Hospital, Kyung Hee University College of Medicine*
[2]*Inje University Haeundae Paik Hospital*
Background: The relationship between central nervous system (CNS) demyelinating diseases and systemic autoimmune diseases such as SLE or RA, remains a topic of debate. The coexistence of multiple sclerosis (MS) and ankylosing spondylitis (AS) is notably rare. Demyelinating lesions are infrequently reported in patients with AS following anti-TNF therapy.
Objective: We report a case of a 37-year-old male with AS, treated with adalimumab, who developed a demyelinating lesion in the brainstem suggestive of multiple sclerosis.
Methods: The patient presented with left facial sensory changes. He had a 10-year history of low back pain and upper limb pain, leading up to diagnosis for AS and ongoing immunotherapy under rheumatology care. Despite the use of adalimumab for the past three years, his symptoms persisted. Despite occasional interruptions in adalimumab treatment, the patient's AS-related symptoms were not significantly aggravated. The patient experienced sudden onset of left facial sensory changes and disequilibrium upon waking, leading to a visit to neurology clinic.
Results: Brain MRI revealed a lesion in the left lateral pons. Pests for paraneoplastic antibodies, anti-aquaporin antibodies, and anti-MOG antibodies were negative, and there were no visual symptoms or abnormalities in visual evoked potentials. Given the potential for recurrence of demyelinating lesions, the treatment was switched to oral immunotherapy with sulfasalazine. The patient has remained stable without new relapses or symptom exacerbation.
Conclusion: Anti-TNF-α agents are effective and generally safe for treating rheumatological diseases; however, the occurrence of multiple sclerosis-like events in patients receiving anti-TNF-α therapy necessitates ongoing discussion.

P-73
An Unusual Presentation of Neuromyelitis Optica Spectrum Disorder after a COVID-19 infection
Jae-Myung Kim[1], Jong-Hee Choi[2]
[1]*Chonnam National University Hospital and Medical School*
[2]*Chonnam National University Hospital*
Background: Although severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, a.k.a. COVID-19) is known to be a neurotropic virus that is commonly accompanied by neurological complications, para-infectious or post-infectious central nervous system (CNS) demyelinating disease including neuromyelitis optica spectrum disorder (NMOSD) has been rarely reported.
Objective: The pathomechanism and causal relationship between the two distinct diseases are still to be elucidated. Herein, we report a case of newly developed NMOSD confirmed by AQP4-Ab right after COVID-19 infection, with a literature review for possible explanation.
Methods: A previously healthy 50-year-old woman complained of headache for three days. She had a

three-day preceding history COVID-19 infection. She had received COVID-19 vaccination (Pfizer) for three times without serious complications. On admission, dull headache associated with neck stiffness was observed. However, fever or respiratory symptoms were absent.
Results: Initial neurologic examinations revealed dysarthria and limb ataxia on the right side with veering tendency to the right. T2-weighted brain magnetic resonance imaging (MRI) documented multifocal high signal intensity lesions (HSIL) including the left internal capsule and cerebral peduncle without contrast enhancement. Cerebrospinal fluid (CSF) analysis showed marked pleocytosis (total nucleated cell count: 427 /μL, lymphocyte: 50.2%), associated with elevated protein concentration (117 mg/dL), but normal serum/CSF glucose ratio (0.5). CSF-PCR test for COVID-19 was negative. During admission, urinary incontinence and left hemiparesis was newly developed. T2-weighted spine MRI revealed multiple long-segmental, centrally located HSIL involving C4-6 and T3-10 level. The diagnosis of NMOSD was confirmed by detection of IgG AQP-4 Ab in her serum (titer: 2+).
Conclusion: Although CSF-PCR test for COVID-19 was negative, direct CNS invasion of SARS-CoV-2 was considered based on marked CSF pleocytosis associated with headache, meningeal irritation signs, and this condition might induce more profound damages.

P-74
Spinal Cord Infarction Attributed To SARS-CoV-2 In A Long-term Asymptomatic Patients With AQP-4 + NMOSD
Jae Young An[1]
[1]*St. Vincent Hospital, The Catholic University of Korea*
Background: Spinal cord involvement after COVID-19 more commonly includes infectious transverse myelitis, para and post infection myelopathy.
Objective: While stroke and lower extremity venous thromboembolic have been commonly reported following acute infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spinal cord infarction or ischemia has been extremely rare.
Methods: We report a 54-year-old woman who developed spinal cord infarction (SCI) with anti-aquaporin (AQP) 4 antibody seropositive after mild SARS-CoV-2. She had myalgia and chills for two days, was diagnosed with COVID-19. While undergoing conservative treatment, she developed a tearing pain in her neck followed by quadriparesis in whom an MRI scan revealed long cervico-thoracic myelopathy. Anterior spinal artery occlusion and possibly longitudinal extensive transverse myelitis were considered as differential diagnosis. The serum examination was reported as positive for anti-aquaporin 4 (AQP4) antibody. She has a history of optic neuritis from 25 years ago but has remained undiagnosed due to the absence of any further attacks. She received empiric pulsed steroids without improvement. Additional intravenous immunoglobulin treatment had no effect on symptom improvement.
Results: A variety of COVID-19-related spinal cord manifestations have been reported. On neuroimaging, a spinal cord infarction and acute transverse myelitis have a close resemblance, and differentiation may be difficult in a patient with COVID-19-associated acute myelopathy.
Conclusion: Despite mild and non-severe COVID-19 symptoms, the presence of thromboembolism in the pulmonary vasculature and deep veins suggests that spinal cord infarction may also be attributed to COVID-19-induced hypercoagulopathy.

P-75
A Case With Late-onset Neuromyelitis Optica Spectrum Disorder Mimicking Wernicke Encephalopathy
Juhyeon Kim[1], Minkyeong Kim[1]

[1]*Department of Neurology, Gyeongsang National University Hospital*
Background: Wernicke encephalopathy (WE) is caused by a lack of vitamin B1, resulting from either insufficient dietary intake or errors in metabolism. In contrast, Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory demyelinating disease affecting the central nervous system.
Objective: WE and NMOSD differ significantly in terms of their etiology, disease mechanisms, and treatments. However, they share some clinical features and radiologic findings, which may lead to misdiagnoses.
Methods: A 64-year-old woman was referred to the emergency room due to intractable vomiting. This severe vomiting led to an inability to eat or drink, resulting in weight loss and general weakness. For a week, she was entirely dependent on nasogastric tube feeding. A few days before her referral, she began experiencing diplopia and dizziness. The patient's vital signs were within normal limits. Neurological examination revealed drowsiness and one-and-a-half syndrome without limb weakness or ataxia. Abdominal computed tomography and tumor markers showed no abnormalities. Brain magnetic resonance imaging (MRI) demonstrated high signal intensities in the periventricular regions, third and fourth ventricles, and cerebral aqueduct, with particular prominence in the right hypothalamus on fluid-attenuated inversion recovery images. Based on the clinical presentation, examination results, and MRI findings, the patient was diagnosed with WE and received high-dose intravenous vitamin B1. On the second hospital day, she became more alert; however, her intractable vomiting persisted despite treatment with metoclopramide, ramosetron, and ondansetron. Additionally, her one-and-a-half syndrome did not improve. On the third hospital day, the patient reported tingling sensations in her trunk and bilateral hands.
Results: Upon neurological examination, the patient demonstrated right peripheral-type facial palsy, tongue deviation to the right, muscle weakness, and augmented pain and pinprick sensations at the thoracic spinal cord level 6 and below. Her Babinski signs were positive bilaterally. A spinal cord MRI showed high signal intensities in the cervical and upper thoracic spinal cord, from C3 to T1, on T2-weighted images, with associated enhancement. The acute onset of longitudinally extensive transverse myelitis, intractable vomiting, brainstem syndrome, and the radiologic findings were consistent with a diagnosis of NMOSD. We initiated high-dose intravenous steroids, leading to significant improvement in the patient's vomiting the following day. However, her muscle weakness persisted, so a second cycle of high-dose steroids was administered. As a result, her muscle strength improved in the bilateral lower extremities. Anti-aquaporin-4 IgG antibodies were positive.
Conclusion: WE and NMOSD share some clinical features and radiologic findings, which can lead to misdiagnoses. Since both conditions require early intervention, alternative diagnoses should be considered based on the disease course or response to treatment.

P-76
Case Presentation: Acute Toxic Hepatitis in a Patient with Multiple Sclerosis Using Dimethyl Fumarate
Mehmet Ufuk Aluclu[1]
[1]*Department of Neurology, Faculty of Medicine, Dicle University*
Background: Drug-induced liver injury is a condition that occurs within 5 days to 12 months after starting the medication and often manifests as sudden onset liver damage. Dimethyl fumarate is a fumaric acid ester used as a first-line treatment for relapsing-remitting multiple sclerosis. An increase in aspartate aminotransferase occurs in 4% of MS patients.
Objective: DMF has neuroprotective, immunomodulatory, and antioxidant effects on the central nervous

system (CNS) and is administered orally at a dose of 240 mg twice daily.
Methods: A female patient with newly diagnosed RRMS who started DMF 240 mg twice daily showed elevated liver function tests three months after initiating the medication. Upon follow-up, the enzyme elevations exceeded five times the normal limit, leading to the discontinuation of the drug. When liver function tests rose to 15 times the normal limit, the patient was admitted to the hepatology clinic. A liver biopsy revealed chronic hepatitis.
Results: Following medical treatment, the patient's liver function tests returned to normal within two months. months or as clinically indicated. This case highlights the importance of laboratory monitoring in patients on DMF treatment and presents a rare instance of acute toxic hepatitis with literature findings.
Conclusion: Patients starting DMF treatment should have monthly AST/ALT and complete blood count tests during the first three months. For long-term follow-up, these tests should be repeated every 6-12 months or as clinically indicated.
Disclosures: Nothing to disclose.

P-77
Herpes Zoster-Induced Myelitis Leading to NMOSD
Seong-il Oh[1]
[1]*Kyung Hee University Hospital, Kyung Hee University*
Background: Herpes zoster (HZ) reactivation can lead to severe neurological complications such as myelitis. The association between HZ and neuromyelitis optica spectrum disorder (NMOSD) is not well understood. NMOSD is an autoimmune condition often associated with aquaporin-4 (AQP4) antibodies, and the potential connection between viral infections like HZ and NMOSD onset or exacerbation is still being explored.
Objective: We report a case of HZ-associated myelitis transitioning into NMOSD with notable AQP4 antibody seroconversion.
Methods: A 70-year-old female with a history of HZ in the right neck and arm developed progressive sensory and motor deficits. Initially, she experienced fatigue and decreased sensation in her right arm, which extended to her left arm and both hands, causing involuntary cramping and twisting. Vesicular lesions were noted on her posterior neck, diagnosed as HZ, and she completed antiviral therapy. Despite treatment, her symptoms progressed to bilateral leg weakness.
Results: MRI revealed acute transverse myelitis from the cervical to the upper thoracic spine. Initial serology was positive for AQP4 antibodies, while MOG-IgG antibodies were negative. Treatment began with high-dose corticosteroids, followed by intravenous immunoglobulin (IVIG) due to an unsatisfactory response. Despite treatment, her condition showed only mild improvement, necessitating ongoing physical rehabilitation. A follow-up study for AQP4 antibodies showed seroconversion to negative after two months.
Conclusion: Herpes zoster can lead to severe neurological sequelae, particularly in immunocompromised individuals or those with pre-existing neurological conditions. This patient's course highlights the potential for VZV reactivation to precipitate or exacerbate

P-78
Afebrile Appendicitis Without CRP Elevation In A Patient With AQP4+NMOSD Under Satralizumab Treatment
Hiroshi Kuroda[1], Kimihiko Kaneko[2], Yuki Matsumoto[2], Chihiro Namatame[2], Hirohiko Ono[2], Yoshiki Takai[2], Toshiyuki Takahashi[2], Tatsuro Misu[2], Kazuo Fujihara[1], Masashi Aoki[2]
[1]*Fukushima Medical University School of Medicine*

[2]*Tohoku University Graduate School of Medicine*
Background: Satralizumab is a biological drug used for relapse prevention of anti-aquaporin-4 antibody-positive NMOSD (AQP4+NMOSD). It exerts biological effects through interleukin-6 (IL-6)/IL-6 receptor blockage, which inhibits C-reactive protein (CRP) production.
Objective: To illustrate clinical and laboratory findings of a patient with AQP4+NMOSD who developed appendicitis under satralizumab treatment.
Methods: A case report.
Results: A female AQP4+NMOSD patient started to undergo satralizumab treatment at the age of 44. After starting satralizumab, prednisolone was tapered off in one year. At the age of 47, two weeks after the 32nd injection of satralizumab, she felt lower abdominal pain and nausea. On outpatient visit, she was afebrile (35.5 degrees C) but presented with right lower abdominal pain and rebound tenderness. Laboratory tests showed normal white blood cell count (6,530 /mL, reference value 3,300 8,600) and normal CRP level (< 0.03 mg/dL) but showed elevated percentage of neutrophils (88.5%). Abdominal CT scan showed a swollen appendix with fecal pellets. She was diagnosed as having appendicitis and underwent laparoscopic appendectomy. She was discharged from hospital 6 days after surgery and restarted satralizumab treatment.
Conclusion: Patients under satralizumab treatment may develop infections with normal body temperature and CRP level. In such conditions, relative neutrophilia may be a clue of infection, and it is important to work-up for avoiding missed diagnoses.

P-79

Adult-Onset Acute Disseminated Encephalomyelitis With Myelin Oligodendrocyte Glycoprotein Antibody Positivity - A Case Report

Thilani Tennakoon [1], Pavithra Thineshan [1], Arjuna Fernando[1]
[1]*Institute of Neurology, National Hospital of Sri Lanka, Colombo, Sri Lanka*
Background: Acute disseminated encephalomyelitis (ADEM) is an immune mediated central nervous system demyelinating disorder, mainly seen in children and rarely in adults. Clinical presentation consists of encephalopathy, brain stem symptoms, pyramidal signs and ataxia. Half of the adult patients can have a precipitating event such as infection or vaccination.
Objective: Objectives of this case report is to highlight the clinical manifestations of ADEM, aetiology of ADEM, differences between adult and childhood ADEM, significance of MOG antibody positivity in ADEM and treatment and prognosis.
Methods: A 47-year-old previously unevaluated male presented with fever for 3 days, altered level of consciousness, dysarthria and unsteady gait for 1 day duration with preceding new onset headache. His neurological examination revealed positive cerebellar signs including ataxia, dysarthria, nystagmus and dysdiadochokinesia. There were no pyramidal signs or cranial nerve palsies. His Magnetic Resonance Image (MRI) Brain showed multiple bilateral focal ill-defined white matter lesions involving corona radiata, corpus callosum and middle cerebellar peduncle more in favour of demyelinating disease. His cerebrospinal fluid (CSF) showed elevated protein and cellular reaction with negative cultures and serum Myelin Oligodendrocyte Glycoprotein (MOG) antibody was positive. He was initially treated with intra venous (IV) antibiotics and then with IV Methylprednisolone followed by oral prednisolone. His symptoms completely recovered with treatment, and he was discharged after arranging follow up visits at neurology clinic. Interestingly this patient has received Measles Mumps Rubella (MMR) vaccination 10 days before the onset of symptoms.

Results: This is a case of ADEM in a middle-aged male who presented with predominant encephalopathy and cerebellar signs. Our patient had typical MRI features of ADEM. We have excluded the possibility of infection, vasculitis and autoimmune rheumatological conditions which highlights the temporal relationship between ADEM and the MMR vaccination. Even though it is rare post vaccination ADEM has occurred with influenza, yellow fever, rubella, poliomyelitis, hepatitis and tetanus vaccines and the pathophysiology is known to be either molecular mimicry or myelinated neuron damage by the direct inflammation. In addition to that our patient was positive for MOG antibodies, MOG Immunoglobulin G (IgG) positivity and ADEM is commonly seen in children and less than 10% in adult cases. In children declining MOG titer is associated with monophasic disease course and persistent MOG positivity is associated with recurrent disease, while prognosis with MOG positivity in adults with ADEM is not well studied.
Conclusion: ADEM is rare among adults which require high degree of suspicion and prompt investigations. MOG positivity is known to occur with ADEM which require follow up since we are lacking data and repeating MOG titers may be helpful in deciding the prognosis.

P-80

Post Infectious Transverse Myelitis Following Dengue Virus Infection- A Case Report

Thilani Tennakoon[1], Arjuna Fernando[1]
[1]*Institute of Neurology, National Hospital of Sri Lanka, Colombo, Sri Lanka*

Background: Transverse myelitis is an inflammatory disorder of the spinal cord presenting with weakness, sensory disturbances and sphincter dysfunction. Aetiologies for this includes primary central nervous system (CNS) demyelinating disorders, infections and paraneoplastic conditions. Dengue virus infection is a rare aetiology for transverse myelitis.
Objective: Objective of this case report is to highlight the several different causes for transverse myelitis, neurological manifestations of dengue infection, when to suspect possibility of post infectious aetiologies and overview of treatment and prognosis.
Methods: A 30-year-old previously unevaluated male presented with bilateral lower limb numbness for 2 days, unsteady gait and urinary retention. He had a preceding history of fever 2 weeks ago. On examination he had T4 sensory level, with normal reflexes, upgoing planters and intact joint position sensation. Motor strength of lower limbs was 4/5 bilaterally. Rest of the neurological examination was normal including normal upper limbs. His Magnetic resonance image (MRI) pan spine showed T2 weighted high signal intensity long segment lesion predominantly involving the anterior horns of spinal cord extending from thoracic D3 to D10 level with nerve root enhancement in the cauda equina region. His cerebrospinal fluid (CSF) showed elevated proteins with negative cultures. He was evaluated for possible underlying aetiology with negative results for Human Immune deficiency Virus, Influenza, Corona virus disease, Epstein Barr Virus, Syphilis and negative CSF studies for Herpes Simplex Virus 1 and 2, Varicella Zoster Virus, Enterovirus and Tuberculosis. His aquaporin 4 and Myelin Oligodendrocyte Glycoprotein (MOG) antibodies were negative. His serum Dengue Immunoglobulin M (IgM) antibodies were positive. He was treated with intravenous (IV) Methylprednisolone followed by oral prednisolone with marked response to treatment.
Results: Here we report a case of transverse myelitis following dengue infection were responded well to IV Methylprednisolone. Neurological manifestations of dengue fever consist of meningitis, encephalitis, myelitis, myositis and neuropathies and these can be either para infectious or post infectious. Post infectious transverse myelitis usually present in 1 to 2 weeks after the onset of infection as in our patient. During post viremia phase diagnosis can be confirmed by detecting Dengue IgM antibodies. Pathophysiology is related to molecular mimicry. Para infectious transverse myelitis can be diagnosed

by detection of dengue virus antigen in the CSF. In addition to transverse myelitis our patient had cauda equina root enhancement which can mimic disorders such as MOG antibody associated disorder and there are few case reports with cauda equina involvement following dengue infection. Mainstay of treatment is with high dose steroids with favourable outcome according to the reported literature.
Conclusion: In patients with transverse myelitis, it's important to consider infectious aetiologies such as dengue infection as same as the primary CNS demyelinating disorder specially in the context of tropical countries where the dengue infection is endemic.

P-81

A case of neurosyphilis presenting as isolated bilateral papillitis

Kyomin Choi[1], Jin Myoung Seok[1]
[1]*Soonchunhyang University Cheonan Hospital, Soonchunhyang University College of Medicine/Department of Neurology*

Background: Bilateral optic neuritis with optic disc edema is one of the characteristic clinical features in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), distinguishing it from other retrobulbar optic neuritis. However, there are many differential diagnoses with similar clinical presentations.
Objective: Here, we report a case of neurosyphilis presenting as isolated bilateral papillitis to highlight important considerations for differential diagnosis in identifying clinical features specific to MOGAD.
Methods: A 25-year-old male presented with bilateral blurred vision over two weeks. The patient reported no pain, headache, or fever. Ophthalmic examination revealed decreased visual acuity with bilateral optic disc edema without other significant ocular findings, including color vision test (Fig 1). Neurological examination was unremarkable, with no signs of meningeal irritation. MRI scans of the brain and orbits were normal, and laboratory tests, including autoantibodies, were unremarkable. Anti-AQP4 and -MOG antibodies were also negative.
Results: Further evaluation for infectious causes showed positive results for serological tests for syphilis (fluorescent treponemal antigen absorbance test (FTA-ABS) IgG and IgM). The cerebrospinal fluid (CSF) study showed slightly elevated opening pressure (23.8 cmH2O), increased white blood cell count (35/mm3) with normal protein level (34.3 mg/dl), and positive CSF treponema pallidum hemagglutination (TPHA) and rapid plasma regain (RPR), confirming neurosyphilis. The patient was treated with intravenous penicillin and discharged. We are well aware that bilateral optic disc edema can occur in clinical situations involving elevated intracranial pressure, such as CNS infections. However, when patients present with bilateral vision loss and optic disc edema without other symptoms suggesting increased intracranial pressure, such as headache, fever, or meningeal irritation signs, as in this case, the diagnosis can be challenging.
Conclusion: This case reminds us that neurosyphilis can cause asymptomatic meningitis and papillitis, and underscores the importance of considering neurosyphilis as a differential diagnosis in cases of bilateral optic neuritis in autoimmune disorders.

P-82

Acute Transverse Myelitis Diagnosed as Neuromyelitis Optica Spectrum Disorder in a Patient with Systemic Lupus Erythematosus: A Case Report

Fauziah Fauziah[1], Riwanti Estiasari[1], Darma Imran[1], Kartika Maharani[1]
[1]*Department of Neurology, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Indonesia*

Background: Transverse myelitis (TM) is an inflammatory spinal cord disorder characterized by motor, sensory and autonomic dysfunction. TM can have various etiologies, including SLE. SLE may coexist with other autoimmune conditions such as neuromyelitis optica spectrum disorders (NMOSD), which is often characterized by optic neuritis, TM and postrema syndrome.
Objective: To report a case of a treated and stable SLE patient who developed NMOSD with positive AQP4 antibodies.
Methods: Case report study.
Results: A 38-year-old woman with SLE presented with progressive weakness, numbness and urinary issues for 2 weeks. Neurological exam showed hypesthesia below C8, upper motor neuron tetraparesis and autonomic disturbances. CSF analysis revealed pleocytosis 60 cells/µL, elevated protein 63 mg/dL and glucose ratio 51%. Spine-MRI showed C3-T10 intramedullary hyperintensities. Despite stable SLE and prior treatment with mycophenolate, HCQ, methylprednisolone, she was diagnosed with TM and treated with high dose methylprednisolone with no-improvement. Given her tuberculosis history and CSF, she diagnosed as tuberculous myelitis and treated accordingly. Following positive AQP4-antibody, she was re-diagnosed with NMOSD. Plasmapheresis led to significant improvement, but some hypesthesia persisted. She discharged with immunosuppressant. 2 weeks later, she experienced intractable vomiting and diagnosed with postrema syndrome and improved with methylprednisolone. 1 year later, she could walk with walker.
Conclusion: NMOSD can coexist with SLE, and the presence of AQP4-antibodies is crucial for distinguishing TM as a manifestation of NMOSD. Early and accurate diagnosis is essential, as delayed recognition and treatment can significantly impact prognosis.
Disclosures: The authors have no conflict of interests

P-83
Recurrent Painless Optic Neuritis in MOGAD: A Case Report from Indonesia
Nita Widjaya[1], Riwanti Estiasari[1], Darma Imran[1], Kartika Maharani[1]
[1]*Department of Neurology, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Indonesia*
Background: MOGAD is a rare demyelinating disease in Indonesia, presenting with symptoms such as optic neuritis, transverse myelitis, or encephalitis. In our hospital, there were 229 outpatient visits for NMOSD and 121 for MS, compared to only 8 visits by 2 patients for MOGAD. Due to its similar clinical presentation, MOGAD can be mistaken for MS or NMOSD.
Objective: To report a rare case of painless recurrent optic neuritis diagnosed as MOGAD.
Methods: Case report
Results: A 57-year-old woman experienced bilateral recurrent visual impairment over 2 years. Her first episode, in December 2022, involved sudden vision loss upon waking, with vision at 1/300 in both eyes and peripapillary haemorrhaging. A head CT showed bilateral optic nerve edema, diagnosing optic neuropathy. Treatment with methylprednisolone 250 mg bid was initiated. Her second episode occurred in May 2024, again with vision at 1/300 in each eye and early papilledema, treated with methylprednisolone 250 mg QID, which improved her visual acuity. However, on June 3, 2024, her vision deteriorated over three days, accompanied by discomfort, fever, and headaches. Vision was 3/60 in the right eye and 1/60 in the left. MRI revealed bilateral optic nerve atrophy, and CSF analysis was normal. Positive anti-MOG antibodies led to maintenance treatment with methylprednisolone 24 mg daily and azathioprine 50 mg daily.
Conclusion: MOGAD can present as recurrent painless optic neuritis. Given its similarity to MS and NMOSD in clinical features, MOG antibody testing is essential for accurate diagnosis and differentiation between these conditions.

P-84

Patient Care Pathways and Diagnostic Delays in Multiple Sclerosis: Insights from a Case Series in Indonesia

Oktavia Maulita Atmajayanti[1], Riwanti Estiasari[2], Darma Imran[2], Kartika Maharani[2]

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

[2]*Department of Neurology, Faculty of Medicine Universitas Indonesia*

Background: Multiple sclerosis (MS) is an autoimmune inflammatory demyelinating disease of the central nervous system. In Indonesia, MS is still considered rare. Despite a growing number of people with MS in the country, delayed diagnosis remains common.

Objective: Describing patient care pathways to identify factors contributing to delayed MS diagnosis in Indonesia.

Methods: A case series of 5 MS patients diagnosed by 2017 McDonald criteria in a tertiary referral hospital in Jakarta, Indonesia.

Results: Among 5 patients, 4 were female and 1 was male, ages ranging from 20 to 35 years. Patient 1 was diagnosed in 2014, patient 2 in 2015, patients 3 and 4 in 2022, and patient 5 in 2023. Their initial symptoms varied, including limb weakness, instability and vision problems. The number of relapse from the onset of symptoms until the diagnosis of MS ranged from 2 to 5. The first healthcare facility visited were primary care centers or secondary hospital, where initial diagnoses including stroke, myopia, dizziness, autoimmune diseases, scoliosis and hypercoagulation. All patients sought a second opinion between 2 and 7 times, consulted various doctors such as general practitioners to orthopaedic surgeons, ophthalmologists and neurologists. None of the patients had an MRI scan at their first visit. In addition to medical treatment, 2 patients also pursued non-medical treatments. On average, it took 11 months (ranging from 3 to 24 months) from the first symptoms to receive a diagnosis of MS.

Conclusion: MS diagnosis is often delayed due to symptom variability, leading to misdiagnosis and multiple consultations. Limited access to specialized care and cultural influences encouraging non-medical treatments also contribute to delays.

Disclosures: There is no conflict of interest.

P-85

A Patient Diagnosed with Intramedullary Spinal Lymphoma Mimicking Neuromyelitis Optica Spectrum Disorder

Byeol-A Yoon[1], Sang-Myung Cheon[1]

[1]*Dong-A University/Department of Neurology*

Background: Primary intramedullary spinal lymphoma is a rare disorder that accounts for less than 1-3% of central nervous lymphomas. Because intramedullary spinal lymphomas look similar to myelitis and show a partial response to corticosteroid treatment, diagnosing intramedullary spinal lymphoma can be challenging.

Objective: We experienced a patient who mimicking myelitis finally diagnosed with primary intramedullary spinal lymphoma.

Methods: A 65-year-old man visited our tertiary center with worsening gait disturbance over the past two weeks. He did not have any previous infection or medical history. Neurologic examination showed mild sensory ataxia without motor weakness. MRI revealed a spinal cord lesion at the level of C3-6 with

contrast enhancement. Cerebrospinal fluid analysis showed 5 lymphocytes with elevated protein (142mg/dL). However, there was no atypical cell in cytopathologic analysis. CSF oligoclonal IgG bands were type 2 positive. There were no abnormal findings in his whole-body CT and tumor markers. The patient was treated with 1g/day methylprednisolone for 5 days, and his symptoms were much improved.
Results: One month later, his gait disturbance worsened again, even though he took oral prednisolone. His follow-up MRI revealed expansion of the previous lesion from lower brainstem to C6 lesion with more intense contrast enhancement. His follow-up CSF study showed 13 lymphocytes with highly elevated protein (349mg/dL). Cytopathologic analysis was negative. The patient took 2nd 1g/day methylprednisolone for 5 days. However, he didn't show any improvement. So, we underwent PET-CT, which revealed only diffuse and focal hypermetabolism in spinal cord of C2-6 and T3 levels. PET-CT was not a profitable tool for differentiating spinal cord tumors and myelitis. Because the patient had no motor weakness, the caregiver refused to undergo spinal cord biopsy. So, we took 3rd dose of methylprednisolone treatment. Ten days after 3rd treatment, his motor weakness worsened to MRC grade 1. He underwent spinal cord biopsy emergently and was finally diagnosed with primary diffuse large B-cell CNS lymphoma.
Conclusion: Primary intramedullary lymphomas are hard to distinguish from myelitis with less-invasive diagnostic modalities, such as repetitive CSF cytopathology (only 2-32% sensitivity), and PET-CT. Only a pathologic diagnosis can confirm the diagnosis.
Disclosures: None

POSTER SESSION – 6
Neuroimaging and Neurophysiology

P-86
Multiple sclerosis in patient with neurogenic locus notch homolog protein 3 mutation
Kyong Jin Shin[1], Suk-Won Ahn[2]
[1]*Department of Neurology, Haeundae-Paik Hospital, Inje University*
[2]*Department of Neurology, Chung-Ang University Hospital, Seoul, Korea*
Background: Multiple sclerosis (MS) is an autoimmune inflammatory disease affecting mainly cerebral white matter. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a hereditary degenerative disease that also involves cerebral white matter.
Objective: Recently, we experienced a MS case with neurogenic locus notch homolog protein (NOTCH) 3 gene mutation. The case has a family history of CADASIL, and, interestingly, showed both characteristic findings of MS and CADASIL on brain MRI.
Methods: An 18-year-old woman presents with a sudden onset right facial palsy. She was healthy and had no prior history of specific disease or taking medications. Her mother was diagnosed with CADASIL with NOTCH 3 gene mutation presenting with stroke and dementia. Brain MRI exhibited multiple high signal intensities in both periventricular white matters and infratentorial area including the right pontine tegmentum, right cervico-medullary junction and left middle cerebellar peduncle and cerebellum. In the T1-weighted image, low signal intensities were also observed in the same area. Some of the lesions were positive for 'central vein sign'. Simultaneous presence of non- and contrast enhancing lesions were observed, some of which showing peripheral enhancement in the form of an open ring. She had also confluent FLAIR-hyperintensive lesions in both anterior temporal lobes without external capsule lesions.

No abnormalities in the bilateral optic nerves, and spine were noted on MRI. Serum antibody assay against aquaporin-4 and myelin oligodendrocyte glycoprotein were negative. Cerebrospinal fluid test exhibited a normal appearance and CSF oligoclonal band was positive. She had also heterozygote pathologic variant with c.328C>T (p.Arg110Cys) in NOTCH 3 gene analysis which also presented with her mother.
Results: Although the case had only one attack of facial palsy so far, the brain MRI scan satisfy the dissemination in time and dissemination in space as a diagnostic criteria of MS because the gadolinium enhanced, and non-enhanced lesions were simultaneously detected in multiple locations on a single MRI scan. A positive CSF oligoclonal band is also an abnormal finding supporting that this case is multiple sclerosis.
Conclusion: She was diagnosed with multiple sclerosis with a trait with NOTCH 3 gene mutation and treated with dimethyl fumarate.
Disclosures: There is no conflict of interest.

P-87
Withdrawn

P-88
Subtypes of Brain and Spinal Cord Spatiotemporal Atrophy in Neuromyelitis Optica Spectrum Disorders and Multiple Sclerosis
Jun Qiu[1], Zhizheng Zhuo[1], Tianyu Gao[1]
[1]*Department of Radiology, Beijing Tiantan Hospital, Capital Medical University*
Background: NMOSD and MS are common inflammatory demyelinating diseases. Brain and spinal cord atrophy, which correlates with cognitive decline and physical disability in both diseases, is important for stratified medicine and prognosis, yet their shared and distinct atrophy subtypes remain undetermined.
Objective: This study aimed to determine their atrophy subtypes and corresponding clinical characteristics.
Methods: Using 3D T1-weighted image derived structural measurements and the Subtype and Stage Inference model, distinct brain and spinal cord atrophy subtypes of NMOSD and MS were identified. The clinical characteristics of disease atrophy subtypes and clinical associations of atrophy stage were investigated. Further, potential atrophy subtype related genes in these diseases were determined based on a genome-wide association study summary for regional brain tissue volumes using a sample size of 33,224 individuals of European ancestry from the UK Biobank.
Results: The results showed that in NMOSD, three atrophy subtypes were identified: (1) cortical subtype with severe cognitive and physical disability (related to BDNF); (2) spinal cord subtype with high number of relapses (related to CUX1); and (3) cerebellum subtype with a favorable prognosis (related to ANCG2). In MS, three atrophy subtypes were identified: (1) cortical subtype featuring severe cognitive decline (related to NQO1); (2) spinal cord subtype featuring high number of relapses (related to CUX1); and (3) subcortical subtype featuring severe physical disability (related to BDNF). Advanced stage in MS spinal cord and subcortical atrophy subtypes associated with severe disability and cognitive decline, while advanced stage in all MS subtypes correlated with disability worsening.
Conclusion: NMOSD cerebellum and MS cortical subtypes had good treatment responses to disease-modifying therapy. We proposed the novel imaging subtypes in NMOSD and MS, which can help interpret disease heterogeneity, develop stratified therapy and assess prognosis.
Disclosures: No conflict of Interest

P-89
Withdrawn

P-90
Study Of Single-subject Morphological Brain Networks In MS, AQP4 Seropositive NMOSD And MOGAD
Ying Jin[1], Yuna Li[1], Zhizheng Zhuo[1], Tiantian Hua[1], Hongfang Li[1], Yaou Liu[1]
[1]*Department of Radiology, Beijing Tiantan Hospital, Capital Medical University, Beijing, 100070, China*
Background: Multiple sclerosis (MS), neuromyelitis optica spectrum disorders (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are inflammatory demyelinating diseases of the central nervous system.
Objective: To construct and topologically characterize single-subject morphological brain networks of MS, NMOSD, MOGAD, and to investigate their clinical relevance.
Methods: 216 patients with relapsing-remitting multiple sclerosis (RRMS), 207 patients with aquaporin 4 antibody positive neuromyelitis optica spectrum disorders (AQP4+NMOSD), 66 patients with MOGAD, and 489 healthy controls (HC) were retrospectively and prospectively included from multiple centers. 3D T1-weighted imaging (T1WI) was obtained to construct and topologically characterize single-subject morphological brain networks of RRMS, AQP4+NMOSD, MOGAD, and HC. For each graph, both global (clustering coefficient, Cp; characteristic path length, Lp; local efficiency, Eloc; and global efficiency, Eglob) and nodal (nodal degree, ki; nodal efficiency, ei; and nodal betweenness, bi) measures were calculated. For measures showing significant alterations in the patients compared with HC, linear regression model was used to examine their associations with clinical and neuropsychological variables. For measures showing significant alterations between patient groups, support vector machine (SVM) models were built to examine their discriminant power in distinguishing between diseases.
Results: (1) Comparison of RRMS, AQP4+NMOSD, MOGAD and HC, no significant alterations were observed in the global measures (FDR correction, $P>0.05$), while statistically significant alterations were observed in the nodal measures (FDR correction, $P<0.05$). (2) Nodal measures with statistically significant differences between RRMS and HC were correlated with disability and cognitive scores, and nodal measures with statistically significant differences between MOGAD and HC were correlated with cognitive scores. (3) Nodal measures with statistically significant differences between diseases could be used for the differential diagnosis of the three diseases, with accuracies of 77.80%, 77.30%, and 74.36% for the differential diagnosis of RRMS vs. AQP4+NMOSD, RRMS vs. MOGAD, and AQP4+NMOSD vs. MOGAD, respectively.
Conclusion: RRMS, AQP4+NMOSD, and MOGAD have characteristic patterns of altered topological properties of single-subject morphological brain networks, which are potentially associated with disability and cognitive level, and better differentiate diseases.

P-91
Clinical Presentations and Imaging Of GFAP Astrocytopathy: A Systematic Review
Ekdanai Uawithya[1], Piyachai Siriphiphatcharoen[2], Ben Benjapibal[2], Sasitorn Siritho[1]
[1]*Siriraj Neuroimmunology Center, Division of Neurology, Mahidol university*
[2]*Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok*
Background: Autoimmune glial fibrillary astrocytopathy is an autoimmune inflammatory central nervous system (CNS) disorder that has been discovered in 2017. Various studies have been conducted since its discovery. However, the clinical presentations, and imaging results are still heterogeneous.

Objective: We conducted this systematic review to elucidate clinical characteristics, and imaging in GFAP astrocytopathy patients.
Methods: We performed systematic reviews using PubMed, Embase, and Scopus from inception until May 2024. The inclusion criteria were (i) case series or observational studies reporting on GFAP astrocytopathy with at least five patients, (ii) majority of patients must be older than 18 years, and (iii) studies must report positive anti-GFAP IgG titers in either cerebrospinal fluid (CSF) or serum. The exclusion criteria were (i) animal studies (ii) studies done in pediatrics population.
Results: Fifteen studies comprising a total of 534 patients were included. Among these patients, 293 were male. The most common clinical presentations were headache (163/466; 45.7%), fever (158/534; 29.6%), psychiatric symptoms (100/467; 21.4%), and altered mental status (100/469; 21.3%). Other symptoms observed were dysautonomia, abnormal movements, weakness, sensory deficits, and visual disturbances. MRI imaging revealed T2 enhancement in 292/434 (67.3%) patients, predominantly in the periventricular area (85/434; 19.6%), followed by subcortical/juxtacortical regions (80/432; 18.5%) and basal ganglia (74/432; 17.1%). Perivascular enhancement was observed in 114/402 (28.4%) patients, while meningeal enhancement was seen in 79/402 (19.7%). Spinal cord abnormalities were detected in 149/297 (50.2%) patients, with long extensive transverse myelitis presented in 64/276 (23.2%) patients.
Conclusion: This review highlights that the most frequently reported clinical presentations of GFAP astrocytopathy were headache, fever, and psychiatric symptoms. The most common lesion locations were found in periventricular area.
Disclosures: I declare that there are no conflicts of interest regarding this study.

P-92
Demyelination secondary to anti-TNF alpha therapy (adalimumab) for ankylosing spondylitis
Young-Do KIM[1], Hansol IM[1]
[1]*Department of Neurology, Incheon St Mary's Hospital, The Catholic University of Korea*
Background: Ankylosing spondylitis is a chronic and progressive inflammatory disease involving the sacroiliac joints with HLA-B27 positivity in 85 % of the patients and radiologically evidence of sacroiliitis. Tumor necrosis factor-α(TNF-α) blockers present a revolutionizing therapeutic choice for ankylosing spondylitis (AS).
Objective: Despite being considered relatively safe, serious side effects associated with immune suppression have been reported, including central and peripheral nervous system (CNS) demyelinating disorders.
Methods: A 25-year-old man with a 11-year history of HLA-B27 positive AS presented with headache, progressive diplopia and ataxia over 30 days. He had been treated with adalimumab for 1 year because of reduced clinical efficacy of methotrexate treatment. There was no prior and family history of neurological disease or multiple sclerosis. Neurological examination revealed left 6th nerve palsy. Routine blood analysis was within normal limits. Brain magnetic resonance imaging (MRI) revealed left frontal periventricular and cerebral peduncle T2 hyperintensities including subtle gadolinium enhancement in the left cerebral peduncle on T1-weighted images (Figure 1). Cervical spine MRI did not reveal any abnormalities. CSF examination was mild leukocytosis and elevated protein without detection of oligoclonal bands. Anti-aquaporin 4 antibody and Myelin oligodendrocyte glycoprotein (MOG) antibody were negative. Other differential diagnostic tests did not show evidence for an infectious inflammation, neurosarcoidosis, vasculitis, vitamin deficiency or metabolic disease.

Results: Adalimumab was discontinued after MRI of the brain and high-dose IV methylprednisolone 1000mg was given for 5 days. His complaints were resolved on the fifth day of the treatment. Three months after cessation of adalimumab control brain MRI demonstrated regression of the lesions and no gadolinium enhancement.
Conclusion: In conclusion, the temporal correlation of neurological symptoms onset with TNF-a blocker administration suggests that even adalimumab like other TNF-a blockers may trigger CNS demyelination.
Disclosures: None

P-93
Withdrawn

P-94
Association Between Volumetric Magnetic Resonance Imaging, and Neuroperformance Measures in Patients with Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease
Tatchaporn Ongphichetmetha[1], Mengke Du[1], Moein Amin[1], Justin Abbatemarco[1], Jeffery Cohen[1], Daniel Ontaneda[1], Amy Kunchok[1], Kunio Nakamura[2], Stephen Jone[2]
[1]*Mellen Multiple Sclerosis Center, Cleveland Clinic Foundation*
[2]*Cleveland Clinic Department of Radiology*
Refer to O-8 in Plenary Oral Presentation - 2

P-95
Cardiovascular Autonomic Dysfunction in Neuromyelitis Optica Spectrum Disorder and Multiple Sclerosis in Asian Population
Chutithep Teekaput[1], Kanokkarn Teekaput[1]
[1]*Chiang Mai University*
Background: Neuromyelitis optica spectrum disorder (NMOSD) and multiple sclerosis (MS) are central demyelinating diseases with overlapping features but distinct cardiovascular autonomic dysfunction profiles. However, the specific patterns in Asian populations remain underexplored.
Objective: To compare clinical profiles, and laboratory findings of patients with NMOSD and MS, focusing on cardiovascular autonomic dysfunction and its associated factors in the Asian population.
Methods: Twenty NMOSD and twenty MS patients were enrolled. Clinical data, number of relapses, and Expanded Disability Status Scale (EDSS) scores were collected. Autonomic dysfunction was assessed using cardiovascular autonomic dysfunction (CAD) and autonomic symptom burden (COMPASS-31) scores. Laboratory parameters were also compared between the two groups.
Results: Cardiovascular autonomic dysfunction was more prevalent in NMOSD patients, with significantly higher CAD scores (2.0 (Interquartile ranges (IQR) 1.0-3.0) vs. 1.0 (0.0-1.5), p=0.001) and COMPASS-31 scores (12.6 (9.7-24.4) vs. 7.4 (4.0-9.0), p<0.001). NMOSD patients had significantly greater adrenergic dysfunction but not cardiovagal dysfunction compared to MS patients (80.0% vs 20.0%, p<0.001, and 65.0% vs 40.0%, p=0.21). Baseline EDSS is an independent factor associated with cardiovascular autonomic dysfunction (adjusted odd ratio 3.2, 95% confidence interval 1.2-8.6, P=0.02).
Conclusion: Asian NMOSD patients exhibited more subjective and objective cardiovascular autonomic dysfunction compared to MS patients. Cardiovascular monitoring should be prioritized in patients with higher disability, especially in Asian NMOSD patients.
Disclosures: None

P-96
Withdrawn

P-97
Seronegative NMOSD: Navigating The Diagnostic Dilemma
Wai Dic Foong[1], Sarah Hasnor Abu Hassan[1], Kok Pin Yong[1]
[1]*National Neuroscience Institute, Singapore*
Background: Central nervous system (CNS) inflammatory demyelinating diseases (IDDs) represent a heterogenous group characterised by injury to the myelin sheath. Systemic autoimmune diseases such as systemic lupus erythematosus (SLE) can affect the CNS and are frequently associated with CNS IDDs, such as neuromyelitis optica spectrum disorder (NMOSD).
Objective: We highlight the utility of neuroimaging in a patient with presumptive SLE, who presented with CNS manifestation.
Methods: A 45-year-old Malay male presented with encephalopathy, which developed over three days. He presented with altered mental status characterised by confusion, disorientation, and visual hallucinations without symptoms suggestive of infection or seizure prior to this. He was diagnosed with mixed autoimmune haemolytic anaemia associated with elevated anti-double-stranded DNA levels. His family history is significant for SLE, affecting both his sisters. He was started on hydroxychloroquine for presumptive SLE but was non-compliant to the medication. Patient did not harbour symptoms suggestive of a SLE flare during this presentation. On current examination, patient was confused and had left eye relative afferent pupillary defect. Additionally, he was later diagnosed with central diabetes insipidus.
Results: Magnetic resonance imaging (MRI) of the brain revealed T2 and FLAIR hyperintensities, mild enhancement and mild mass effect, without restricted diffusion, involving the bilateral medial thalami and basal ganglia, the posterior aspect of the left frontal lobe, bilateral fornices, optic chiasm, and optic tracts. Cerebrospinal fluid (CSF) analysis showed pleocytosis and elevated protein, with negative CSF specific oligoclonal bands, infective and autoimmune panels. Serum testing for aquaporin-4 immunoglobulin G returned negative. Further MRI cervicothoracic spine and whole-body positron emission tomography scan revealed no significant abnormalities. A trial of intravenous methylprednisolone followed by oral prednisolone led to near resolution of the radiological lesions and his mini-mental state examination score improved from 14 on presentation to 21 post-treatments.
Conclusion: Patient was diagnosed with seronegative NMOSD, as supported by clinical and radiological involvement of diencephalon and optic chiasm. Our case illustrates the importance of neuroimaging in early diagnosis with resultant appropriate treatment.
Disclosures: No

P-98
Evaluation of Enlarged Perivascular spaces (EPVS) in patients with Neuromyelitis Optica Spectrum Disorder (NMOSD) in a Tertiary Hospital.
Nasheeda Saeed[1], Juen Kiem Tan[1], Rathika Rajah[2], Intan Bazilah[3], Muhammad Aminuddin Bin Ashari[4], Hui Jan Tan[1], Shahizon Azura Binti Mohamed[4], Rabani Remli[1]
[1]*Department of Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia*
[2]*Hospital Canselor Tuanku Muhriz*
[3]*International Islamic University Malaysia*

[4]*Department of Radiology, Faculty of Medicine, University Kebangsaan Malaysia*

Background: EPVS play an important role in the pathogenesis of NMOSD and have been found as an independent factor to predict disease severity in NMOSD patients.
Objective: To demonstrate the features of EPVS detected by Magnetic Resonance Imaging (MRI) in our study population.
Methods: This retrospective study included eleven Aquaporin-4 IgG seropositive NMOSD patients from Hospital Canselor Tuanku Muhriz, Malaysia, reviewed from January 2018 to December 2022. MRI images were evaluated by two neuroradiologists, and EPVS were graded as mild or severe based on their presence and total number in the centrum semiovale, basal ganglia, and midbrain.
Results: Out of the 11 patients,10 were females (90.9%). Six patients (54.5%) had mild EPVS, while five (45.5%) had severe EPVS. The mean EPVS count was 13.45 (SD ±11.86), with the mean of 11.67 (SD ±4.82) in mild group and 29.60 (SD ±8.62) in severe group. The mean ages were 53.0 (SD ±11.45) and 54.4 (SD ±15.88) years for mild and severe groups, respectively. Cerebrospinal fluid (CSF) protein levels were 495.17 mg/dL (SD ±164.29) in mild group and 869.2 mg/dL (SD ±589.87) in the severe group. The median albumin level for mild group is 40.50 g/L (IQR 35.25-44.00) while the mean albumin of 36.2 g/L (SD ±4.60) was found in the severe group.
In the mild EPVS group, one patient presented with optic neuritis (ON), three patients with longitudinally extensive transverse myelitis (LETM), and one with both. In the severe EPVS group, two patients presented with both ON and LETM, and three patients with LETM alone.
Conclusion: Higher CSF protein levels and lower serum albumin levels in patients with severe EPVS suggesting some differences in the clinical and laboratory profiles of NMOSD patients. EPVS could serve as a biomarker for disease activity and prognosis in NMOSD.

P-99

Intravascular B-Cell Lymphoma Presenting as Conus Myelitis Mimicking Myelin Oligodendrocyte Glycoprotein (MOG) Antibody-Associated Disease

Pritam Majumdar[1], Thomas Mathew[1], Vyom Buch[1], Sharath Kumar GG[1], Bevinahalli Nandeesh[2], Chandana Nagaraj[1], Shagun Bhardwaj[1], Abhinaya Reddy[1]
[1]*St Johns National Academy of Health Sciences Bengaluru*
[2]*NIMHANS, Bangalore*

Background: Central nervous system (CNS) lymphoma is one of the most deceptive conditions in neurology, often mimicking various other neurological diseases owing to its reputation as a great imitator.
Objective: To describe a rare presentation of CNS lymphoma mimicking MOGAD.
Methods: Case - A previously healthy 61-year-old man presented to the emergency department with acute paraplegia and urinary retention, preceded by a week of lower back pain. On examination, he appeared confused and exhibited weakness in both lower limbs with a power of 1/5 and hyperreflexia. MRI of the spine showed a linear hyperintense lesion in the conus region. At the same time, an MRI of the brain revealed multiple asymmetrical cortical and subcortical T2/FLAIR hyperintense lesions which were large and fluffy, predominantly in the right frontal and temporal regions, with no contrast enhancement observed.
Results: A diagnosis of MOGAD was initially considered based on conus myelitis and brain lesions, but tests for MOG and aquaporin-4 antibodies were negative. Detailed paraneoplastic and autoimmune workups were also negative. Elevated serum neurofilament light chain levels were observed at 1721.2 pg/ml. The patient did not respond to high-dose IV methylprednisolone and IVIg, deteriorating and becoming delirious. Further tests were negative, including a serum ANA profile, angiotensin-converting enzyme levels, and

HRCT chest. CSF analysis showed high protein levels (279 mg/dl) with normal cell counts and glucose levels. An FDG PET scan revealed hypermetabolic lesions in the liver, adrenal glands, and brain. Due to the inaccessibility of the adrenal glands, a brain biopsy was performed after obtaining informed consent which showed histological features consistent with intravascular large B-Cell lymphoma, superior frontal gyrus.
Conclusion: Lymphoma should be included in the differential diagnosis of myelitis, particularly in elderly patients exhibiting features atypical for a demyelinating disease and negative conventional diagnostic tests.
Disclosures: There is nothing to disclose.

P-100

Neurosarcoidosis presented with long extended myelitis

Azize Esra Gürsoy[1], Didem Savaşçı[1]
[1]*Çam and Sakura City Hospital*

Background: Sarcoidosis is a multisystem granulomatous disorder affecting the lungs, skin, joints. Neurosarcoidosis (NS) is reported in %5-34 of patients with systemic sarcoidosis. Spinal cord involvement is reported in %19-26 of patients with NS. Longitudinally extensive myelitis (LETM) from NS is relatively common and must be distinguished from other causes
Objective: In this report, we aimed to present 2 patients who presented with LETM and were diagnosed with NS.
Methods: The data of our 2 patients were obtained from the records of Başakşehir Çam and Sakura City Hospital. In this presentation, clinical features, radiological, laboratory and pathological results and changes before and after treatment are reported.
Results: Case 1: A 43-year-old woman presented with a complaint of numbness starting in the left arm and spreading to the whole body. Spinal MRI showed a T2 hyperintense lesion between C5 and T2 levels with Gd enhancement. Investigation for neurosarcoidosis was performed upon detection of trident sign on MRI. Thorax CT showed hilar lymphadenopathies and PET examination revealed hypermetabolic multiple lymph nodes. The diagnosis of sarcoidosis was made by endobronchial ultrasound-guided transbronchial biopsy (EBUS)
Case 2: A 47-year-old woman presented with complaints of neck pain, numbness in the arms and legs and mild unsteadiness. Spinal MRI showed T2 hyperintensity between C4 and T2 levels located posteriorly with contrast enhancement. Serum ACE level was found to be high, hilar lymphadenopathies were detected on thorax CT and sarcoidosis was diagnosed by EBUS.
Both patients improved with 1000 mg iv methylprednisolone followed by oral methylprednisolone and azathioprine.
Conclusion: Sarcoidosis should be kept in mind as a differential diagnosis in patients with LETM. In the differential diagnosis of LETM, knowing the radiological features of spinal cord involvement contributes greatly in reaching the correct diagnosis.

P-101

Monoclonal Gammopathy Presenting as Atypical Optic Neuritis: A Diagnostic Challenge

Oranuch Chuapakdee[1]
[1]*Chula Neuroscience Center, King Chulalongkorn Memorial Hospital, Division of Neurology, Department of Internal Medicine, Chulalongkorn University*

Background: Optic neuritis (ON) is an inflammatory of optic nerve which often associated with

demyelinating condition including multiple sclerosis, NMOSD and MOGAD. However, ON can also signal hematologic malignancies, especially when presented with atypical ON. Recognizing and treating underlying conditions is crucial for patient outcomes.
Objective: To present a case of monoclonal gammopathy with clinical significance manifesting as atypical optic neuritis.
Methods: We report a 70-year-old male with hypertension and dyslipidemia who presented with acute, relapsing, painless visual impairment in the right eye and a positive relative afferent pupillary defect (RAPD). Two months prior, he had a similar episode affecting both eyes, which improved with 3 days of IVMP. Fundoscopy at presentation revealed dot blot haemorrhages, marked pallid disc edema, and dilated tortuous vessels. Temporal artery ultrasound was negative for giant cell arteritis. MRI of the orbit showed long segment T2 hyperintensity with post-gadolinium enhancement of the intraorbital-intracanalicular right optic nerve and optic nerve head. MRA, MRV, and MRI vessel wall studies were unremarkable. Immune-mediated optic neuritis tests, including oligoclonal bands, AQP4-IgG, and MOGAD-IgG, were negative. Serum VDRL was positive, but CSF TPPA and VDRL were negative. Hematologic evaluation showed increased small lymphocytes in CSF cytospin and suspected B cell lymphoma on CSF flow cytometry, though no malignant cells were detected in the CSF. ESR and hs-CRP were mildly elevated; ANA and ANCA were negative.
Results: IVMP and maintenance oral prednisolone were administered. Bone marrow flow cytometry showed 13% positivity for kappa light chain with CD5+CD19+ B cells. Immunofixation revealed IgM kappa monoclonal gammopathy with a Kappa/Lambda ratio of 2.795. A whole-body PET scan showed no extracranial involvement. Monoclonal gammopathy of clinical significance was diagnosed. Chemotherapy with rituximab and high-dose methotrexate was initiated. On follow-up, visual acuity improved significantly, and optic nerve head enhancement resolved.
Conclusion: This case underscores the importance of differential diagnosis in atypical and steroid-dependent optic neuritis. In addition to immune-inflammatory etiologies, it is crucial to consider hematologic malignancies such as MGCS. Comprehensive diagnostics and timely intervention are vital for improving patient outcomes.
Disclosures: No disclosure.

P-102
Exploring Myelin Water Imaging in Spinal Cord: Correlating Changes with Clinical Outcomes in Multiple Sclerosis
Jiake Wu[1]
[1]*UBC*
Background: Around 80% of MS patients develop spinal cord lesions. Advanced imaging techniques like myelin water imaging (MWI) could better understand and track disease progression. To our knowledge, the correlation between MWF changes in the spinal cord and long-term disability outcomes in progressive MS remains unexplored.
Objective: Correlate 2-year-changes in spinal cord myelin water fraction (MWF) across both lesions and normal appearing white matter with clinical outcomes, as measured by the EDSS, 9HPT, and Timed 25-Foot Walk over a five-year period.
Methods: Myelin Water Fraction Analysis: Myelin water fraction (MWF) analysis will utilize the non-negative least squares algorithm on multi-component T2 decay curves, focusing on MS lesions, perilesional

zones, and normal-appearing white matter (NAWM). MWF will also be quantified in the dorsal and lateral columns. It is hypothesized that higher mechanical stress in the upper cervical cord will correlate with reduced MWF, indicating increased tissue damage and inflammation.
Clinical Assessment: Clinical evaluations, conducted annually over five years, include the Expanded Disability Status Scale (EDSS), Nine-Hole Peg Test (9HPT) for manual dexterity, and Timed 25-Foot Walk (T25FW) for mobility. Disability progression is defined per Hauser, with significant changes recognized as an increase of at least 1.0 EDSS point from baseline if initial scores were ≤5.5, or a 0.5-point increase for scores >5.5. For 9HPT and T25FW, a change is defined as a ≥20% increase.
Statistical Analysis: A mixed-effects model will analyze longitudinal data to evaluate the relationship between changes in MWF and clinical outcomes. Adjustments will be made for age, disease duration, and treatment status. The focus will be on correlating myelin loss in spinal segments with worsening disability scores.
Results: It is anticipated that areas with significant myelin loss at baseline, particularly in the upper cervical cord, will show strong correlations (predict) with increased (worsening) disability scores. Specifically, we predict that both lateral corticospinal tracts will show a stronger correlation with worsening disability compared to the ventral corticospinal tracts. This is consistent with findings from previous studies indicating that lateral tracts are more susceptible to damage in MS, impacting motor functions more significantly (Smith et al., 2017). These results could provide pivotal insights into the spatial patterns of myelin degradation and their differential impact on neurological functions. By highlighting the specific tracts most predictive of disability progression, our findings could guide more targeted therapeutic strategies and improve prognosis accuracy in MS management.
Conclusion: This project examines changes in myelin within and around lesions, in normal appearing white matter (NAWM), and various spinal cord tracts in MS patients, correlating these changes with five-year clinical outcomes using established clinical measures.

P-103
Withdrawn

P-104
Clinical and Radiological Features of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD): A Case Series
Burcu Altunrende[1], Ahmet Yabalak[2], İpek Arslan[3], Furkan Talha Tokdemir[3], Gulsen Akman[4]
[1]Health Sciences University, Department of Neurology, Taksim Education and Research Hospital
[2]Düzce University Faculty of Medicine Hospital, Department of Neurology
[3]Taksim Education and Research Hospital
[4]Retired Faculty Member, Istanbul University Çapa Faculty of Medicine
Background: Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) is a demyelinating disease spectrum characterized by the presence of autoantibodies targeting myelin oligodendrocyte glycoprotein (MOG). Differentiating MOGAD from other demyelinating diseases is crucial due to differences in treatment and prognosis.
Objective: This study aims to present the clinical and radiological features, as well as the clinical course, of 10 cases diagnosed with MOGAD.
Methods: Data from 10 patients diagnosed with MOGAD at the demyelinating diseases outpatient clinic of

Taksim Training and Research Hospital, Department of Neurology, were retrospectively evaluated. Patients were assessed based on gender, age at diagnosis, clinical involvement, antibody seropositivity (Anti-NMO antibody, Anti-MOG antibody), lumbar puncture (LP) and radiological imaging results, comorbid diseases, clinical attacks, and treatment criteria.
Results: The study included 7 women (70%) and 3 men (30%) with an average age of 30 years. The average follow-up period was 28.1 ± 36.5 (2-108) months. Initial attack symptoms included optic neuritis in 6 patients (bilateral in two), concurrent brainstem and myelitis attacks in 1 patient, myelitis attacks in 2 patients, and optic neuritis, myelitis, hemispheric and brainstem attack like ADEM in 1 patient. In follow-up 18 relapse was seen in 9 patients. MRI findings revealed perineural enhancement of optic nerve, H sign, ADEM like hemispheric lesions, brainstem and longitudinally extensive transverse myelitis. 9 patient received disease modifying therapy (4 rituximab, 5 azathioprine) and 1 patient had an attack under rituximab treatment.
Conclusion: In differential diagnosis of MOGAD, clinical findings, along with radiological features are guiding factors. Early diagnosis and effective treatment initiation are crucial to prevent morbidity and mortality.
Disclosures: No disclosures.

P-105
Optical Coherence Tomography Angiography in Multiple Sclerosis: A single center experience.
Fatma Balci[1], Aytul Mutlu[2], Mine Ozturk[3]
[1]*Haseki Education and Research Hospital*
[2]*Haseki Education and Research Hospital, Neurology Department*
[3]*Haseki Education and Research Hospital, Ophthalmology Department*
Background: Optical coherence tomography angiography (OCTA) is a fast, non-invasive and inexpensive method that provides non-invasive imaging of the retina and choroidal vasculature. Considering that the retina is anatomically an extension of the brain, microvascular cross-sectional images of the retina can provide information about the CNS.
Objective: We aimed to evaluate the changes in retinal vascular structure in patients with multiple sclerosis (MS) by OCTA.
Methods: A total of 70 MS patients (15 clinically isolated syndrome [CIS], 40 relapsing remitting MS [RRMS], 15 secondary progressive MS [SPMS]) and 70 healthy controls participated in the study. Demographic and clinical data of the patients, optic neuritis (ON) history, ophthalmic examination findings and OCTA data were recorded. OCTA parameters: The vascular density in the retinal superficial capillary plexus included the deep capillary plexus and radial peripapillary capillaries. Additionally, the retinal nerve fiber layer was evaluated as a structural spectral domain optical coherence tomography parameter.
Results: Superficial and peripapillary vascular plexus densities and retinal nerve fiber layer thickness values were significantly decreased in MS patients compared to healthy controls ($p = 0.004$). Patients with a history of ON (ON+) showed a significant reduction in VD compared to control groups ($p=0.001$). Likewise, patients without a history of ON (ON-) showed a significant decrease in VD compared to the control groups ($p = 0.001$). Deep capillary plexus densities did not differ between groups ($p = 0.385$). Perifoveal values were lower in the SPMS group than in RRMS and CIS patients, and in RRMS patients than in the CIS group ($p=0.014$; $p=0.03$; $p=0.039$). EDSS and VD values were inversely proportional ($r=- 0.272$; $p=0.003$). No significant difference was found between the MS and control groups in the foveal avascular region ($p = 0.456$).
Conclusion: OCTA showed that peripapillary and superficial vascular plexus densities were reduced in MS.

Vascular regression and microvascular damage caused by decreased metabolic demand, inflammation could be demonstrated non-invasively with OCTA in MS.
Disclosures: No conflict of interest.

POSTER SESSION – 7
Neuropathology

P-106
Clinical characteristics and diagnosis delay in NMOSD: A retrospective study at University Medical Center Ho Chi Minh City.
Huong Dinh[1,21], Hieu Dinh[2]
[1]*Neurology Department, University Medical Center HCMC, Vietnam*
[2]*Neurology Department, University of Medicine and Pharmacy HCMC, Vietnam*
Refer to O-5 in Plenary Oral Presentation - 1

P-107
Spinocerebellar Ataxia Type 6 Combined With Neuromyelitis Optica Spectrum Disorder
Hye Ryung Kwon[1]
[1]*Department of Neurology, St. Vincent Hospital, The Catholic University of Korea*
Background: Spinocerebellar Ataxia type 6 (SCA6) is a late-onset hereditary cerebellar ataxia caused by a CAG repeat expansion in the CACNA1A gene and sometimes preceded by an episodic symptom such as dysarthria, nystagmus and vertigo. Neuromyelitis optica (NMO) is a rare idiopathic, autoimmune inflammatory demyelinating syndrome.
Objective: We report the unusual case of a patient who developed NMOSD 3 years after onset of symptoms of SCA6.
Methods: A 59-year-old woman who was diagnosed with transient ischemic attack 3 years ago was admitted to another hospital with paraesthesia in the right hand, dysarthria, and numbness below the T4 dermatome. Brain and spinal cord magnetic resonance imaging studies showed mild cerebellar atrophy, posterior medullar lesion and longitudinal extensive myelitis from C1 to C6. Serum aquaporin4-Ab was positive. The patient was diagnosed with NMOSD and treated with intravenous high dose steroid and immunosuppressant.
Results: The patient admitted in our hospital for the second opinion because she showed aggravated dysarthria and tonic spasm in the right upper limb 1 month after discharge. Transient dysarthria and gait disturbance were repeated after tonic spasm improved with topiramate. Genetic analysis revealed a mutation of –16 G>T q.22 and insertion of a penta-nucleotide repeat expansion (3.3 kb). Therefore, she was diagnosed with SCA6 combined with NMOSD.
Conclusion: This case suggests that the immune response in SCA6 could be involved in the pathogenesis of NMOSD although the role of the polyglutamine tract in triggering the immune response is still unclear.

P-108
Serum Neurofilament Light Chain Levels in an Indian Cohort of Multiple Sclerosis Patients: A Clinico-Radiological Retrospective Study
Pritam Majumdar[1], Thomas Mathew[1], Shagun Bhardwaj[1], Sharath Kumar GG[1], Sai Kanth[1], Sonia Shivde[1],

Sagar Badachi[1], Raghunandan Nadig[1], Surabhi Garg[1], Akshatha Huddar[1], Sudheeran Kannoth[2], Sindhu V Nambiar[1], Gosala Raja Kukkuta Sarma[1]
[1]*St Johns National Academy of Health Sciences Bengaluru*
[2]*Amrita Institute of Medical Sciences, Kochi*
Background: Serum neurofilament light chains (sNfL) appear to be a promising biomarker in Multiple Sclerosis (MS). Here, we present the first study of this biomarker in Indian patients.
Objective: To investigate sNfL as a potential biomarker for disease activity and treatment response in MS patients.
Methods: In this retrospective study, sNfL levels were tested in 40 consecutive MS patients satisfying the 2017 McDonald criteria. All patients were clinically stable for at least one month. sNfL was tested by sandwich enzyme-linked immunosorbent assay technique using a digital immunoassay (Cloud Clone Corp USA, catalog number: SEE03Hu). The sNfL positivity (defined as values above the cut-off for normal age-matched controls) and titers were correlated with various parameters like clinical, neuroimaging, and treatment profiles of patients.
Results: The median age of the patients was 33 years (range 24-71), with most being female (80%). The median follow-up duration was 84 months (range 10-240), and the median sNfL level was 0.65 ng/ml (range 0-5.5). 32 (80%) patients had sNfL levels above the age-normal cutoff for age. sNfL positivity was significantly associated with longer disease duration (Median [IQR]: 72 [36-108] months, p=0.01). Non-significant trends of association were also observed with a higher number of relapses (Median [IQR]: 3 [2-4] months, p=0.08), cerebral atrophy (64.7% vs. 43.2%, p=0.1), and progressive disease (67% vs. 46.2%, p=0.2) but no association was found with higher EDSS scores (p=0.9), time since the last attack (p=0.9), time to start disease-modifying therapy (DMT) (p=0.8), different doses of Rituximab (p=0.5), number of hyperintense T2 lesions (p=0.9), or CSF Oligoclonal bands positivity (p=0.3).
Conclusion: sNfL levels are elevated in a high proportion of MS patients, with a positive correlation observed with the total duration of the disease. Studies involving larger cohorts are needed to understand the usefulness of serum sNfL in the Indian context.
Disclosures: Nothing to disclose.

P-109
Characteristics of Complement Deposition Pattern in MOGAD, Comparison with NMOSD
Yoshiki Takai[1]
[1]*Tohoku University Hospital*
Refer to O-9 in Plenary Oral Presentation - 2

P-110
Serum Neurofilament Light Chain Levels: A Biomarker For Monitoring Disease Progression And Treatment Response in Multiple Sclerosis
Marzena Pedrini[1], William M Carroll[2], Alexandra Maceski[3], Jens Kuhle[3], Allan G Kermode[1]
[1]*Perron Institute for Neurological and Translational Science, University of Western Australia, Australia; Centre for Molecular Medicine and Innovative Therapeutics, Murdoch University, Austral*
[2]*Perron Institute for Neurological and Translational Science*
[3]*Neurologic Clinic and Policlinic, Departments of Medicine, Biomedicine, and Clinical Research, University Hospital Basel, University of Basel, Basel, Switzerland*
Background: The neurofilament light chain (NfL) has become an important biomarker for assessing

disease activity, progression, and treatment response in multiple sclerosis (MS). Following axonal injury, neurofilament proteins are released into the extracellular space, and their levels in cerebrospinal fluid and blood can indicate the extent of axonal damage.
Objective: This study aims to evaluate the efficacy of serum NfL as a biomarker for tracking disease activity and progression, as well as its utility in monitoring treatment response in MS patients.
Methods: Serum NfL levels were assessed in a total of 552 individuals with demyelinating diseases, including clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS), and healthy controls (HC) using single-molecule array technology (SIMOA). Treatment options were categorized as “no treatment”, “low efficacy” and “high efficacy”.
Results: Serum NfL levels (pg/mL) were significantly elevated in patients with CIS, RRMS, SPMS and PPMS compared to HC (23.6 vs 12.3, $p<0.05$; 29.4 vs 12.3, $p<0.05$; 38.4 vs 12.3, $p<0.001$; 38.5 vs 12.3, $p<0.001$, respectively). Additionally, higher NfL levels were correlated with increased disability levels. A statistically significant difference in NfL levels was observed between early-stage disease (CIS/RRMS) and progressive disease (PPMS/SPMS) in individuals without treatment (35.2 vs 42.0, $p<0.01$, adjusted for age). Furthermore, treatment demonstrated a notable reduction in NfL levels in RRMS compared to those receiving no treatment (24.4 vs 36.9, $p<0.01$, adjusted for age). In individuals with RRMS, both “low efficacy” and “high efficacy” therapies led to reduction in serum NfL levels. Notably, a statistically significant difference was observed only with “high efficacy” treatments compared to “no treatment”.
Conclusion: Our findings provide support for the potential utility of serum NfL as an indicator of disease activity, progression, and treatment response in multiple sclerosis.
Disclosures: Marzena J. Fabis-Pedrini has received a travel sponsorship from Merck Serono Australia. Jens Kuhle received speaker fees, research support, travel support, and/or served on advisory boards by the Swiss MS Society, Swiss National Research Foundation (320030_189140/1), University of Basel, Progressive MS Alliance, Bayer, Biogen, Celgene, Merck, Novartis, Roche, Sanofi. William M. Carroll has received speaker honoraria and scientific advisory board fees from Bayer, BioCSL, Biogen-Idec, Lgpharma, Merck, Novartis, Roche, Sanofi-Aventis, Sanofi-Genzyme, and Teva. Allan G. Kermode has received speaker honoraria and scientific advisory board fees from Bayer, BioCSL, Biogen-Idec, Lgpharma, Merck, Novartis, Roche, Sanofi-Aventis, Sanofi-Genzyme, Teva, NeuroScientific Biopharmaceuticals, and Mitsubishi Tanabe. Aleksandra Maceski report no conflicts of interest to disclose.

P-111
Association Between Multiple Sclerosis and Parkinson’s Disease: A Systematic Review and Meta-Analysis
Sanjeev Kharel[1], Rajeev Ojha[2]
[1]*Tribhuvan University Teaching Hospital*
[2]*Department of Neurology Tribhuvan University Teaching Hospital*
Background: Parkinson’s Disease (PD) is a neurodegenerative disorder affecting 1-2% of persons over 60 and is more common as people age. A prevalent demyelinating illness, multiple sclerosis (MS) is characterized by plaques in the white matter of the periventricular and juxtacortical regions, as well as in the basal ganglia and, more frequently, the brainstem.
Objective: To perform a systematic review and meta-analysis to show the association between MS and PD.
Methods: The study was conducted per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline. Researchers searched PubMed, EMBASE, and Google Scholar for English literature from inception to July 1, 2024. Observational studies showing association were included. The

analysis was done by STATA 16.
Results: Six studies were included in our study. Three studies showed a statistically significant pooled Hazard Ratio (HR) between MS and PD [HR: 1.23 95% C.I.:0.62-1.85, p=<0.001, I2=76.53%]. One study showed no overall increased risk of PD of [Standardized Incidence Ratios (SIR) 0.98, 95% CI 0.67-1.44] while another showed increased risk of subsequent PD[SIR:1.66,1.05-2.50]. Another study showed no increased risk [Odds ratio (OR): 0.49 (0.22-1.06)].
Conclusion: Our systematic review and meta-analysis showed a significant association between MS and PD regarding HR while other studies showed contrasting results. Further studies are warranted to know the nature of the association, and additional clarification.
Disclosures: None

P-112
Withdrawn

POSTER SESSION – 8
Patient Reported Outcomes and Programs that Support Quality of Life

P-113
Rituximab for the treatment of relapsing-remitting multiple sclerosis in Thailand: an economic evaluation and budget impact analysis
Saharat Aungsumart[1], Metha Apiwattanakul[1]
[1]*Neurological institute of Thailand*
Background: FDA-approved disease-modifying therapies (DMTs) for treating MS are costly, making them inaccessible to most MS patients in Thailand due to cost-effectiveness concerns. Rituximab, although used off-label, is both cost-effective and highly efficient for treating MS. However, its cost-effectiveness in Thailand has not been extensively evaluated.
Objective: This study aims to evaluate the cost-utility and budget impact of rituximab and its biosimilar for multiple sclerosis treatment compared with best supportive care, the standard practice in Thailand.
Methods: A Markov model with a one-month cycle length and lifetime horizon was applied to compare the costs and outcomes of rituximab and best supportive care from a societal perspective. Incremental cost-effectiveness ratios were estimated, and probabilistic and one-way sensitivity analyses were conducted to address parameter uncertainty. Additionally, the Markov model was used to assess the 5-year budget impact from the government perspective. The highlight of this study is to provide policy recommendations for including rituximab in the Thai list of essential medicines.
Results: A rituximab biosimilar demonstrated higher effectiveness and lower associated costs compared to best supportive care, with a 70% probability of being cost-effective. The probability of relapse was identified as the most sensitive parameter in the one-way sensitivity analysis. The calculated budget impact of treating multiple sclerosis patients in Thailand was 26,360,000 Thai baht (THB) or 844,255 United States dollars (USD) in the first fiscal year, and approximately 20,810,000-23,080,000 THB (666,608-739,388 USD) in each of the subsequent four fiscal years.
Conclusion: In Thailand, a rituximab biosimilar would be cost-effective and reduce overall treatment costs. The evidence from this study supports the policy decision to include rituximab in the Thai National List of Essential Medicines as of March 2024.
Disclosures: The authors declare no conflict of interest.

P-114

Comparison of Visual Outcomes in Patients with AQP4-IgG Positive, MOG-IgG Positive, and Double Seronegative Optic Neuritis with Severe Visual Impairment

Rawipreeya Laosirirat[1], Saharat Aungsumart[2]
[1]*National Institute of Thailand*
[2]*Neurological Institute of Thailand*

Background: Optic neuritis is frequently idiopathic in origin, yet clinical data on idiopathic autoimmune-mediated optic neuritis remains sparse. Most previous studies have focused on visual acuity at specific time points post-treatment, lacking longitudinal comparisons.

Objective: This study aims to compare the visual outcomes in patients with severe visual impairment from optic neuritis who are AQP4-IgG positive, MOG-IgG positive, or double seronegative.

Methods: We conducted a retrospective longitudinal study at the Neurological Institute of Thailand, analysing visual outcomes of three patient groups (AQP4-IgG, MOG-IgG, and double seronegative) presenting with severe visual impairment (defined as best corrected visual acuity (BCVA) of 20/200 or worse) between June 2020 and May 2023. Visual outcomes were assessed by time to good visual recovery (defined as ≥ 66.77% improvement in BCVA from after attack to baseline) and complete visual recovery (defined as BCVA returning to baseline).

Results: A total of 30 patients with 45 affected eyes were included. Individual eyes were analysed independently, including AQP4-IgG (n=10), MOG-IgG (n=5), and double seronegative (n=30). Demographic data showed a female-predominant population with a median age of 39 years old. Median BCVA at onset was logMAR 1.7.

Using MOG-IgG as a comparator, the hazard ratios for complete visual recovery in AQP4-IgG and double seronegative groups were 0.158 (P= 0.135) and 0.421 (P =0.288), respectively. For good visual recovery, the AQP4-IgG group and double seronegative group had a hazard ratio of 0.187 (P=0.013) and 0.189 (P=0.005), respectively.

Within 2 months, all MOG-IgG patients achieved good visual recovery compared to less than 50% of AQP4-IgG and double seronegative group, with some AQP4-IgG and double seronegative patients experiencing further recovery beyond three months.

Conclusion: Patients in the MOG-IgG group exhibited the best visual prognosis and the shortest recovery times compared to the AQP4-IgG group and double seronegative group.

Disclosures: Authors declare no conflict of interest.

P-115

Cyclical IVIG as a safe and effective treatment option in pregnancy in a patient with NMOSD and concurrent SLE: A Case Report.

Suhailah Abdullah[1]
[1]*University Malaya*

Background: NMOSD and SLE are associated with a higher risk of relapse and complications in pregnancy. However, there are limited options for disease-modifying treatment in pregnancy given the safety concerns for the developing fetus.

Objective: To report the efficacy of cyclical IVIG in pregnancy.

Methods: This case report showcases a patient with a concomitant diagnosis of NMOSD and SLE who received cyclical IVIG throughout the conception and intrapartum period as a replacement for IV Rituximab for prevention of relapse and exacerbation of SLE.

Results: Rituximab has a product label of Grade C for pregnancy. However, recent real-world case series

and reports seem to suggest a favorable safety profile in preventing relapse in NMOSD during conception and intrapartum periods. However, its efficacy in the treatment of moderate to severe SLE is controversial. On the other hand, IVIG is safe in pregnancy but has limited data as a preventive therapy for NMOSD. Nevertheless, there is more robust evidence of its efficacy in the treatment of refractory SLE. This case report showcases the timeline of the treatment switch from Rituximab to IVIG from conception to the intra and postpartum periods that resulted in a successful pregnancy as manifested by the absence of relapse in NMOSD, exacerbation of SLE, and the delivery of a healthy infant.
Conclusion: Her successful pregnancy highlighted the possible efficacy of cyclical IVIG as a safe and effective treatment option in pregnancy.
Disclosures: The author has received travel expenses and honoraria for lectures and/or educational activities from Merck Serono, Novartis, and Sanofi.
Nevertheless, there is no conflict of interest.

P-116
Review Study: Factors Affecting the Well-Being of Multiple Sclerosis Patients
Yasar Altun[1], Berfin Altun[2]
[1]*Adiyaman University, Medical Faculty, Department of Neurology*
[2]*Üsküdar University, Faculty of Humanities and Social Sciences, Department of Psychology*
Background: Due to the chronic character of multiple sclerosis (MS), non-drug treatment can be applied. While there are factors that affect MS positively, there are also factors that affect it negatively. In addition, there may be complementary treatments that have a positive effect on standard pharmacological treatment for MS patients.
Objective: In this study, it was aimed to review the studies conducted between 2013 and 2023 (the last 10 years), excluding undergraduate and postgraduate theses that evaluated studies evaluating psychological well-being in multiple sclerosis (MS) patients and
Methods: A total of 34 studies, one in Turkish and 33 in English, were included in the study, and the articles included in the study were examined using the document analysis technique.
Results: When the distribution of articles by years is examined, it is seen that there is a rapid increase in the number after 2020. It has been observed that the studies in the literature mostly examine the reasons that affect psychological well-being positively and negatively, and there are studies on awareness. In the period from 2000 to the present; It has been observed that the number of studies on awareness of MS patients published in Google Scholar, TR Index and PubMed databases is higher than the number of studies on reasons that positively affect psychological well-being. In the articles examined, it was determined that both quantitative and qualitative research methods were preferred as research methods, and measurement tools such as scales, surveys and forms were used as data collection tools, and the interview method, one of the qualitative research methods, was used.
Conclusion: Only one study has been conducted in our country and it has been shown that psychological well-being in MS patients has a positive effect on the patients' disability score. The number of studies written from outside our country has increased rapidly.
Disclosures: There is no conflict of interest.

P-117
Potential Determinants of Reduced Work Efficiency And Unemployment In Demyelinating Diseases
Monalisa Vegda[1], Akshatha Sudhir[1], Lekha Pandit[1], Mary Anitha D'Cunha[1], Suresha Kharvi[1]

[1]*Centre for Advanced Neurological Research, KS Hegde Medical Academy, Nitte University, Mangalore, India*
Background: Chronic demyelinating diseases such as MS and NMOSD are associated with both physical and psychological disabilities that impacts work efficiency and employment.
Objective: To study direct impact of physical disability, fatigue, pain and depression on work place efficiency among those employed and among students and home makers with chronic demyelinating disorders.
Methods: We analysed data from 292 patients, who answered a questionnaire in person or telephonically. Details regarding their symptoms, employment, work efficiency and dependence was collected. Average and subgroup employment loss was calculated. Linear regression analysis determined the impact of fatigue, pain and depression on employment loss.
Results: There were 292 patients with mean age of 40.32 years and mean age of disease onset of 32.24 years. Among them, 42 (14.38%) students, 74 (25.34%) homemakers and 137 (46.91%) employed and primarily unemployed (35) adults were seen. In all 28.46% became unemployed after diagnosis, more in myelitis (52.5%) and bilateral ON (31.25%) subgroups. Fatigue was a recurring complain (48.95%) with 17.12% people attributing work loss to it. Mean work hour loss of 9.70 hours (26.36%) was seen in employed patients. Fatigue ($p < 0.00003$), depression ($p < 0.0002$) and pain (0.00132) were contributors of unemployment. Significant depression was noted among students (95.23%) as compared to other group of patients (48.63%) (Chi- 42.65, $P < 0.00001$). Among homemakers, pain (40.54%) and fatigue (52.70%) contributed to reduced work efficiency. Dependence on care giver was 80.47% among patients with 4.1% caretakers admitting to switching jobs, 3.1% reducing work hours and 2% temporarily stopping work.
Conclusion: Impact of disease existed beyond physical disability that affects work efficiency, livelihood, health care and financial security.

P-118

Outcome prediction models in a large international multicentre cohort of myelin oligodendrocyte glycoprotein antibody-associated disease

Ki Hoon Kim[1], Silva Messina[2], Vyanka Redenbaugh[3], Patrick Schindler[4], Regina Stegher[5], Laura Cacciaguerra[6], John Chen[7], Eva-Maria Dorsch[4], Anne-Katrin Fietz[5], Ruth Geralds[2], Jae-Won Hyun[8], Su-Hyun Kim[8], Maria Isabel Leite[2], Sean Pittock[9], Gilberto Solorza Buenrostro[4], Friedemann Paul[4], Jacqueline Palace[2], Eoin Flanagan[10], Ho Jin Kim[8]

[1]*Department of Neurology, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Korea*
[2]*Nuffield Department of Clinical Neurosciences, Oxford University Hospitals, Neurology, Oxford, United Kingdom*
[3]*Mayo Clinic, Neurology, Rochester, United States*
[4]*Charité-Universitätsmedizin Berlin, Neurology, Berlin, Germany*
[5] *Charité-Universitätsmedizin Berlin, Institut fur Biometrie und Klinische Epidemiologie, Berlin, Germany*
[6] *Mayo Clinic, Neurology, Center for MS and Autoimmune Neurology, Rochester, United States*
[7] *Mayo Clinic, Neurology, Ophthalmology, Center for MS and Autoimmune Neurology, Rochester, United States*
[8] *Research Institute and Hospital of National Cancer Center, Neurology, Goyang, South Korea*
[9] *Mayo Clinic, Neurology, Laboratory Medicine and Pathology, Center for MS and Autoimmune Neurology, Rochester, United States*
[10]*Mayo Clinic*

Background: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an autoimmune

inflammatory disease affecting the optic nerves, spinal cord and brain.
Objective: To assess predictors of disability and factors that may influence outcomes, large datasets are needed to power the analysis.
Methods: Patients with MOG-IgG on the cell-based assay and compatible clinical phenotype were included. Datasets from the UK (Oxford), USA (Mayo Clinic), South Korea (National Cancer Center), and Germany (Charite) were combined to investigate risk factors for a relapsing course and disability (EDSS score at last follow up), employing logistic regression models and time-to-event analysis.
Results: We included 655 patients (72.3% White; 19.4% Asian; 8.3% others) with 163 (24.5%) <18 years old at onset and 402 (60.5%) females. The median disease onset age was 32 years. Optic neuritis was the most common onset attack (51.6%) followed by transverse myelitis (19.7%). By the last follow-up (median, 3.62 years), 381 (57.3%) had a relapsing course with a median of 3 attacks (range, 2-14); optic neuritis accounted for 81.2% of relapses. In relapsing patients, the median time to the 2nd attack was 0.67 years (range 0.05-39.94). MOG-IgG sero-positivity was persistent (≥6 months) in 298/409 (72.9%). At last follow-up, 183/647 (28.3%) had an EDSS of 0; 94 (14.5%) had an EDSS ≥3; 22 (3.4%) had an EDSS ≥6; and 106/628 (16.9%) had a visual acuity ≤6/12; 12/628 (1.91%) had a visual acuity ≤20/200 or ≤6/60 in at least one eye. Risk factors for an EDSS ≥3 were older onset age [30-59years vs 0-11years odds ratio (OR) 2.72 95% CI (1.32-6.15)] and longer disease duration [OR 1.07 95% CI (1.03-1.10)].
Conclusion: In this large international multicentre study of MOGAD, the overall disability outcomes were favourable with approximately 85% having no or minimal disability (EDSS <3) at last follow-up. Older age was associated with a greater risk of disability.
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Dr Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, and Astellas. He's received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, and UCB. His institution has

received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/ MedImmune, Roche/Genentech.
He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)—issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties. He is working as a consultant in the Mayo Clinic Neuroimmunology laboratory clinical service. The Mayo Clinic Neuroimmunology Laboratory commercially offers MOG-IgG testing, but revenue accrued does not contribute to salary, research support, or personal income.
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Friedemann Paul has received honoraria and research support from Alexion, Bayer, Biogen, Chugai, MerckSerono, Novartis, Genyzme, MedImmune, Shire, and Teva Pharmaceuticals, and serves on scientific advisory boards for Alexion, MedImmune, Novartis, and UCB. He has received funding from Deutsche Forschungsgemeinschaft (DFG Exc 257), Bundesministerium für Bildung und Forschung (Competence Network Multiple Sclerosis), Guthy-Jackson Charitable Foundation, EU Framework Program 7, and National Multiple Sclerosis Society of the USA. He serves on the steering committee of the N-Momentum study with inebilizumab (Horizon Therapeutics) and the OCTiMS Study (Novartis). He is an associate editor with Neurology, Neuroimmunology, and Neuroinflammation and academic editor with PloS One Jacqueline Palace has received support for scientific meetings and honorariums for advisory work From Merck Serono, Novartis, Chugai, Alexion, Roche, Medimmune, Argenx, Vitaccess, UCB, Mitsubishi, Amplo, Janssen. Grants from Alexion, Argenx, Roche, Medimmune, Amplo biotechnology. Patent ref P37347WO and licence agreement Numares multimarker MS diagnostics Shares in AstraZeneca. Her group has been awarded an ECTRIMS fellowship and a Sumaira Foundation grant to start later this year. A Charcot fellow worked in Oxford 2019-2021. She acknowledges partial funding to the trust by Highly specialised services NHS England. She is on the medical advisory boards of the Sumaira Foundation and MOG project charities, Is a member of the Guthy Jackon Foundation Charity and is on the Board of the European Charcot Foundation and the steering committee of MAGNIMS and the UK NHSE IVIG Committee and chairman of the NHSE neuroimmunology patient pathway and ECTRIMS Council member on the educational committee since June 2023. On the ABN advisory groups for MS and neuroinflammation and neuromuscuscular diseases.
Eoin Flanagan has served on advisory boards for Alexion, Genentech, Horizon Therapeutics and UCB. He has received research support from UCB. He has received speaker honoraria from Pharmacy Times. He received royalties from UpToDate. Dr Flanagan is a site principal investigator in a randomized clinical trial of Rozanolixizumab for relapsing myelin oligodendrocyte glycoprotein antibody-associated disease run by UCB. Dr Flanagan is a site principal investigator and a member of the steering committee for a clinical trial of satralizumab
for relapsing myelin oligodendrocyte glycoprotein antibody-associated disease run by Roche/ Genentech. Dr Flanagan has received funding from the NIH (R01NS113828). Dr Flanagan is a member of the medical advisory board of the MOG project. Dr Flanagan is an editorial board member of Neurology, Neuroimmunology and Neuroinflammation, The Journal of the Neurological Sciences and Neuroimmunology Reports. A patent has been Submitted on DACH1-IgG as a biomarker of paraneoplastic autoimmunity.
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P-119

Enhancing Quality of Care for Patient Requiring Intravenous Rituximab: Reducing Door-to-Infusion Time at a Single Tertiary Centre

Wai Hian Ho[1], Si Yan Leo[1], Chen Yu[1], Mei Lian Goh[1], Su Rong Fam[1], Xuejuan Peng[1], Janis Siew Noi Tye[1], PeiPei Shen[2], Mai Moh Moh Thu[2], Anne Hui Ting Neo[2], Freddy Huang Mook Tang[2], Kevin Tan[1], Jeanne May May Tan[1], Josiah Yui Huei Chai[1], Tianrong Yeo[1]
[1]*National Neuroscience Institute*
[2]*Tan Tock Seng Hospital*

Refer to O-10 in Plenary Oral Presentation - 2

P-120

Evaluation of "Invisible Symptoms" in Multiple Sclerosis Patients Using Personal Health Records (PHRs): A Pilot Study

Kenzo Sakurai[1], Kei Kaburagi[1], Riyoko Ko[1], Yoko Nakano[1], Kenji Isahaya[1], Yoshihisa Yamano[1]
[1]*St. Marianna University School of Medicine*

Background: Patients with Multiple Sclerosis (MS) often experience a decrease in quality of life (QoL) due to "invisible symptoms" such as fatigue and depression, even without evident relapses, progression, or neurological deficits. However, collecting and evaluating these "invisible symptoms" is challenging in clinical practice.

Objective: The aim of this study is to explore factors that correlate with the "invisible symptoms" of MS patients using digital biomarkers available through PHRs.

Methods: We targeted MS patients at the Department of Neurology, St. Marianna University School of Medicine, and evaluated QoL (SF-36), fatigue (FAS), depression (BDI-II), and daytime sleepiness (JESS) as "invisible symptoms" through Patient Reported Outcomes (PRO). Additionally, we measured biometric markers such as steps, sleep duration, and sleep heart rate using a smartwatch as PHRs and explored their correlation with the "invisible symptoms."

Results: Forty-seven patients participated in this study. The patient demographics were mean age 39.2 ± 10.3 years, 39 females (84.8%), median disease duration of 7 years, and median EDSS of 1.25. Strong correlations were observed between QoL and depression, QoL and fatigue, and depression and fatigue (r=-0.78, -0.86, 0.90, respectively). However, no correlation was found between these "invisible symptoms" and steps, sleep duration, or sleep heart rate. Similarly, no correlation was observed between daytime sleepiness and sleep duration or sleep heart rate. On the other hand, PHRs were useful in visualizing patients' activity levels and sleep patterns and were beneficial in evaluating some "invisible symptoms."

Conclusion: In this study, no direct correlation was found between "invisible symptoms" and biometric markers obtained from PHRs. However, PHRs were shown to be potentially useful on a case-by-case basis.

Disclosures: N/A

POSTER SESSION – 9

Symptom Management and Rehabilitation

P-121
Withdrawn

P-122
A rare case of severe hyperglycemia related central pontine myelinolysis
Sang-Mi Noh[1], Yoonha Hwang[1]
[1]*St.Vincent's Hospital, The Catholic University of Korea*
Background: Central pontine myelinolysis (CPM) is well recognized to occur in a variety of clinical settings, but particularly following rapid correction of severe hyponatraemia. Although the rapid correction of hyponatremia is a dominate cause of CPM, a variety of other medical conditions have been associated with the development of CPM, independent of change
Objective: Most CPM cases with hyperosmolar hyperglycemia are related with acute correction of hyperglycemia. We report here a CPM case without correction of hyponatremia and hyperglycemia.
Methods: A 52-year-old woman with diabetes developed dysarthria, dysphagia and paraparesis. Initial the serum glucose was 810 mg/dl, sodium 123 mEq/L, potassium 4.1 mEq/L, blood urea nitrogen 1 mg/dl. There was no ketoacidosis, consistent with a hyperosmolar hyperglycemic state. Neurological examination showed the findings of gait ataxia and parapresis (MRC grade IV) and also revealed mild dysarthria and dysphagia. The other examination was unremarkable. Diffusion MRI of the brain performed on the same day demonstrated a region of high signal in the pons with decreased ADC value. These findings were consistent with CPM.
Results: The CPM associated with the rapid development of severe serum hyperosmolality in the absence of rapid correction of preceding hyponatremia is very rare.
Conclusion: Proposed mechanism between oligodendrocyte shrinkage and myelinolysis may be faster hypertonia than the rate of compensation of brain cells can result in CPM.

P-123
Therapeutic Challenges in A Complex Case of Refractory Neuromyelitis Optica Spectrum Disorder with Coexisting Sjögren's Syndrome
Juen Kiem Tan[1], Jack Son Wee[2], Nasheeda Saeed[1], Rathika Rajah[1], Alvin Oliver Payus[3], Aida-Widure Mustapha Mohd Mustapha[1], Hui Jan Tan[1], Rabani Remli[1]
[1]*Universiti Kebangsaan Malaysia*
[2]*Ministry of Health Malaysia*
[3]*Universiti Malaysia Sabah*
Background: Primary Sjögren's syndrome affect the CNS possibly through vasculitic processes and autoimmune demyelination. Combined with NMOSD, the resulting disease is refractory and challenging to manage.
Objective: To elucidate the clinical course and management of NMOSD with coexisting Sjögren's syndrome. We illustrate a case presenting to our center.
Methods: A 46-year-old Chinese woman initially presented with right leg weakness early 2022. She denied headache, nausea, vomiting, dysphagia, constitutional symptoms, fever, rashes, joint pain, and incontinence. Serum anti-MOG, oligoclonal bands, and Aquaporin-4 was negative, but Sjögren's antibody (Anti-Ro) was positive. She was diagnosed with seronegative NMOSD and treated with pulse IV methylprednisolone and six cycles of cyclophosphamide.

She relapsed twice in April and September 2023, with bilateral leg weakness. CSF protein was 424mg/L and was acellular. MRI showed hyperintense signals over bilateral cerebral hemisphere and central intramedullary hyperintensities from T9 to the conus medullaris. She received two cycles of rituximab six months apart, when it was complicated with herpes zoster ophthalmicus. Plasma exchange (PLEX) was commenced for the second relapse, but she developed seizures during PLEX and was discharged on levetiracetam and mycophenolate mofetil, with an EDSS of 7.
Results: She had a severe relapse in March 2024, when she was treated with sepsis and non-convulsive status epilepticus. She was given antibiotics, IV MTP, IVIg and later, PLEX. MRI showed increasing confluence of white matter hyperintensities throughout both cerebral hemispheres. She was discharged with low-dose prednisolone, clonazepam, perampanel, valproate, and levetiracetam. Monthly IVIg cycles improved her seizure control and mentation. Unfortunately, she deteriorated acutely three months after discharge with sepsis and eventually succumbed.
Conclusion: This case highlights the complexities of managing seronegative NMOSD with severe, recurrent relapses and recurring infections. A multidisciplinary approach forms the basis of management long term to improve outcomes in such cases.
Disclosures: None to disclose.

P-124
Meningomyelitis-like onset of neuromyelitis optica spectrum disorder
Joong-Yang Cho[1]
[1]*Department of Neurology, Ilsan Paik Hospital, Inje University College of Medicine*
Background: Neuromyelitis optica spectrum disorder (NMOSD) is a rare inflammatory demyelinating disease. Abnormal cerebrospinal fluid (CSF) findings such as leukocytosis with concentration >50/ul are one of the characteristics of NMOSD, but these were not specific for identifying other infective neurological diseases.
Objective: Here we describe a rare case of NMOSD with CSF findings suggestive of bacterial meningomyelitis.
Methods: A 51-year-old female was admitted to our hospital with acute both leg weakness with dysuria one day ago. On neurological examination, the patient was alert and oriented. Her visual acuity was normal. Meningeal irritation was negative. Her strength of lower extremities was MRC grade II, and sensation was decreased in all modalities. Bilateral Babinski's sign was positive.
Spine MRI showed long segmental cross-sectional cord signal intensity change with diffuse cord swelling. Brain MRI revealed non-enhancing T2 high signal intensity on left periventricular white matter, corpus callosal splenium. Cerebrospinal fluid analysis revealed elevated protein (407 mg/dl) with pleocytosis (1500/ul, granulocyte 69%), and decreased glucose (43 mg/dl, serum glucose 112 mg/dl) level.
Results: An initial diagnosis of long extensive myelitis with brain involvement, such as NMOSD established, but bacterial meningomyelitis was not excluded. The patient was administered antibacterial treatment with high dose methylprednisolone for 5 days. After high dose steroid therapy, she experienced mild recovery of motor power in the lower limbs, and sensory loss. Serum anti-aquaporin-4 (AQP-4) antibody was positive. Final diagnosis was seropositive NMOSD with CSF examination mimicking bacterial meningomyelitis. Additionally, plasma exchange was performed, which improved her symptoms gradually.
Conclusion: Bacterial meningitis-like presentation was a rare presentation in attack phase of NMOSD. In this case, corticosteroid should be considered as initial treatment.

P-125
Withdrawn

P-126
Syncope Attack in Neuromyelitis Optica Spectrum Disorder: Case Series Report and Literature Review
Xueping Zheng[1], Yuyuan Yang[1], Xiaosa Chi[1]
[1]*The Affiliated Hospital of Qingdao University*
Background: Neuromyelitis Optica Spectrum Disorders (NMOSD) is characteristic of optic neuritis (ON) and acute myelitis, as well as encompasses the cerebral, diencephalic, and brainstem lesions. However, syncope related to NMOSD was rarely reported. Here, we reported two cases diagnosed with AQP4-positive NMOSD and presented with recurrent syncope.
Objective: Two relapsing NMOSD cases presenting with recurrent syncope attack were reported.
Methods: Brain and cervical spine magnetic resonance imaging (MRI) were conducted, and serum AQP4-IgG was assayed. Besides, NMOSD patients with such syncope attack presentation were reviewed and summarized.
Results: Two cases were reported, and 3 cases were literature reviewed. Both of our patients had syncope attack following nausea and vomiting and lesions were showed in medulla oblongata. All of the patients were AQP4 positive and markedly improved after high dose intravenously methylprednisolone treatment. One reported patient even needs pacemaker implantation for the severe syncope. All of the patients had lesions in medulla oblongata or posterior cervical spinal cord., indicating complex anatomical connection with syncope.
Conclusion: Syncope could occur in NMOSD patients, especially with medulla oblongata lesions. Much more attention should be paid to these patients in case of pacemaker implantation.
Disclosures: No

POSTER SESSION – 8
Patient Reported Outcomes and Programs that Support Quality of Life

P-127
A Qualitative Study on the Impact of Symptoms and Adverse Events of Oral Glucocorticoids on Daily Life in Patients with Neuromyelitis Optica Spectrum Disorder
Ichiro Nakashima[1], Yuko Shimizu[2,3], Ryotaro Ikeguchi[3], Tadashi Nagatsuka[4], Katsuhisa Yamashita[4], Yuta Fukuoka[5], Tatsunori Murata[5], Kazuo Fujihara[6,7]
[1]*Division of Neurology, Tohoku Medical and Pharmaceutical University*
[2]*Department of Medical Safety, Tokyo Women's Medical University*
[3]*Department of Neurology, Tokyo Women's Medical University*
[4]*Chugai Pharmaceutical Co., Ltd*
[5]*CRECON Medical Assessment Inc*
[6]*Department of Multiple Sclerosis Therapeutics, Fukushima Medical University School of Medicine*
[7]*Multiple Sclerosis and Neuromyelitis Optica Center, Southern TOHOKU Research Institute for Neuroscience*
Background: The use of oral glucocorticoids (GCs) is reported to be effective in relapse prevention of neuromyelitis optica spectrum disorder (NMOSD) and is widely used in Japan. The long-term use of GCs may cause several adverse events (AEs). Collectively, both the symptoms of NMOSD and GC-associated AEs are known to reduce patient quality of life (QoL).

Objective: To conduct a qualitative study evaluating the causal relationship between the subjective symptoms of NMOSD and patient experience of AEs due to GCs and their impact on patient daily life and emotions.
Methods: This interview survey of Japanese patients with aquaporin-4 antibody–positive (AQP4[+]) NMOSD was conducted using an interview guide prepared based on a literature search and expert opinions. Well-trained interviewers conducted the interviews with patients, with each interview lasting 60 minutes. Conversations with the patients were recorded and transcribed verbatim. Qualitative analysis was performed by coding and categorizing data and assessing the causality of symptoms and GC-related AEs with patients' daily life and emotions using the records of verbatim transcripts.
Results: Qualitative interviews were conducted with 15 patients with AQP4[+] NMOSD. The median patient age was 53 years, and almost all patients were female (n=14). All patients had a prior history of GC treatment, and 9 patients were currently prescribed GCs at the time of the survey completion. The overall degree of neurological findings based on the modified Rankin Scale was 'normal' in 4 patients, 'very mild signs of impairment' in 7 patients, and 'mild impairment' and 'relatively severe impairment' in 2 patients each.
Results of the causality assessment obtained from patients showed that both symptoms of NMOSD and AEs due to GCs affected various daily activities, including interpersonal relationships, going out, employment, and schooling, as well as impacted patient's emotional burden.
Conclusion: NMOSD symptoms and GC-related AEs impacted the QoL, including patients' lifestyle and values. Based on these results, we are planning a survey questionnaire to assess patient preferences for tailored treatment options for NMOSD.
Disclosures:
I.N. serves on the scientific advisory boards for Chugai Pharmaceutical, Biogen Japan, and Novartis, and receives honoraria for speaking engagements with Chugai Pharmaceutical, Alexion Pharmaceuticals, Biogen Japan, Mitsubishi Tanabe Pharma, and Novartis.
Y.S. and R.I. received speaker honoraria from Chugai Pharmaceutical.
T.N. and K.Y. are employees of Chugai Pharmaceutical.
Y.F. and T.M. are employees of CRECON Medical Assessment Inc. and they receive consultation fees from Chugai Pharmaceutical.
K.F. serves as an advisor on the scientific advisory boards for Biogen, Mitsubishi Tanabe Pharma, Novartis, Chugai Pharmaceutical, Roche, Alexion Pharmaceuticals, Viela Bio/Horizon Therapeutics, UCB, Merck, Japan Tobacco, and AbbVie; has received funding for travel and speaker honoraria from Biogen, Eisai, Mitsubishi Tanabe Pharma, Novartis, Chugai Pharmaceutical, Roche, Alexion Pharmaceuticals, Viela Bio, Teijin, Asahi Kasei, Merck, and Takeda Pharmaceuticals; and has received grant-in-aid for scientific research from the Ministry of Education, Culture, Sports, Science and Technology of Japan and grant-in-aid for scientific research from the Ministry of Health, Labour and Welfare of Japan.

EUROPEAN CHARCOT FOUNDATION SYMPOSIUM

Managing progressive MS today

ECF1 -Treatment of progressive MS in practice

Hans-Peter Hartung
Professor of Neurology, Heinrich-Heine-University Düsseldorf, Germany
Honorary Professor at Brain and Mind Center, UnMedical Faculty, University of Sydney, Australia

While a broad range of disease modifying treatments are available for relapsing forms of MS, there is a paucity of drugs effective in progressive MS. Only 2 drugs have been approved so far: Siponimod for active SPMS and ocrelizumab for PPMS. Their effect size is moderate and hence there is a pressing need to develop new treatments. New hope has been generated by the outcomes of the phase 3 trial of the BTK inhibitor tolebrutinib.
I will discuss various strategies based on current concepts of the pathomechanisms underlying progression in MS.
I will also discuss the recent attempts to redefine progression (RAW vs PIRA) and how that may impact our treatment algorithms.
In practical terms early detection of progression along the course of MS is of paramount importance. Management requires an integrated multidisciplinary approach with a combination of DMTs, symptomatic treatments, physiotherapy, and rehabilitation.

ECF2 - Patient Reported outcomes in the assessment of treatment response

Giancarlo Comi
Honorary Professor Vita Salute San Raffaele University (Milan)
Centro Sclerosi Multipla Gallarate (Italy)
Casa di Cura Igea, Milan (Italy)

From patients, patients organizations and health authorities there is an increased demand for more active engagement of persons with the disease in the definition of processes of care. This is particularly true in chronic diseases as multiple sclerosis (MS). No therapy can be developed without establishing patient centric metrics because the success of an intervention, in term of clinical efficacy and safety depends on its specific impact on the life of every single person with multiple sclerosis. Patient reported outcome (PRO) defines any information of a patient health condition that comes directly from the patients, without interpretation by a clinician or anyone else. Despite a large number of Patient Reported Outcome measures (PROs) developed in these years, very few have been regularly used in clinical practice and in registries and, perhaps with the exception of some questionnaires evaluating quality of life, very few have been used

as outcome measures in clinical trials. The global Patient Reported Outcome for Multiple Sclerosis (PROMS) initiative has been promoted to represent an unified view on PROs and to promote its role in clinical trials and clinical practice. Results of an International survey to prioritize functional domains that matter most to person with MS will be presented and the use of PROs in monitoring Progressive MS will ve analysed.

ECF3 - Advances in neurorehabilitation

Letizia Leocani
University Vita-Salute San Raffaele, Milan

Traditionally, rehabilitation aims at restoring function or implement compensatory strategies for deficits in sensorimotor and cognitive domains. Technology-supported rehabilitation holds the promising potential to augment and improve further results in clinical practice. Rehabilitative technology has traditionally been defined as aids that help people recover their functioning after injury or illness. This approach can be broadened to include technology enabling measurement of motor or cognitive performance (wearable sensors, digital testing, nervous conduction), enhancing treatment (robotics, virtual reality, non invasive neuromodulation), monitors and promotes physical activity, or allows monitoring and feedback. In MS, the appearance of symptoms and disability progression tend most often to emerge with increasing disease duration, so that it is possible to detect demyelination of eloquent pathways and initial loss of function before advanced neurodegenerative processes take place. The possibility of predicting future yet still contrastable disability will help changing the goal of rehabilitation, from restoring and recovery of evident symptoms and functional loss and symptoms to their prevention.

ECF4 - Symptomatic therapy

Kazuo Fujihara M.D.
Professor, Department of Multiple Sclerosis Therapeutics, Fukushima Medical University School of Medicine. Director, Multiple Sclerosis & Neuromyelitis Optica Center, Southern TOHOKU Research Institute for Neuroscience (STRINS), Koriyama, Japan.

Multiple sclerosis (MS) may cause a variety of symptoms and functional disabilities, such as weakness, spasticity, ataxia, tremor, bladder and bowel disturbances, sexual dysfunction, fatigue, cognitive and affective disorders, and they impair activity of daily living and reduce quality of life more severely in the progressive phase of the disease. Since disease modifying therapies of progressive MS are still limited in number and their efficacy is insufficient, symptomatic therapy as well as rehabilitation remains important in the management of the patients. In this presentation, an overview of current symptomatic therapies in progressive MS will be provided and the challenges will be discussed.

PHARMA EDUCATIONAL SYMPOSIA

Chugai Pharmaceutical Co., Ltd
Thursday, 31 October 2024

How Satralizumab changed treatment strategy in NMOSD

Exploring the Diverse Functions of IL-6 in NMOSD: A Japanese Clinical Perspective

Yusei Miyazaki
Department of Neurology, National Hospital Organization Hokkaido Medical Center

Most patients with NMOSD have AQP4 autoantibodies in their circulation, which can penetrate the central nervous system (CNS) and mediate destructive inflammation once the blood-brain barrier is compromised. Early research suggested that IL-6 is involved in the pathogenesis of NMOSD by promoting the survival and proliferation of plasmablasts, the putative source of AQP4 antibodies. Satralizumab, an IL-6 receptor inhibitor, has been shown to significantly reduce NMOSD relapse rates compared to placebo in the Sakura Sky and Sakura Star trials. Additionally, more recent basic and clinical studies indicate that IL-6 plays a role in various aspects of NMOSD, including not only the survival of plasmablasts but also the regulation of peripheral immune systems, the integrity of the blood-brain barrier, and the function of resident CNS cells. This presentation will explore the multifaceted role of IL-6 in NMOSD and discuss the experience of using satralizumab in Japan.

New Era Treatment Strategy of NMOSD - RWD of Satralizumab

Ichiro Nakashima
Professor,Department of Neurology, Tohoku Medical and Pharmaceutical University, Sendai, Japan.

NMOSD is a neurological autoimmune disorder characterized by severe optic neuritis and myelitis. The discovery of AQP4 antibodies has clarified the clinical features of antibody-positive patients, and the development of disease modifying drugs has advanced. Currently, five biologics are available in Japan. Glucocorticoids and immunosuppressants have been used as a relapse prevention therapy in Japan, but there are patients in whom recurrence cannot be suppressed by conventional treatment, in addition there are patients in whom treatment cannot be continued due to adverse events even if relapse is suppressed. However, the treatment strategy has changed with the launch of biologics.
Satralizumab is a biologic agent targeting the IL-6 receptor for NMOSD developed in Japan. In this session, evidence of the efficacy and safety of satralizumab will be reviewed, including real-world data accumulated since post marketing in Japan.

ASTRAZENECA
Friday, 1 November 2024

Complement in Focus: Clinical and Real-World Evidence for the Prevention of Relapses in AQP4-Ab+ NMOSD

Prof. Ho Jin Kim
National Cancer Center, Seoul, South Korea
Prof. Sasitorn Siritho
Bumrungrad International Hospital Bangkok, Thailand
Prof. Jin Nakahara
Keio University Hospital, Tokyo, Japan

This symposium will focus on the role of the complement system in neuromyelitis optica spectrum disorder (NMOSD) and present clinical and real-world evidence on the use of complement component 5 inhibitors (C5i)—eculizumab and ravulizumab—for the prevention of relapses in AQP4-Ab+ NMOSD patients. Attendees will gain insights into the complement-mediated pathophysiology of NMOSD and the therapeutic benefits of targeting C5 to prevent relapses. Data from key clinical trials, including PREVENT and CHAMPION-NMOSD, will be discussed alongside real-world safety outcomes, particularly focusing on the reduction of relapse rates and the management of meningococcal infection risk. The symposium will also explore the long-term safety of these therapies and their impact on reducing corticosteroid use, improving patient quality of life, and minimizing relapse risk. Through expert presentations and a panel discussion, attendees will better understand how to integrate C5 inhibitors into clinical practice for optimal patient outcomes.

Mitsubishi Tanabe Pharma Corporation
Friday, 1 November 2024

CD19-targeted therapy for NMOSD

Inebilizumab: a new era of treatment for neuromyelitis optica spectrum disorder

Chung-Hsing Chou, M.D.
Department of Neurology, Tri-Service General Hospital, Taiwan

Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease characterized by recurrent and disabling attacks of acute inflammation affecting the optic nerves and spinal cord, and sometimes the brainstem or cerebrum. B cells contribute to NMOSD pathophysiology by secreting antibodies against AQP4 and driving T-cell responses through pro-inflammatory cytokine secretion and antigen presentation.
Inebilizumab is presumed to involve binding to the B cell, resulting in antibody-dependent, cell-mediated cytotoxicity. Thus, B cell depletion is expected to suppress the inflammatory attacks characteristic of NMOSD. Recently, the long-term safety and efficacy of inebilizumab with continued and sustained clinical benefit has been shown in a double-blind, randomized, placebo-controlled, phase 2/3 N-MOmentum trial.

B Cell Targeting in NMOSD: Therapeutic Implications of Inebilizumab

Yusei Miyazaki, M.D., Ph.D.
Department of Neurology, National Hospital Organization Hokkaido Medical Center

NMOSD is an inflammatory disease of the CNS that is clinically characterized by recurrent neurological attacks. Most patients have AQP4 autoantibodies in their circulation, which, upon the breakdown of the blood-brain barrier, penetrate the CNS and mediate destructive inflammation. Recent studies have highlighted the central role of circulating plasmablasts as the source of these autoantibodies.
Inebilizumab is a humanized monoclonal antibody specific to CD19, which is exclusively expressed on B-lineage cells, including plasmablasts. In the N-MOmentum study, inebilizumab significantly suppressed NMOSD relapses compared to placebo, leading to its approval in several countries. Interestingly, in addition to removing autoantibody-producing plasmablasts, paraclinical data obtained from the N-MOmentum study suggested therapeutic mechanisms independent of reducing anti-AQP4 antibodies. In this lecture, I will discuss both the antibody-dependent and -independent roles of B-lineage cells and the therapeutic mechanisms of inebilizumab in NMOSD. Additionally, I will share our experiences with inebilizumab in Japan.