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Pan-Asian Committee
for Treatment and Research in Multiple Sclerosis

THE 14th PAN-ASIAN COMMITTEE FOR RESEARCH AND TREATMENT IN MULTIPLE SCLEROSIS CONGRESS

24 to 26 November 2022

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Pan-Asian Committee for Treatment and Research in Multiple Sclerosis

Alexion-organized and -sponsored satellite symposium at the 14th Congress of the Pan-Asian Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS)

INVITATION

Targeting complement in neuroimmunological diseases during the coronavirus pandemic

16:30–18:00 SGT | Friday 25 November 2022

Island Ballroom | Shangri-La Singapore | Singapore

SPEAKERS

Chair: Professor Jin Nakahara
(Japan)

Professor Heinz Wiendl
(Germany)

Professor John Vissing
(Denmark)

Professor Maria Pia Sormani
(Italy)

AGENDA

16:30–16:40	Welcome and introductions	Chair: Professor Jin Nakahara (Japan)
16:40–17:00	The importance of complement in the pathophysiology and targeted treatment of neuromyelitis optica spectrum disorder and generalized myasthenia gravis	Professor Heinz Wiendl (Germany)
17:00–17:15	Real-world evidence of targeting complement in patients with neuromyelitis optica spectrum disorder	Professor Jin Nakahara (Japan)
17:15–17:30	Terminal complement inhibition for generalized myasthenia gravis during the coronavirus pandemic	Professor John Vissing (Denmark)
17:30–17:45	Can we apply learnings from the treatment of multiple sclerosis during the coronavirus pandemic to neuromyelitis optica spectrum disorder?	Professor Maria Pia Sormani (Italy)
17:45–18:00	Questions and close	All

This is an educational meeting organized and funded by Alexion, AstraZeneca Rare Disease, and is intended for healthcare professionals only.

These presentations will focus on data relating to neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 antibody-positive (AQP4+) and on data relating to refractory generalized myasthenia gravis (gMG) in patients who are anti-acetylcholine receptor antibody-positive (AChR+).

Please note, data relating to an Alexion product will be presented as part of this meeting. Product registration conditions differ internationally, and prescribing information may vary depending on approval in each country.

Please note that eculizumab is not licensed for NMOSD or gMG in Singapore.

The views expressed in this symposium are based upon the clinical experience of the presenters.

ALEXION
AstraZeneca Rare Disease

M/INT/UNB-g/0095 September 2022

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WELCOME NOTE

Dear Friends and Colleagues,

We would like to welcome you to the 14th Congress of the Pan-Asian Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS) that will take place in Singapore from 24 to 26 November 2022.

PACTRIMS is an annual event that aims to provide clinical and scientific updates in the care of patients with multiple sclerosis (MS), neuromyelitis optica and related conditions in the Asia-Pacific region. Patients in this region face different challenges where clinical care could vary depending on different healthcare reimbursements, perceptions of disease and accessibility to diagnostic assays and medications. PACTRIMS 2022 strives to provide opportunities for participants representing their MS communities to exchange knowledge, acquire skills, share experiences, foster collaborations and work towards our shared vision of improving the care and lives of patients with MS and other CNS inflammatory demyelinating diseases.

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

On behalf of the organizing committee, we welcome you and wish you a fruitful congress in Singapore.

Yours sincerely,

Amy Quek May Lin
Chair, Local Organising Committee
PACTRIMS 2022

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PROGRAM OVERVIEW

Thursday 24 November 2022	
15.00-15.05	Welcome Address by the Local Organizing Chair, Amy Quek (Singapore)
15.05-15.10	Opening Address by the President, Kazuo Fujihara (Japan)
15.10-15.15	Special Address by Guest of Honour
	Plenary 1: NMO and MOGAD – state of the art chaired by Naraporn Prayoonwiwat (Thailand) and Alvin Seah (Singapore)
15.15-15.40	L1.How to use new(ish) therapies for NMOSD: real world experience from Japan 2019-2022 - Yusei Miyazaki (Japan)
15.40-16.05	L2. 2022 Consensus Diagnostic Criteria and clinical decision making in MOGAD - Sudarshini Ramanathan (Australia)
16.05-16.30	L3. Attack-independent neuroaxonal damage in MS, NMO and MOGAD? Implications for therapy - Ho Jin Kim (Korea)
16.30-16.45	Panel Q&A
16.45-17.15	Coffee Break
17.15-18.45	Novartis Symposium
19.30-21.30	Welcome Reception Cocktail (Please wear your badge for entry)
Friday, 25 November 2022	
08.00-09.30	Mitsubishi Tanabe Symposium
09.30-10.00	Coffee Break & Poster Viewing Session One
	Plenary 2: Neurodegeneration in MS: from pathophysiology to treatment chaired by Kazuo Fujihara (Japan) & Michael Barnett (Australia)
10.00-10.25	L4. Innate immunity, neurodegeneration and the slowly expanding MS lesion - V Wee Yong (Canada)
10.25-10.50	L5. Imaging Neurodegeneration in MS - beyond the T2 lesion - Jin Nakahara (Japan)
10.50-11.15	L6. Bruton Tyrosine Kinase Inhibition in Multiple Sclerosis – dual targeting of inflammation and neurodegeneration - Heinz Wiendl (Germany)
11.15-11.30	Panel Q&A
11.30-12.30	Oral Presentation Part One
12.30-13.30	Lunch
	Plenary 3: Infection, Immunology and Inflammatory Demyelination: at the Crossroads Chaired by C T Tan (Malaysia) & Stephen Adelstein (Australia)
13.30-13.55	L7. Vaccination, MS and immunotherapy – a practical, evidence-based approach - Lekha Pandit (India)

13.55-14.20	L8. Epstein-Barr Virus: are we on the cusp of targeted immunotherapy for MS? - Bruce Taylor (Australia)
14.20-14.45	L9. Infectious consequences of immunosuppression - Stephen Reddel (Australia)
14.45-15.00	Panel Q&A
15.00-16.00	Oral Presentation Part Two
16.00-16.30	Coffee Break & Poster Viewing Session Two
16.30-18.00	Alexion Symposium
19.00-22.00	Presidential Dinner at LeVel33 (Please wear your badge for entry)

Saturday, 26 November 2022	
08.00-09.30	Chugai-Roche Symposium
09.30-10.00	Coffee Break
	Plenary 4: CNS inflammation at the extremes of age – special considerations chaired by Kevin Tan (Singapore) & Kieren Po (Australia)
10.00-10.25	L10. Pediatric and transitional MOGAD: distinctive features and pathogenesis - Pin Fee Chong (Japan)
10.25-10.50	L11. Immunotherapy in patients with pediatric multiple sclerosis and other demyelinating disorders of the CNS: practical considerations - Russell Dale (Australia)
10.50-11.15	L12. CNS demyelination in the Elderly: clinical course and treatment strategies - Ju-Hong Min (Korea)
11.15-11.30	Panel Q&A
	Closing and Award Ceremony
11.30-11.40	Poster Award ceremony
11.40-11.45	Closing Remarks by PACTRMS Vice-President, Ho Jin Kim (Korea)

INVITED LECTURES

L-1

How to use new(ish) therapies for NMOSD: real world experience from Japan 2019-2022

Yusei Miyazaki, M.D., Ph.D.

Department of Neurology, National Hospital Organization Hokkaido Medical Centre, Japan

Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory disease of the central nervous system (CNS) clinically characterized by recurrent attacks of neurological symptoms. Most patients have anti-aquaporin 4 autoantibodies in the circulation. Upon breakdown of the blood-brain barrier, these autoantibodies penetrate the CNS and trigger destructive inflammation. Progression of disability in NMOSD is dependent exclusively on the occurrence of attacks. Apart from rituximab, treatments for preventing NMOSD relapse basically worked through nonspecific immunosuppression and had incomplete effectiveness as well as a broad spectrum of side effects. In 2019 and 2020, the effectiveness of four monoclonal antibodies—eculizumab, satralizumab, inebilizumab, and rituximab—was demonstrated one after the other in randomized controlled trials, and the results have led to the approval of these drugs in many countries. All these monoclonal antibodies have definite effectiveness in preventing NMOSD relapses with acceptable safety profiles. With the advent of these monoclonal antibody therapies, the treatment of NMOSD has entered a new era. In this lecture, I will share our experience treating NMOSD using these new monoclonal antibodies and discuss the best treatment strategy for NMOSD at present.

L-2

2022 Consensus Diagnostic Criteria and clinical decision making in MOGAD

Sudarshini Ramanathan BSc (Med) MBBS (Hons) FRACP PhD

Neurology Staff Specialist, Concord Hospital, Sydney, Australia

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is now recognised as a disease entity distinct from multiple sclerosis and neuromyelitis optica spectrum disorder. This presentation will highlight the scientific and clinical evolution of our understanding of this condition, and the role of laboratory biomarkers and their strength and limitations in characterising this disorder. We will review the expanding clinical spectrum of MOGAD, and the clinical and radiological profiles which can distinguish this condition from other demyelinating syndromes and facilitate expedited diagnosis. This presentation will outline the development of the 2022 International MOGAD Diagnostic Criteria and discuss therapeutic decision making both at disease onset and in the case of relapsing disease.

L-3

Attack-independent neuroaxonal damage in MS, NMO and MOGAD? Implications for therapy

Ho Jin Kim, MD, PhD.

Department of Neurology, National Cancer Center, Goyang, Republic of Korea

Multiple sclerosis (MS), aquaporin-4 IgG seropositive neuromyelitis optica spectrum disorder (AQP4-IgG+ NMOSD) and myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD) are three main relapsing form of autoimmune CNS diseases.

In MS, the major burden of disability is thought to be a consequence of progressive disease independent of clinical attacks and new MRI activity. By contrast, attack-independent progression appears extremely rare in AQP4-IgG+ NMOSD and MOGAD, where disability is thought to derive almost exclusively from severe attacks, resulting in permanent tissue damage and poor recovery.

In the same vein, subclinical neuroaxonal damage in the absence of overt clinical attacks occurs in all stages of MS, while it is yet a matter of controversy in AQP4-IgG+ NMOSD and MOGAD. Identifying such an attack-independent tissue damage is essential, as it should be accounted for when evaluating treatment response, in order to achieve best clinical outcome.

In this talk, I will review and discuss the current evidence on the occurrence of subclinical attack-independent tissue damage in patients with AQP4-IgG+ NMOSD and MOGAD.

L-4

Innate immunity, neurodegeneration and the slowly expanding MS lesion

V. Wee Yong

Professor, University of Calgary, Canada

The slowly expanding lesion (SEL) detected by brain imaging grows gradually over years in the brain of people living with MS, particularly those with progressive MS. The number of SELs has been correlated with progression of disability. Analysis of postmortem MS samples highlights pro-inflammatory microglia at the rim of SELs, and several of these have iron deposition in their midst. Correspondent with these features are accumulation of oxidized phosphatidylcholines and signs of axonal pathology. In tissue culture, our studies show that ferrous iron, oxidized phosphatidylcholines and pro-inflammatory microglia are toxic to neurons (e.g. Dong et al., Nature Neurosci 2021). While we lack medications to antagonize iron or oxidized phosphatidylcholines in SELs, the toxicity of microglia may be ameliorated by repurposed hydroxychloroquine and the family of Bruton's tyrosine kinase inhibitors (e.g. Yong, Neuron, Epub ahead of print).

L-5

Imaging Neurodegeneration in MS - beyond the T2 lesion

Jin Nakahara

Professor, Department of Neurology, Keio University School of Medicine, Tokyo, Japan

The T2 lesion on magnetic resonance imaging (MRI) remains the most important paraclinical tool to identify demyelination and to diagnose multiple sclerosis (MS). However, the clinico-radiological paradox has been well recognized: There are only modest correlations between irreversible neurological disability and T2 lesion load in MS. Given the increasing number of available disease-modifying drugs (DMDs) with varying mechanisms of action, precise evaluation of individual MS immuno-pathology and neurodegeneration with advanced imaging may identify those who are at a risk of progressive disease course and ultimately lead to better choice of DMD to improve his/her prognosis. In the current lecture, current imaging modalities and their potential utility in MS will be reviewed and summarised.

L-6

Bruton Tyrosine Kinase Inhibition in Multiple Sclerosis – dual targeting of inflammation and neurodegeneration

Heinz Wiendl, MD

Professor, Department of Neurology with Institute of Translational Neurology, Germany

Current therapies for multiple sclerosis (MS) effectively reduce relapses and relapse-associated worsening caused by transient infiltration of peripheral immune cells into the CNS. However, they are less effective at slowing disability accumulation in both relapsing and progressive MS, possibly because they do not penetrate the blood-brain barrier (BBB) to act on CNS-resident innate immune cells that have been proposed to drive disability.

Bruton's tyrosine kinase (BTK) is an intracellular signalling molecule regulating maturation, migration, survival, and activation of B cells and myeloid cells, particularly microglia. B cells and microglia are central players in MS immunopathogenesis and contribute to disease progression. As such, CNS-penetrant inhibitors of BTK (BTKis) hold promise to target adaptive and innate immunity concurrently on both sides of the BBB.

Originally developed as a B-cell malignancy treatment, BTKis emerge as a promising therapeutic approach on the horizon of MS treatments. Currently, five BTKis are undergoing clinical trials in MS. These BTKis differ in selectivity, strength of BTK inhibition, binding mechanisms, and ability to modulate immune cells within the CNS.

Here, BTK function in signalling pathways of different immune cells relevant to MS will be reviewed, and overview of preclinical data and clinical trial results will be provided.

L-7

Vaccination, MS and immunotherapy – a practical, evidence-based approach.

Lekha Pandit, MD, DM, PhD.

Professor of Neurology, Director of Centre for Advanced Neurological Research, Nitte University, Karnataka, India

Vaccinations are integral to preparing patients for long term immunotherapy in autoimmune disorders such as multiple sclerosis. Vaccinations on one hand protect patients on disease modifying therapy against specific infections, but on the other, may have varied efficacy on these very patients by virtue of their underlying disease and concurrent medications. In addition, vaccination may trigger new / first attack of a demyelinating disorder. Geographically, susceptibility for specific infections vary and patients with multiple sclerosis may be on disease specific or "off label" therapies. These in turn increase the challenges in advocating vaccinations and especially timing of the latter in relation to ongoing therapy. The COVID-19 pandemic and COVID-19 vaccinations offer a good example for analysing the relationship between vaccinations, MS and immunotherapy. A review of real-life based evidence on vaccinations in MS patients on immunotherapy, including in a low-middle income set up will be presented.

L-8

Epstein-Barr Virus: are we on the cusp of targeted immunotherapy for MS?

Bruce Taylor

Professor, University of Tasmania and conjoint consultant neurologist Royal Hobart Hospital, Australia

Epstein Barr Virus EBV is a ubiquitous human herpes virus that is known to be associated with several human illnesses including MS. Recent work has indicated that infection with EBV is an obligate risk factor for developing MS and that there may be molecular mimicry between EBV epitopes and CNS proteins. These important recent discoveries have raised the possibility of targeted therapies against EBV, or even vaccination against EBV as potential therapeutic options in the prevention or treatment of MS. This lecture will examine the current understanding of the role of EBV in MS causation and progression, the role of immunotherapy including T Cell therapies, and antivirals in the treatment of MS the potential role of anti-retroviral therapies in EBV control and the controversies surrounding the potential benefits and harm from an EBV Ivaccine.

L-9

Infectious consequences of immunosuppression

Stephen Reddel, MB BS PhD FRACP

Staff Specialist Neurologist, Concord Repatriation & General Hospital, Sydney, Australia

Autoimmunity in increasingly recognised as a cause of human and neurological disease, and unlike many diseases is treatable. The alloimmune response is not necessarily the same as the autoimmune response. The alloimmune response has prominent pattern recognition pathways (danger signals), innate immune system responses, and redundancy of pathways for defending against the pathogen.

Nevertheless, as a general principle it is safer to assume that immunosuppressive drugs are likely to affect an alloimmune pathway that exists to fight an infection, at some time, somehow, somewhere. The absence of a signal in a selective population controlled randomised trial does not prove that such a drug is without risk in the real-world application.

The recent global pandemic has illustrated how mechanisms of alloimmunity in the context of particular immunosuppression can anticipate what happens in a real test not seen in trials, for instance with pulsed anti-CD20 monoclonals in COVID-19 severity and vaccination responses. There are many other anticipatable risks for infection with our therapies that will be discussed.

L-10

Paediatric and transitional MOGAD: distinctive features and pathogenesis

Pin Fee CHONG

Department of Pediatrics, Graduate School of Medicine, Kyushu University, Japan

Over the past few years, autoantibodies against myelin oligodendrocyte glycoprotein (MOG-Abs) have been consistently identified in a variety of demyelinating syndromes. Although MOG-Abs were initially reported in children with acute disseminated encephalomyelitis (ADEM), the clinical spectrum of these MOG-Ab-associated disorder (MOGAD) is expanding and somehow differs between paediatric and adult patients. Recent studies using cell-based assays have demonstrated a higher frequency of MOG-Abs detection in paediatric than adult patients with acquired CNS demyelinating diseases. Typical paediatric MOGAD presentations usually show ADEM in younger, and optic neuritis and transverse myelitis in older children (age >9 years). A proportion of these children experience a relapsing disease course. Until recently, clinical, and radiological evaluation has expanded the spectrum of MOGAD including those showing atypical features such as encephalitis- or leukodystrophy-like appearance and other unclassifiable phenotypes. While there is a lack of knowledge about the pathogenic roles of MOG, an increasing number of studies have shown that MOG is a protein that can elicit demyelinating immune response in animals. This review discusses the diversity in clinical phenotypes in paediatric MOGAD and present our recent data from both clinical and experimental perspectives.

L-11

Immunotherapy in patients with paediatric multiple sclerosis and other demyelinating disorders of the CNS: practical considerations

Russell Dale

Professor of Paediatric Neurology, University of Sydney, Australia

A considered approach is required to the child or adolescent with acute or relapsing demyelination of the CNS. Firstly, the underlying clinical and syndrome and underlying pathophysiology differs in the very young child: The young child is more likely to present with acute disseminated encephalomyelitis (ADEM) or bilateral optic neuritis than an adult. In a young child with new onset CNS demyelination, it is more likely they have MOG antibody associated disease than multiple sclerosis. In the adolescent, multiple sclerosis becomes the more likely diagnosis in the child presenting with CNS demyelination. This distinction is essential, because the therapeutic approach is different between the autoantibody associated syndromes (MOGAD or AQP4 ab disease) and multiple sclerosis.

Secondly, neuroinflammation is inherently problematic to the developing brain, and can result in disruption of synaptic connectivity, and consequently neurodevelopment. Hence, treating neuroinflammation speedily and adequately, is an important consideration. The cognitive sequelae of multiple sclerosis in adolescents, and neurodevelopmental problems such as ADHD after ADEM, are increasingly recognised.

Thirdly, balancing the need for adequate immune modulation with side effects of treatment is important, to avoid harmful side effects to the young. Thankfully there is now good safety data regarding the use of immune therapies in children and adolescents with CNS demyelination, to aid the clinician in decision making.

Fourthly, therapeutic compliance is a major consideration in the adolescent, and combination of respectful education plus empowerment is important.

L-12

CNS demyelination in the Elderly: clinical course and treatment strategies

Ju-Hong Min

Professor, Department of Neurology, Sungkyunkwan University School of Medicine, Samsung Medical Centre, Republic of Korea

Immunosenescence is a process of immune dysfunction with aging and includes changes in the composition and function of lymphoid organs in the elderly. This is closely related to the development of autoimmunity and neurodegeneration and can contribute to co-morbidities in aging population. With increased

life span and effective disease modifying therapies (DMTs), the number of elderly patients with CNS demyelinating diseases is growing. In addition, late-onset patients with such as multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), and myelin oligodendrocyte glycoprotein (MOG) antibody associated disorder (MOGAD) show different clinical characteristics, compared to early-onset patients, although the interactions of immunosenescence with pathomechanisms remain unclear. Particularly in MS, current DMTs reduce relapse activity and slow disease progression, but cannot prevent the accumulation of disability, which may be explained by the impact of immunosenescence on the immune system and disease progression. Moreover, most clinical trials for DMT were not designed focusing on aging patients and the risk of their comorbidities can negatively affect the disease course, which can make the therapeutic strategies more challenging in elderly patients with CNS demyelination.

INNOVATION BEYOND IMAGINATION

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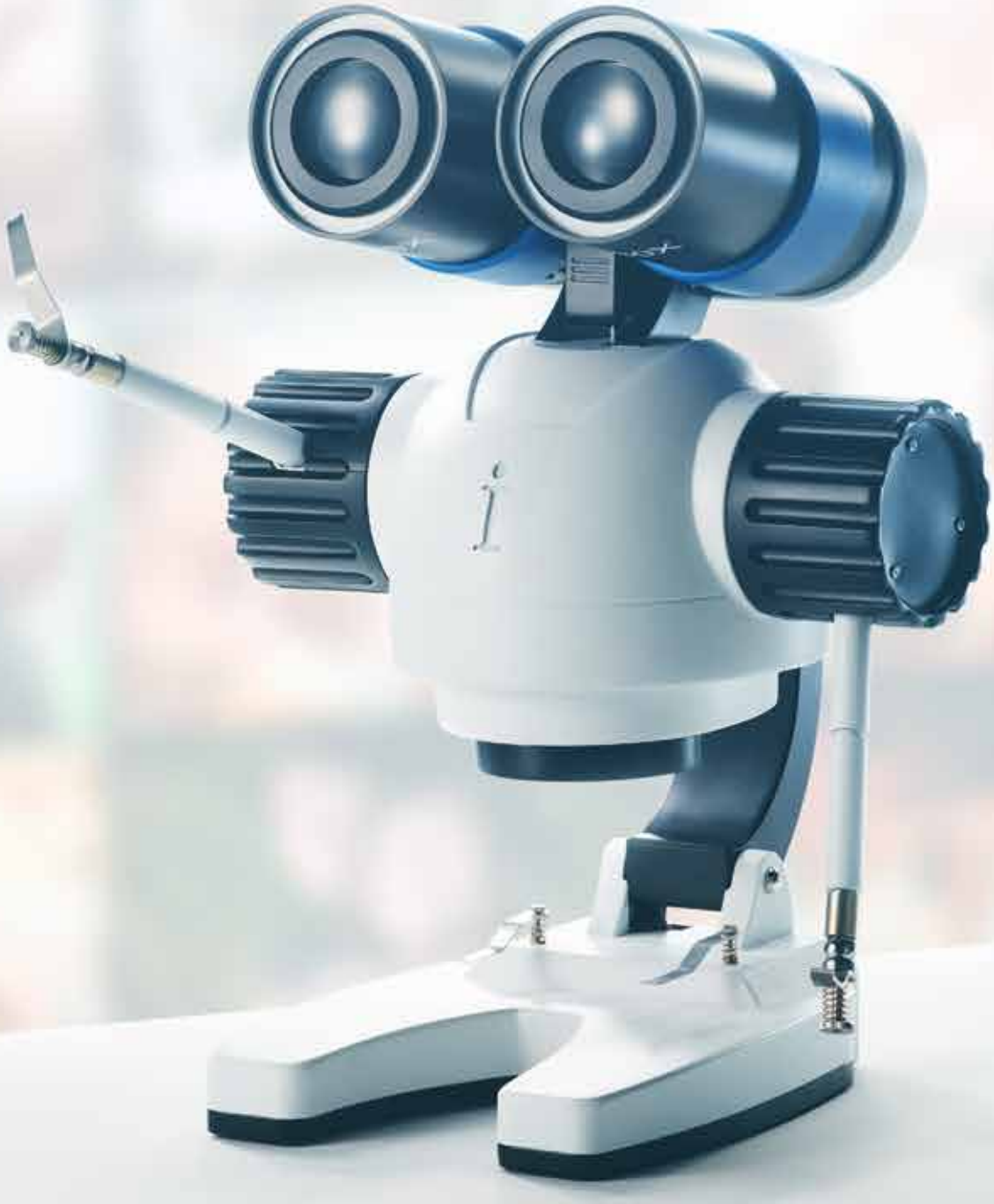

ORDINARY SUBMISSION

PLENARY ORAL PRESENTATION - 1

Advances in Technology and Methods of Care

O-1

Evaluation of a new enzyme-immunodot assay for AQP4-IgG for large-scale rapid use: a prospective multicentre diagnostic accuracy study

Jin Bi[1], Ying Fu[1]
[1]*The First Affiliated Hospital of Fujian Medical University*

Background: Cell-based assays (CBA) are now the most sensitive and specific laboratory tests for AQP4-IgG in neuromyelitis optica spectrum disorder (NMOSD). However, the requirement of special instruments limits their widespread use in routine laboratories at different hospitals.
Objective: To develop an enzyme-immunodot (IDoT) assay for the simple and rapid detection of the IgG autoantibodies to aquaporin 4 (AQP4-IgG).
Methods: This was a prospective multicenter diagnostic study. Patients with NMOSD and healthy controls from the Third Affiliated Hospital of Sun Yat-sen University in Guangzhou and the First Affiliated Hospital of Fujian Medical University in Fuzhou were included from April to December 2020. The positive group comprised patients clinically diagnosed with NMOSD who were AQP4-IgG-positive according to CBA. The negative group comprised healthy controls who were AQP4-IgG-negative according to CBA. To further verify performance characteristics of the IDoT assay, we also conducted it in other disease controls, cross-validation and follow-up test.
Results: The serum samples of 200 patients in the positive group and 200 healthy controls was tested for AQP4-IgG by the IDoT assay using the blind method. Compared with the CBA, the IDoT assay had a 99% sensitivity (95%CI 0.960–0.998), 99% specificity (95%CI 0.960–0.998), 99% positive likelihood ratio (95%CI 0.960–0.998), and 0.01 negative likelihood ratio (95%CI 0.002–0.040). The area under the receiver operating characteristic curve was 0.99 (95%CI 0.979–1.001), and the Kappa coefficient was 98% (95%CI 0.960–1.000), suggesting that the detection efficiencies of the two detection methods were consistent. The results of the IDot assay were scored according to the depth of the color difference. Spearman correlation analysis of the IDoT assay and serum AQP4-IgG titer results showed a moderate correlation ($r = 0.627$, $P < 0.001$). There was one false positive patients in IDoT assay of other disease controls.
Conclusion: The IDoT assay has the same efficacy as CBA in detecting the AQP4-IgG.

Basic Science and Pathophysiology

O-2

Complement Activation is associated with Relapse in MOGAD

Jae-Won Hyun[1], Yeseul Kim[1], Rosah May Palermo Payumo[2], Ki Hoon Kim[1], Su-Hyun Kim[1], Ho Jin Kim[1]
[1]*Department of Neurology, National Cancer Center*
[2]*National Cancer Center Graduate School of Cancer Science and Policy*

Background: Complement (C5) inhibition is a therapeutic option in aquaporin-4 antibody neuromyelitis optica spectrum disorder, and elevation of activated complement proteins in myelin oligodendrocyte glycoprotein antibody disease (MOGAD) was recently reported. However, it is yet unclear whether complement activation is associated with relapse in MOGAD.

Objective: We aimed to evaluate the association of complement activation and relapse in MOGAD.
Methods: The levels of activated complement proteins (C5a and soluble C5b9 (sC5b9)) were measured in 22 paired relapse and remission serum samples from the same patients with MOGAD, and 10 age- and sex- matched healthy volunteers. Relapse samples were obtained within median 20 (range 1 - 59) days from the attacks, and remission samples were collected after median 35 (range 4 – 103) months from the previous attacks. Serum levels of C5a, and sC5b9 were measured by enzyme-linked immunosorbent assay. Major and minor relapses were defined by Opticospinal Impairment Score.
Results: The C5a and sC5b9 levels in MOGAD patients at relapse were significantly higher than those in MOGAD patients at remission as well as those in healthy controls (C5a: median 38.6 vs. 11.5 (p
Conclusion: Increased levels of activated complement proteins were associated with relapse in MOGAD. These findings suggest potential benefit from activated complement (C5) inhibition in MOGAD patients.
Disclosures: Kim Y, Payumo, Kim KH report no financial disclosures. Hyun has received grants from the National Cancer Center and National Research Foundation of Korea. Kim SH has lectured, consulted, and received honoraria from Bayer Schering Pharma, Biogen, Genzyme, Merck Serono, and UCB and received a grant from the National Research Foundation of Korea. Kim HJ received a grant from the National Research Foundation of Korea and research support from Aprilbio and Eisai; received consultancy/speaker fees from Alexion, Aprilbio, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll BioPharma, MDimune, Merck Serono, Novartis, Roche, Sanofi Genzyme, Teva-Handok, UCB, and Viela Bio; is a co-editor for the Multiple Sclerosis Journal and an associated editor for the Journal of Clinical Neurology.

O-3
Serum Neurofilament Light Chain Levels as a Biomarker of Disease Activity, Progression and Treatment Response in Patients with Multiple Sclerosis
Marzena Fabis-Pedrini[1], Belinda Kaskow[1], Stephanie Trend[1], William Carroll[1], Sue Walters[1], Aleksandra Maceski[2], Jens Kuhle[2], Allan Kermode[1]
[1]Perron Institute for Neurological and Translational Science, University of Western Australia, Australia; Centre for Molecular Medicine and Innovative Therapeutics, Murdoch University, Australia
[2]Neurologic Clinic and Policlinic, MS Centre and Research Centre for Clinical Neuroimmu-

nology and Neuroscience Basel, University Hospital Basel, University of Basel
Background: The neurofilament light chain (NfL) has emerged as a promising biomarker of multiple sclerosis (MS) disease activity, progression, and response to treatment. During axonal injury, neurofilament proteins are released into the extracellular space and their levels in CSF and blood are reflecting the degree of axonal damage in MS.
Objective: To measure the value of serum NfL as a biomarker of disease activity and progression, and its usefulness to monitor treatment response in patients with MS.
M**ethods**: Serum NfL levels were measured in 542 patients with demyelinating disease, including clinically isolated syndrome (CIS; n=20), relapsing-remitting MS (RRMS; n=341), secondary progressive MS (SPMS; n=138), primary progressive MS (PPMS; n=43) and 10 healthy controls (HC) using single-molecule array technology (SIMOA). Treatment strategies were classified as "no treatment", "injectable" and "high efficacy". The Expanded Disability Status Scale (EDSS) score and patients' demographics were also analysed.
Results: Serum NfL levels were significantly higher in patients with CIS vs HC (23.6 +/- 3.4 vs 12.3 +/- 1.6, p
Conclusion: Our findings support the potential value of serum NfL as a measure of disease activity and progression, and treatment response in multiple sclerosis.
Disclosures: Marzena J. Fabis-Pedrini has received travel sponsorship from Merck Serono Australia. Jens Kuhle received speaker fees, research support, travel support, and/or served on advisory boards by 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, 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. Belinda Kasow, Stephanie Trend, Sue Walters, Aleksandra Maceski report no conflicts of interest to disclosure.

O-4
Astroglial Connexin 43 is a Novel Therapeutic Target for a Chronic Multiple Sclerosis Model
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Background: Connexin (Cx) 43 gap junction channel proteins are overexpressed in chronic lesions of multiple sclerosis (MS) and its animal model, experimental autoimmune encephalitis (EAE), at chronic phase, reflecting reactive astrogliosis.

Objective: We aimed to elucidate the role of overexpressed Cx43 in MS by therapeutic administration of a novel CNS-permeable pan-Cx blocker, INI-0602, in chronic EAE.
Methods: EAE was induced by immunizing MOG35-55 in 35 C57BL6 mice. Following the peak of acute EAE, INI-0602 (40 mg/kg) or saline was intraperitoneally administered every other day from day postimmunization (dpi) 17 to dpi 50.
Results: The clinical signs of EAE were significantly attenuated in the chronic phase in INI-0602-treated mice. Demyelinated areas and infiltration of CD3+ T cells, Iba1+ microglia, F4/80+ macrophages, C3+GFAP+ A1 astroglia in lumbar spinal cord lesions were reduced in INI-0602-treated mice compared to saline-treated mice. Flow cytometry analyses of CD4+ T cells isolated from the CNS tissues of INI-0602 treated mice revealed a significant decrease in the proportions of Th17 and Th17/Th1 cells at dpi 24 and Th1 cells at dpi 50. INI-0602 treatment of astroglia in vitro reverted A1 phenotype formation of astroglia by suppressing calcium-orientated communication through gap junctions and significantly decreased the Cx43 expression density.
Conclusion: These results suggest that the overexpressed astroglial Cx43 in chronic EAE and MS lesions exacerbate neuroinflammation. Thus, astroglial Cx43 is a novel promising therapeutic target for chronic progressive MS.

O-5
Central Nervous System Inflammatory Diseases after mRNA SARS-CoV-2 Vaccination
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Background: Central nervous system inflammatory diseases (CNSID) have been observed in close temporal association following mRNA SARS-CoV-2 vaccination; vaccine causality remains uncertain.
Objective: To describe CNSID occurring in close temporal association with mRNA SARS-CoV-2 vaccination in Singapore and to classify vaccine causality based on proposed criteria.
Methods: We conducted a prospective observational cohort study of CNSID (encephalitis, meningitis, transverse myelitis (TM) and/or optic neuritis [ON]) patients hospitalized in 7 public acute hospitals who had received at least one dose of either BNT162b or mRNA-1273 COVID vaccine within the preceding 6 weeks between December 2020 and August 2021.

Clinical, laboratory and radiological findings were collated. Vaccine causality was assessed by applying Butler criteria: 1) temporal relationship to vaccine, 2) diagnosis of an alternative cause, and 3) individual risk factors for the CNSID. Cases were classified as: probable, possible and unlikely.
Results: From 4,515,469 vaccinated individuals, 31 (<0.00001%) patients presented with CNSIDD post-vaccination. Disease onset was at a median of 8 days (range 1-40) following first vaccination (n=17) and 14.3 days (range 1-33) following second vaccination (n=14). CNSIDs reported were: meningitis (n=5), encephalitis (n=5), meningoencephalitis (n=6), CNS inflammatory demyelinating diseases (ON [n=8], TM, [n=4], new MS brain lesion, [n=1]) and cerebellitis (n=2). Causality was classified as "probable" in 8 patients, "possible" in 15 patients and "unlikely" in 8 patients. Among the patients with meningoencephalitis classified as "possible" vaccine causality, 3 had neural autoantibodies detected (GFAP-IgG, MOG-IgG, AMPAR-IgG and GABAB-IgG).
Conclusion: CNSID post-mRNA COVID vaccination is extremely rare; only a minority have no specific aetiology. A causal relationship remains unconfirmed but plausible.

Disease-modifying therapies

O-6
VISIONARY-MS Top-line Results: A Phase 2, Randomized, Double-Blind, Parallel Group, Placebo-controlled Study to Assess the Safety and Efficacy of CNM-Au8, a Catalytically Active Gold Nanocrystal Suspension in Relapsing Multiple Sclerosis
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Background: CNM-Au8 an oral suspension of catalytically-active gold nanocrystals supports brain energy metabolism resulting in neuroprotection and remyelination in preclinical models. The VISIONARY-MS trial investigated CNM-Au8 for the treatment of relapsing MS (RMS). The trial was suspended due to COVID-19 related enrolment challenges, enrolling 73/150 pts.
Objectives: The objectives of the VISIONARY-MS trial were to assess the efficacy and safety of CNM-Au8 for the treatment of stable RMS patients with chronic optic neuropathy on top of background disease-modifying therapy (DMT).

Methods: VISIONARY-MS was a Phase 2, multicentre, randomized, double-blind, placebo-controlled study assessing the efficacy and safety of CNM-Au8 versus placebo over 48 weeks in stable RMS patients on top of background DMTs. Enrolled subjects were randomized 1:1:1 to CNM-Au8 15mg/day, 30mg/day, or placebo. Key inclusion criteria: age 18-55 years, RMS diagnosis with disease duration 70µm in both eyes.
The primary endpoint was the change in BC-LCLA score in the clinically most affected eye, analysed using a mixed effect model with repeated measures through week 48. Secondary efficacy outcomes assessed global neurological function by the modified MS Functional Composite (mMSFC) including 25-Foot Timed Walk, Symbol Digit Modality Test, 9-Hole Peg Test (dominant and non-dominant), and LCLA (affected and fellow eye) from baseline through week 48. Primary analyses were conducted in the modified intent to treat population (mITT), which censored invalid data from 1 of 11 clinical trial sites. The threshold for statistical significance was prespecified at p=0.10. CNM-Au8 doses were combined for these analyses.
Results: The primary outcome, BC-LCLA, LS-mean difference versus placebo in the affected eye was 3.13 (95% CI: -0.08 to 6.33; p=0.056). 2 of 3 key secondary outcomes were significant: (i) LS-mean difference of the mean standardized mMSFC score: 0.28 (95% CI: 0.04 to 0.52; p=0.0197); (ii) LS-mean difference of the mMSFC average ranked sum score: 13.4 (95% CI: 2.8 to 23.9; p=0.0138); and (iii) time to repeated mMSFC improvement in two or more domains by >15% (36% vs. 22%, log-rank p=0.399). Exploratory endpoints included multi-focal visual evoked potentials, MRI, and OCT metrics, which demonstrated improvement. CNM-Au8 was well tolerated. There were no serious adverse events assessed as related to CNM-Au8. Treatment emergent adverse events were transient, and predominantly mild-to-moderate in severity.
Conclusion: These data provide preliminary evidence for improved global neurological function in stable RMS patients treated with CNM-Au8 as adjunct to standard-of-care and support continued investigation of CNM-Au8 in confirmatory trials.
Disclosures: Michael Barnett and Alexander Klistorner are consultants to Sydney Neuroimaging Analysis Centre, which was contracted to provide blinded analysis of MRI and VEP data in VISIONARY-MS. Robert Sergott is a consultant for Annesley EyeBrain Center, which was contracted to provide blinded quality review of LCLA data and blinded analyses of OCT data in VISIONARY-MS. Austin Rynder, Karen S. Ho, Jacob Evans, Jeremy Evans Alan Hartford, Robert Glanzman, and Michael Hotchkin are employees of Clene Nanomedicine, Inc

PLENARY ORAL PRESENTATION - 2
Disease-modifying therapies

O-7
Efficacy of Rituximab in patients with CNS Inflammatory Demyelinating Diseases: a

single institutional cohort in Singapore

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Background: Rituximab is a monoclonal antibody directed against the CD20 antigen on the surface of B lymphocytes resulting in B cell depletion. It is widely used as an off-label treatment in MS, AQP4-Ab NMOSD and MOGAD with various observational studies showing reduced relapse rates after treatment.
Objective: To determine the efficacy of Rituximab in patients with MS, AQP4-Ab NMOSD and MOGAD in the National Neuroscience Institute of Singapore.
Methods: Clinical data of patients with Multiple Sclerosis (MS), Aquaporin-4 antibody (AQP4-Ab) Neuromyelitis Optica Spectrum Disorders (NMOSD) and Myelin Oligodendrocyte Glycoprotein Antibody Associated Disease (MOGAD) who received Rituximab were reviewed. Annualized Relapse Rates (ARR) before and after initiation of Rituximab were calculated.
Results: Eighty patients who received Rituximab were identified – 32 RRMS, 9 SPMS, 2 PPMS, 34 AQP4-Ab NMOSD and 3 MOGAD. Seventy were females (87.5%), with a mean age of 45.6 years (SD 15.2) and median disease duration of 6.6 years (IQR 14.7) at Rituximab initiation. ARR 1 year after Rituximab was significantly lower than ARR 1 year prior to Rituximab [0.12 (SD 0.48) vs. 1.20 (0.88), p
Conclusion: Relapse rates were significantly reduced in patients after Rituximab therapy confirming that it is an effective maintenance therapy for CNS Inflammatory Demyelinating Diseases.

O-8

Immune cell profiles as biomarkers in treatment of SPMS with Siponimod: towards precision medicine

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Background: Relapsing-remitting multiple sclerosis (RRMS) has been linked to autoimmune processes, but the chronic form of MS, Secondary Progressive form (SPMS) has unclear pathogenesis and diverse mechanisms. Recently active immune responses are highlighted in SPMS; however, drugs that target immune cells have proved effective in RRMS often fail to help SPMS.
Objective: To determine biomarkers of pathogenic mechanisms in play in individual SPMS cases that are related to the efficacy of the lymphocyte-targeting drug Siponimod (Mayzent), thus allowing screening to indicate rational drug choice for SPMS treatment.
Methods: Although RRMS lymphocyte-targeting drugs showed promise in some SPMS cases, they ultimately failed in trials, suggesting chronic neuroinflammation can result from different active immune process in particular individuals. Siponimod, a S1Pr modulator targeting lymphocyte trafficking, has now been approved for SPMS treatment. However, it is unclear which lymphocyte populations it targets in some cases or why this treatment succeeds in where similar modulators

have failed. Identification of the particular immune processes involved is critical to enable effective personalised medicine for SPMS treatment. Our studies also link SPMS and active immune responses, with a new T helper cell (Th cell) subset found in some actively worsening SPMS (Raveney et al., PNAS 2021 and Raveney et al.). Thus it is critical to identify the profile of ongoing immune mechanisms in disease to allow for the correct drug targeting. To this end, we investigated Siponimod efficacy in correlation with immune mechanism. Multiparameter flow cytometry and serum analysis was used to examined immune profiles in peripheral blood from 48 MS subjects pre-Siponimod treatment and at 3, 6 and 12 months and compared with subsequent clinical indicators.
Results: Preliminary data in our novel mouse model of SPMS (Nat. Commun. 2015) that is driven by cytotoxic like Th cell subsets indicated that Siponimod ameliorated chronic neuroinflammatory disease symptoms (p=0.0033), supporting a role for Siponimod treatment in targeting T cell mediated pathogenesis.
For human MS, clinical improvement was observed in 12 out of 48 subjects that were switched to Siponimod treatment. Effective Siponimod treatment was linked to a reduction in proportions of peripheral Th cells with an activated/effector phenotype (p
Conclusion: Differential drug efficacy in SPMS likely relates to individual pathogenic mechanisms. Pre-treatment T cell profiling could drive personalized medicine, targeting the correct treatment for the particular pathogenic Th cell

Epidemiology, Genetics, and Epigenetics

O-9
The First Multiple Sclerosis Study in Mongolia; Predictors of Disability and Depression in Mongolian MS Patients

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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. Multiple sclerosis (MS) has not been investigated in Mongolia; there were a few MS case reports.
Objectives: We aimed to investigate the characteristics of MS in Mongolia, for the first time, particularly focusing on the association between MS-related parameters and depression levels.
Methods: We initiated the cross-sectional analyses, using data from 27 MS patients, aged 20-60 in Ulaanbaatar, Mongolia. Patients completed a questionnaire on their lifestyles and clinical information in January-April, 2022. We classified MS patients into two groups based on the disability levels assessed by expanded disability status scale (EDSS): “mild disability,” score
Results: We classified MS patient based on their EDSS scores: 11.1% mild disability and 88.9% moderate to severe disability, or based on their PHQ-9 scores: 44.4% mild depression, 40.7% moderate depression, and 14.8% severe depression. Disability levels were associated with vision problems (P< 0.05), but not any treatment (corticosteroid, 48%; methotrexate, 19%; plasmapheresis, 4%). Odds ratios (OR) for disease onset age were associated with EDSS scores (OR, 1,00; P< 0.001; 95% CI (1.02-4.39); OR for treatment duration had an effect on the EDSS scores (OR,1,02; P< 0.01; 95% CI (1,00-1,17). Depression levels were associated with corticosteroid treatment (P< 0.05) but not disability levels (P= 0.3).
Conclusions: MS onset age and treatment duration were independent predicting factors influencing the level of disability. Our findings provide epidemiological evidence for the beneficial early intervention of MS.

O-10
The Risk of Dementia in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder: a Nationwide Cohort Study in South Korea
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Background: Cognitive impairment is a common feature of multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD). However, knowledge regarding the association between MS or NMOSD and dementia risk is limited.
Objective: In the present study, the risk of dementia in MS and NMOSD patients in South Korea was estimated.
Methods: Data analyzed in this study were obtained from the Korean National Health Insurance Service (KNHIS) database between January 2010 and December 2017. The study included 1,347

MS patients and 1,460 NMOSD patients > 40 years of age who had not been diagnosed with dementia within 1 year prior to the index date. Matched controls were selected based on age, sex, and the presence of hypertension, diabetes mellitus, or dyslipidemia.
Results: In MS and NMOSD patients, the risk of developing Alzheimer's disease (AD; adjusted hazard ratio (aHR) = 2.23; 95% confidence interval (CI) = 1.70–2.91 and aHR = 1.99; 95% CI = 1.38–2.88, respectively) and vascular dementia (aHR = 3.75; 95% CI = 1.91–7.35 and aHR = 3.21; 95% CI = 1.47–7.02, respectively) was higher compared with the matched controls. NMOSD patients had a lower risk of AD compared with MS patients after adjusting for age, sex, income, hypertension, diabetes, and dyslipidemia (aHR = 0.62; 95% CI = 0.41–1.93). In stratified analyses of MS and NMOSD, the AD risk was significantly higher in the younger patient group (40–64 years of age) and in the patient group without hypertension.
Conclusion: The risk of AD and vascular dementia increased in MS and NMOSD patients and AD risk was higher in MS than in NMOSD. This is the first study in which the risk of AD and vascular dementia was investigated in MS and NMOSD within the same population.
Disclosures: JHM has lectured, consulted, and received Honoria from Bayer Schering Pharma, Merck Serono, Biogen Idec, Sanofi Genzyme, Teva-Handok, UCB, Samsung Bioepis, Mitsubishi Tanabe Pharma, Kolon Life Science, and Roche; received a grant from the National Research Foundation of Korea and SMC Research and Development Grant. ECJ, SYJ, JHJ, YY, HJK, KH, and DWS has nothing to disclose.

O-11

COVID-19 infection after at least two doses of SARS-CoV-2 mRNA vaccine in Multiple Sclerosis, AQP4-antibody NMOSD and MOGAD during the Omicron BA.1/2 wave in Singapore

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Background: Although the Omicron variant appears to cause mild disease, its high transmissibility remains a concern amongst people with neuroimmunological diseases, especially those on disease-modifying therapies (DMTs).
Objective:.To determine the factors associated with breakthrough COVID-19 infection despite at least two SARS-CoV-2 mRNA vaccines in MS, AQP4-Ab NMOSD and MOGAD patients during the Omicron BA.1/2 wave in Singapore.
Methods: This is a prospective study conducted at the National Neuroscience Institute (NNI), Singapore during the Omicron BA.1/2 wave from 1st January to 30th April 2022. Data was collected via clinic and/or teleconsultation from January 2022 through to August 2022 to ensure accurate data capture which included demographics, disease history, DMTs, vaccination records and COVID-19 infection status.
Results: Two hundred and one patients were included – 125 MS, 65 AQP4-Ab NMOSD, and 11 MOGAD. Forty seven had COVID-19 infection of whom 14 were on anti-CD20 therapies and

4 on fingolimod. Two infections were of moderate severity while the rest were mild. As a group, anti-CD20 therapies and fingolimod were associated with COVID-19 infection (p=0.039) while the other DMTs were not. On survival analysis, time to infection after 3 vaccinations was shorter in anti-CD20 therapies and fingolimod (as a group) compared to other DMTs (HR 2.96, p=0.006) and to no DMTs (HR 2.74, p=0.025). Receipt of a third vaccine was associated with fewer infections (33/176, 18.8%; crude rate of 11.3 infections per 1000 person-years) compared to 2 vaccines only (14/25, 56.0%; crude rate of 21.8 infections per 1000 person-years) (p<0.0001).
Conclusion: Patients on anti-CD20 therapies and fingolimod are at higher risk of COVID-19 infection after vaccinations although the majority of infections are mild. Receipt of third vaccine confers extra protection, supporting the vaccination strategy in this group.

Neuroimaging and Neurophysiology

O-12
Chi-Separation Imaging for Diagnosis of Multiple Sclerosis versus Neuromyelitis Optica Spectrum Disorder

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Background: Chi-separation imaging can provide surrogates for iron and myelin that relate closely to pathologic changes in multiple sclerosis (MS) lesions.
Objective: To evaluate the appearances of MS and neuromyelitis optica spectrum disorder (NMOSD) brain lesions on Chi-separation maps and explore their diagnostic value in differentiating the two diseases.
Methods: This prospective study included participants with MS and NMOSD who underwent Chi-separation imaging from October 2017 to October 2020. Using local frequency shifts and R2' (= R2*- R2), positive (Chi_pos) and negative susceptibility (Chi_neg) were separately estimated. R2 mapping was obtained using machine-learning approach. For each lesion, presence of the central vein sign (CVS) and paramagnetic rim sign (PRS) and signal characteristics on Chi_neg and Chi_pos maps were assessed and compared. For each participant, the proportion of lesions with CVS, PRS, and hypodiamagnetism was calculated. Diagnostic performances were assessed using receiver operating characteristic (ROC) curve analysis.
Results: Thirty-two participants with MS (mean age, 34 ± [SD] 10 years; 25 women) and 15 with NMOSD (52 ± 17 years; 14 women) were evaluated, with a total of 611 MS and 225 NMOSD brain lesions. On the Chi_neg maps, 80.2% (490/611) of MS lesions were categorized as hypodiamagnetic versus 14.2% (32/225) of NMOSD lesions (P
Conclusion: On Chi-separation maps, MS lesions tend to be hypodiamagnetic, which can serve as an important hallmark for differentiating MS from NMOSD.

POSTER SESSION - 1
Advances in Technology and Methods of Care

P-1
Non-Invasive Brain Neuromodulation For Fatigue Reduction In People With Multiple Sclerosis
Alice Dias[1], Demetrios Agourakis[2], Andre Caetano[3], Giovanna Vidigal[3], Juliana Telles[2], Bruna Sciarinni[2], Mauricio Bando[2], Carlos Monteiro[4], Talita Silva[4]
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Background: Fatigue is as very common symptom in the structure of neurological disorders in patients with Multiple Sclerosis (MS), which deepens disability and affects quality of life. Non-invasive neuromodulation, in this case rhythmic transcranial magnetic stimulation (rTMS), can act as a tool by activating or inhibiting certain areas of the brain cortex, in
Objective: The aim of the present study was to evaluate the overall fatigue improvement by applying rTMS in a group of MS patients.
Methods: 7 patients (33 to 68 yrs), both genders, answered the MFIS (Modified Fatigue Scale Impact Scale) before starting to receive rTMS and at the end of the study. The two scores were then tested for statistical significance, considering statistically significant, values of p
Results: 7 patients joined the study, and all of them showed some degree of overall fatigue improvement in both motor and psychosocial aspects. The MFIS mean score, before the rTMS was 32.43±9.78 (p
Conclusion: The rTMS has a positive effect on the manifestations of fatigue in MS. Non-invasiveness, safety and the possibility of differentiated use allow use of rTMS in the clinic and become an important component of non-drug rehabilitation of patients.
Disclosures: There is no conflict of interest between the authors.

P-2
Physiotherapy Associated With Transcranial Magnetic Stimulation For Rehabilitation Of Fatigue, Balance And Gait In Multiple Sclerosis
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Background: Multiple Sclerosis (MS) is a demyelinating autoimmune disease that causes

Central Nervous System damage and disabling symptoms. Transcranial Magnetic Stimulation (TMS) has benefits in the rehabilitation process when combined with therapeutic interventions.
Objective: To evaluate the influence of TMS combined with physiotherapy on the balance, gait and fatigue of people with MS.
Method: Participated of this study 20 people with MS, 14 women and 6 men, aged 33 to 68 years (SD 50,0) and Kurtze Expanded Disability Status Scale (EDSS) between 0 and 6,5. The study was done at Brazilian Association of Multiple Sclerosis. The protocol consisted of 10 TMS sessions and 6 physiotherapy sessions with a protocol for lower limb strength training and static and dynamic balance. Participants were randomized and divided into 2 groups: Group I) with real stimulus, so that 10 received the TMS stimulus (primary motor cortex (Cz): 50 pulses per time, 30 trains, 20 seconds of interval, totaling 1500 pulses at 90% of resting motor threshold and left dorsolateral prefrontal cortex (F3):10Hz, 50 pulses per train, 40 trains, 20 seconds interval, totaling 2000 pulses at 110% of resting threshold), and Group II) sham, that received the application without TMS stimulation (10 patients). All underwent physiotherapy. The Berg Balance Scale, Timed up and Go Test (TUG) and Modified Fatigue Impact Scale (MFIS) was applied before the combined interventions and after 60 days.
Results: It was found that 70% of participants showed improvement in balance, 20% a decrease and 10% a plateau on Berg Balance Scale. At the Timed up and Go Test, it was found 70% of improvement and 30% of decrease in performance. At the fatigue evaluation with Modified Fatigue Impact Scale, in Cognitive domain, it was found 90% decrease in fatigue values and 10% increase. In the physical domain, it was analyzed that 65% had an improvement in the indexes, 25% a worsening and 10% remained the same. In the psychosocial domain, 70% showed a decrease in fatigue levels, 20% an increase and 10% remained unchanged.
Conclusion: This preliminary study suggests that TMS associated with physiotherapy has great potential in the rehabilitation of balance, gait and fatigue on people with MS.
Disclosures: There is no conflict of interest between the authors.

P-3
Gait analysis using a wearable sensor in CNS inflammatory disease
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Background: Gait disturbance is a significant factor that causes overall deterioration in daily life and greatly deteriorates the quality of life in central nervous system (CNS) neuroimmunologic diseases such as multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). For evaluation of gait disorders, 6-minute walk test (6MWT), timed 25-foot walk test (T25FWT), and timed up and go test (TUG) are mainly used, but recently, wearable devices are being used for the research field.
Objective: In this study, we analyzed gait disturbance by comparing gait scales through questionnaires and gait parameters using wearable devices in CNS neuroimmunologic diseases.
Methods: We investigated the clinical variables, gait parameters, and gait disturbance questionnaire in CNS inflammatory disease in a stable state. Clinical variables included age, sex, disease duration, expanded disability status scale (EDSS), gait disability, BMI, and muscle power. Self-re-

ported questionnaires for walking disability, ADL, and fatigue were measured by the multiple Sclerosis Walking Scale-12 (MSWS-12), Multiple Sclerosis Impact Scale (MSIS-29), and fatigue severity scale (FSS). The gait parameter were measured with a wearable accelerometric device, the BTS G-Walk R (G-Sensor). It is a portable, wireless, inertial system with wearable sensors. The device could obtain spatiotemporal parameters, including gait speed, cadence, stand, swing duration, TUG, 6MWT, turning gait.
Results: A total of 28 CNS neuroimmunological disease patients were measured for gait dysfunction, and by disease, 3 MS, 13 NMOSD, 4 MOGAD, two optical neuritis, five transverse myelitis, and one rhombencephalitis were included. Although gait speed was associated with EDSS and T25WT, it was not associated with MSWS-12, MSIS-29, and FSS.
Conclusion: In this study, it would be suggested that gait parameters using a wearable device can be measured and that it would be used in clinical settings as an index to predict disease and disability. Through this preliminary study, it will be necessary to confirm further the clinical significance of the study expanding more patients and subjects with stratified classification.

Disclosures: Disclosure Statement
The authors report no financial disclosures.

P-4
Evaluation of a new enzyme-immunodot assay for AQP4-IgG for large-scale rapid use: a prospective multicentre diagnostic accuracy study
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Refer to O-1 in Plenary Oral Presentation - 1

P-5
Smartphone monitoring of cognition in people with multiple sclerosis: A systematic review
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Background: Current cognitive monitoring of people with multiple sclerosis (pwMS) is sporadic, resource intensive and insensitive for detection of real-world cognitive performance and decline. Smartphone applications may provide us with a more sensitive biomarker for cognitive decline that reflects real-world performance.
Objective: The goal of this study was to perform a systematic review and qualitative synthesis of all current smartphone apps monitoring cognition in pwMS.
Methods: A systematic search of five major online databases (PubMed/Medline, Scopus, Web of Science, Cumulative Index of Nursing and Allied Health Literature and IEEE Xplore) was performed in accordance with the Cochrane Handbook and Preferred Reporting Items for

Systematic Reviews and Meta-Analysis (PRISMA) statement. We included all studies with at least one measure of phone-based digital biomarkers for monitoring cognition in pwMS above the age of 18.
Two authors independently screened the articles retrieved. Data on test-retest reliability, validity coefficients, feasibility and practice effects were extracted from the studies identified. Critical appraisal of the studies was performed using the National Institute of Health quality assessment tool for observational cohort and cross-sectional studies.
Results: 12 articles covering six smartphone apps were included in this review. All articles had a low risk of bias, though sample size calculation was rarely performed. Of the six apps, five used smartphone versions of the symbol digit modalities test. The final app examined keystroke features passively.
Test-retest reliability ranged from good to excellent. Concurrent validity was demonstrated through moderate to strong correlation with neuropsychological tests. Construct validity was shown with weak to moderate correlations with EDSS, radiological biomarkers and patient-reported outcomes. Mobile apps performed comparably, and in some cases outperformed established cognitive tests. Whilst reported acceptability was high, significant attrition rates were present in longitudinal cohorts. There were significant short and long-term practice effects. Overall, smartphone versions of the symbol digit modalities test (SDMT) showed strong psychometric properties across multiple apps.
Conclusion: Smartphone applications are reliable and valid biomarkers of real-world cognition in pwMS. Further longitudinal data would allow for a better understanding of their predictive and ecological validity.
Disclosures: Yi Chao Foong has received conference travel support from Biogen.

POSTER SESSION - 2
Basic Science and Pathophysiology

P-6
Serum and CSF metabolomics detect clinically-silent neuroinflammatory lesions earlier than neurofilament-light in a focal delayed-type hypersensitivity multiple sclerosis rat model
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Background: There are currently no validated biofluid markers for the detection of subclinical neuroinflammation in multiple sclerosis (MS) although neurofilament-light (NfL) appears promising. The dynamic nature of metabolic changes, as measured by metabolomics, may allow early identification of clinically-silent neuroinflammation.
Objective: Using the delayed-type hypersensitivity (DTH) MS rat model, we investigated the serum and cerebrospinal fluid (CSF) metabolomics profiles and NfL levels arising from a focal, clinically-silent neuroinflammatory brain lesion.
Methods: Nuclear magnetic resonance (NMR) spectroscopy metabolomics and NfL measurements (Simoa® assay) were performed on serum and CSF at Days 12, 28 and 60 after DTH lesion initiation. Supervised multivariate analyses were used to determine metabolomics differences between DTH animals and controls. Rat brains were harvested, cryosectioned and stained for markers of neuroinflammation and neurodegeneration.
Results: Serum and CSF metabolomics perturbations were detectable in DTH animals at all time points – the greatest change occurred at the earliest time point (Day 12) when neuroinflammation was most intense (serum: mean accuracy [SD], 80.6 [10.7]% vs. 45.9 [20.6]%, p
Conclusion: While NfL levels were elevated late in the pathogenesis of the DTH lesion, serum and CSF metabolomics were able to detect early, clinically-silent neuroinflammation and should be explored as biomarkers for subclinical disease activity in patients.

P-7

Safety and Efficacy of Inebilizumab in AQP4+ NMOSD Participants with history of Immunosuppression Treatment prior to N-MOmentum Study

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Background: Inebilizumab, an anti-CD19 B cell-depleting antibody, is approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults seropositive for aquaporin-4 antibody (AQP4+). Immunosuppressants were prohibited during the N-MOmentum pivotal trial, although many participants had a history of immunosuppressant therapy before enrolment.
Objective: To evaluate long-term outcomes of inebilizumab treatment in AQP4+ NMOSD participants from the N-MOmentum trial with a history of immunosuppressant therapy as compared to those without.
Methods: N-Momentum (NCT02200770) was a 28-week randomized phase 2/3 trial of inebilizumab vs placebo, with an optional Open-Label Extension (OLE) (>2 years). Immunosuppressant medication for the prevention or treatment of NMOSD relapses was allowed prior to dosing on Day 1. In this post hoc analysis, AQP4+ participants who received inebilizumab (through the OLE) were grouped by no history of immunosuppression therapy beyond treatment of acute NMOSD attacks (naïve), or prior azathioprine (AZA) and/or mycophenolate mofetil (MMF) therapy. Outcomes compared for these two groups included annualized relapse and hospitalization rates, as well as safety assessments.
Results: Among participants who received inebilizumab during the study, 94 received prior AZA/MMF and 103 were immunosuppressant naïve. The total patient-years of inebilizumab treatment in the prior AZA/MMF group was 300.35 and for immunosuppressant naïve participants, 335.7. The annualized relapse rate (95% confidence interval [CI]) for participants with prior AZA/MMF was 0.11 (0.07, 0.17), compared to 0.08 (0.05, 0.14) for naïve. The annualized NMOSD-related inpatient hospitalization rate (annualized rate [95% CI]) for prior AZA/MMF was 0.15 (0.08, 0.27), and 0.12 (0.06, 0.22) for naïve. The percentage of participants with ≥1 study drug-related treatment-emergent adverse event (TEAE) was 30.9% (29/94) in prior AZA/MMF and 47.6% (49/103) of naïve; 4.3% (4) of prior AZA/MMF and 5.8% (6) of immunosuppressant-naïve reported ≥1 study drug-related serious adverse event. Most adverse events were infection-related for both groups; (72.3% (68/94) for prior AZA/MMF and 77.7% (80/94) for naïve).
Conclusion: This post hoc analysis evaluating long-term outcomes of inebilizumab in AQP4+ NMOSD participants treated with prior AZA/MMF therapy demonstrated a similar efficacy and safety profile as participants without prior immunosuppressant therapy.
Disclosures: F. Paul has received research support, speaker honoraria and travel reimbursement from Bayer, Biogen Idec, Merck Serono, Novartis, Sanofi Genzyme, and Teva; is supported by the German Research Council (DFG Exc 257) and the German Competence Network for Multiple Sclerosis; has received travel reimbursement from the Guthy-Jackson Charitable Foundation; and serves on the steering committee of the OCTIMS study, sponsored by Novartis.
R. Marignier reports personal fees for consulting from Alexion, Horizon Therapeutics, Roche, and UCB.
J.W. Lindsey reports personal compensation for speaking or consulting for Banner Life Sciences, Biogen, Celgene, EMD Serono, Genentech, Genzyme, Mapi Pharmaceuticals, and TG Therapeutics; is participating in clinical trials funded by Anokion, Atara, Biogen, EMD Serono, and Genen-

tech; and has received research funding from Genentech and the National MS Society.
H.J. Kim has received a grant from the National Research Foundation of Korea; consultancy/speaker fees or research support from Alexion, Aprilbio, Alto Biologics, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll BioPharma, Handok, Horizon Therapeutics, MDimune, Merck Serono, Mitsubishi Tanabe Pharma Corporation, Novartis, Roche, Sanofi Genzyme, Teva-Handok and UCB; serves on a steering committee for MedImmune/Horizon Therapeutics; and is a co-editor for the Multiple Sclerosis Journal and an associate editor for the Journal of Clinical Neurology.
D. She, D. Cimbora, and K. Patterson are employees and stockholders of Horizon.
B.A.C. Cree reports personal compensation for consulting from Alexion, Atara, Autobahn, Avotres, Biogen, EMD Serono, Gossamer Bio, Horizon, Neuron23, Novartis, Sanofi, TG Therapeutics, Therini and has received research support from Genentech.
Medical writing and funding were provided by A. Cohen and Horizon Therapeutics.

P-8

Glial immunity in patients with Wilson's disease

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Background: Wilson's disease (WD) is a classic hereditary disease in which abnormal copper metabolism is a predominant factor causing central nervous system (CNS) damage, though whether other factors besides copper toxicity contribute to neurodegeneration remains unknown. Growing evidence reveals that neuroinflammation is common in patients with WD.
Objective: In this study, we attempted to further reveal the glial-immune in the pathogenesis of WD.
Methods: A total of 117 WD patients were enrolled in this study. We performed Translocator protein 18 kDa (TSPO) PET imaging with radioligand [18F]DPA-714[N,N-diethyl-2-(2-(4-(2-[18F] fluoroethoxy)phenyl)-5,7-dimethylpyrazolo[1,5-a]pyrimidin-3-yl)acetamide] of 10 WD patients to track neuroinflammation in vivo. [18F]DPA-714 uptake was assessed by ROIs in the brain. The relationship between neuroinflammation and disease was demonstrated by analyzing the uptake of [18F]DPA-714. We investigated the novel autoantibody in WD patients by immunoprecipitation to primary neuronal cells, mass-spectrometry analysis, an antigen-binding assay on an antigen-overexpressing cell line, siRNA knockout cell lines and transgenic mice, and in vitro stimulation experiments. Extensive samples were collected to verify the autoantibody frequency.
Results: The results show that high uptake of [18F]DPA-714 in basal ganglia, brainstem, and cerebral cortex of WD patients. Compared with those in the stable WD group, significant regional elevations of [18F]-DPA-714 SUVmax in the basal ganglia in the progressive WD group. Meanwhile, we identified GFAP autoantibodies (GFAP-Abs) and GFAP antigen-specific B cells in WD patients. GFAP-Abs were identified in 11 enrolled WD patients (9.6%), and 25% of WD patients with epilepsy are GFAP-Abs positive.
Conclusion: We found that both glial innate immune and anti-glial autoimmune can be involved in the neurodegeneration of WD. These results could help interpret the mechanism of WD patients with neurological manifestations.

P-9

Complement Activation is associated with Relapse in MOGAD

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P-10

Persistent Expression of TNFR1 Ligands in the Meninges as a Cause of Neurodegeneration in MS Cortical Grey Matter

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Background: Meningeal immune cell infiltrates play an important role in cortical grey matter pathology in the MS brain via the release of pro-inflammatory cytokines that may cause underlying tissue damage. Tumour necrosis factor (TNF) and lymphotoxin-alpha (LTa) play key roles in lymphoid organ development and cellular cytotoxicity in the immune system.

Objective: Here we investigate how persistently increased levels of TNF or LTa in the cerebral meninges can give rise to lymphoid-like structures and underlying multiple sclerosis-like cortical pathology.

Methods: Stereotaxic injections of lentiviral vectors carrying the human TNF and LTa genes were performed into the midline subarachnoid meningeal space in adult Dark Agouti rats to produce chronic localised over-expression of the cytokine. The brain tissues were then analysed ex-vivo at varying time points up to 3 months post-injection, including gene and protein expression and immunohistochemistry.

Results: Injection of TNF and LTa vectors both induced extensive lymphoid-like immune cell aggregates, maintained over 3 months, including T-cell rich zones containing podoplanin+ fibroblastic reticular stromal cells and B-cell rich zones with a network of follicular dendritic cells, together with expression of lymphoid chemokines and their receptors. Extensive microglial and astroglial activation and marked progressive neuronal loss occurred in the underlying cortical parenchyma. Significant levels of subpial demyelination only occurred following prior sub-clinical immunisation against myelin oligodendrocyte glycoprotein, whereas neuronal loss was present irrespective of immunisation. Conditioned medium from LTa treated microglia was able to induce a reactive phenotype in astrocytes.

Conclusion: Our results show that chronic TNF or LTa overexpression alone is sufficient to induce formation of meningeal lymphoid-like structures and subsequent neurodegeneration, mimicking that seen in the progressive multiple sclerosis brain.

P-11

Extracellular Vesicles Released by Neutrophils Citrullinated Myelin to Accelerate Inflammatory Demyelination in Multiple Sclerosis

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Background: Being innate immune cells, neutrophils were underestimated players in multiple sclerosis (MS). Neutrophils have been detected in the cerebrospinal fluid (CSF) of MS patients at disease onset or the early stage of a relapse phase, and neutrophil-to-lymphocyte ratio (NLR) was higher in patients experiencing relapsing phase compared to remission.
Objective: To study the potential roles of neutrophils in the pathogenesis of MS and whether neutrophils could be a potential therapeutic target for MS.
Methods: Single cell RNA sequencing (scRNA) and flow cytometric analysis were performed to demonstrate dynamic changes and molecular pathways of neutrophils in MS and Experimental autoimmune encephalomyelitis (EAE). Cerebellar organotypic cultures were prepared to study how neutrophils affect myelination. Spinal cord stereotaxic injection was performed to study the drainage pathway of myelin antigen to lymph nodes. Bone marrow derived neutrophils were isolated to study the molecular pathway.
Results: ScRNA and flow cytometric analysis verified quick infiltration of neutrophils into central nervous system (CNS) as early as day 11 after immunization (onset) and peak at day 15-21 (peak). The infiltrated proinflammatory neutrophils caused subsequent inflammatory demyelination of EAE. Blocking of neutrophil infiltration contributed to alleviating physical disability. After stimulated with myelin debris, neutrophils released extracellular vesicle (EV) to citrullinate myelin protein. The citrullinated myelin obtained antigenicity and drained into lymph nodes to induce immune response. Contents analysis of EV indicated PADI4 as a functional molecule. Consistently, injection with PADI4 inhibitor helped to downregulate incidence rate of EAE model.
Conclusion: Neutrophils infiltrated into CNS in MS/EAE and released EVs containing PADI4 after stimulation of myelin debris. PADI4 in the EVs were able to citrullinate myelin protein which activate immune response and thus accelerating inflammatory demyelination.

P-12

The Anti-Inflammatory Effects of FLT3 inhibitor in Mice with Experimental Autoimmune Encephalomyelitis (EAE).

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Background: Multiple sclerosis (MS) is a T-lymphocyte-mediated autoimmune disease that is characterized by inflammation in the central nervous system (CNS). Although many disease-modifying therapies (DMTs) are presumed effective in patients with MS, studies on the efficacy and safety of DMTs for preventing MS relapse are limited.

Objective: FMS-like tyrosine kinase 3 (FLT3) signaling has been shown to indirectly expand T cells through increasing dendritic cell number. Therefore, it is plausible that inhibition of FLT3 signaling pathways may also decrease the T cell activation in autoimmune diseases. We hypothesized that FLT3 inhibitors would decrease the DC-induced stimulation of T cells, thereby inhibiting autoimmune responses in MS, and tested the anti-inflammatory effects of FLT3 inhibitor on MS with using mice model of experimental autoimmune encephalomyelitis (EAE).
Methods: The EAE mice were randomly assigned into three experimental groups: the phosphate-buffered saline (PBS)-treated EAE group and FLT3 inhibitor-treated EAE group. After EAE mice induction by auto-immunization against the myelin oligodendrocyte glycoprotein peptide, we evaluated EAE symptom scores and biochemical analyses such as infiltration of inflammatory cells and demyelination of the spinal cord. Furthermore, western blotting was performed using the spinal cords of EAE mice.
Results: In the behavioral study, the FLT3 inhibitor-treated EAE mice (12 mice with 30mg/kg and 12 mice with 60mg/kg) showed favorable clinical scores compared with PBS-treated EAE mice (12 mice) during the symptomatic periods of EAE mice. Additionally, the biochemical studies revealed that FLT3 inhibitor exhibited less inflammatory infiltration and demyelination, also weak immunoreactivity for all of the immunization biomarkers in the EAE mice.
Conclusion: This study suggests that FLT3 inhibitor has anti-inflammatory and neuroprotective effects in the EAE mice, so it could be a new promising therapeutic agent for MS.

P-13
Serum Neurofilament Light Chain Levels as a Biomarker of Disease Activity, Progression and Treatment Response in Patients with Multiple Sclerosis
Marzena Fabis-Pedrini[1], Belinda Kaskow[1], Stephanie Trend[1], William Carroll[1], Sue Walters[1], Aleksandra Maceski[2], Jens Kuhle[2], Allan Kermode[1]
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P-14
CD8+ T Cell Epitope Discovery from Immediate Post-mortem Multiple Sclerosis Lesions
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Background: The autoimmune inflammatory process in Multiple Sclerosis (MS) is mostly

trapped within the central nervous system. Access to precious tissue samples from post-mortem human brain allows us to conduct epitope discovery assays on the actual cells within a brain lesion to identify the target antigen(s) responsible for triggering autoreactive T cells.
Objective: In this study, we identify dominant T cell receptors (TCRs) and their cognate HLA-restricted antigens from CD8+ T cells present within white matter lesions and normal-appearing white matter (NAWM) isolated from immediate post-mortem MS brain tissue.
Methods: We performed single-cell TCR sequencing on CD8+ T cells isolated from immediate postmortem MS white matter lesions and NAWM (post-mortem index.
Results: Screening studies of three TCRs with pools of peptides identified TCR activity with TCR1 and B*15:01. Follow-up analysis using single peptides identified the peptide TTGAVRQIFGDYKTT, AA92-AA107 of Myelin proteolipid protein as triggering TCR1 when presented by B*15:01 (116 +/- 3.0 unstimulated vs 281+/- 18.03 stimulated, p
Conclusion: We have successfully established a TCR reporter assay to assess CD8+ T cell receptors and HLA class I interactions in the presence of MS-relevant peptides.

P-15
Antigen-Independent Production of IL-17A by Bystander Activated CD4+ T Cells in Multiple Sclerosis
So Yeon Kim[1], Yeseul Kim[1], Su-Hyun Kim[1], Sang-Min Han[1], Hyewon Park[1], Rosah May Payumo[1], Ha Eun Kim[1], Ki Hoon Kim[1], Eunjig Lee[2], Ho Jin Kim[1]
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Background: Multiple sclerosis (MS) is a demyelinating CNS disease that auto-antigen recognizing CD4+ T cells, however, recent studies revealed that antigen non-related bystander-activated T cells can trigger experimental autoimmune encephalomyelitis (EAE) by secreting effector cytokines. With discovery that IL-17A producing CD4+ T cells which were bystander-activated by proinflammatory cytokines (IL-1β and IL-23) contribute to the development of EAE, studies are required to determine the activity of bystander-activated CD4+ T cells in MS patients.
Objective: Investigate the difference in immunophenotypes and cytokine producing functions of bystander-activated CD4+ T cells between HC and MS patients.
Methods: In this study, 28 MS patients from the National Cancer Center (Male, n=13; Female, n=15. Mean age, 33±9 years) and 22 age- and sex-matched healthy controls (HC; Male, n=11; Female, n=10. Mean age, 30.3±6.8 years) were included. We examined the expression of IL-1R1 on CD4+ T cells and the frequency of IL-17A producing bystander-activated CD4+ T cells in MS compared to HC both in ex vivo and in vitro stimulation with IL-1β and IL-23 by flow cytometry.
Results: We found that IL-17A producing memory CD4+IL-1R1+ cells, known as bystander-activated CD4+ T cells, were increased in MS patients after in vitro stimulation with IL-1β and IL-23, while there was no difference in the frequency of ex vivo CD4+IL-1R1+ T cells in the periphery. Interestingly, this phenomenon was not observed in the presence of other immune

cells (in periphery blood mononuclear cell culture). Co-culture of CD56+ cells with CD4+ T cells decreased IL-17A producing memory CD4+IL-1R1+ T cells, suggesting that CD56+ cells may attenuate IL-17A production by bystander-activated T cells.
Conclusion: Our study implies that IL-17A producing bystander-activated CD4+ T cells have the potential to contribute to disease exacerbation of MS.
Disclosures: This study was supported by the Advanced Research Center Program of the National Research Foundation funded by the Ministry of Science & ICT (NRF 2018R1A5A2023127) and sponsored by Eisai Korea Inc. (TEC-IIS-M082-0001).

P-16
In Vitro Generation Of Disease-Specific Autoantibodies Produced By B Cells From Patients With Neuromyelitis Optica Spectrum Disorder And Myelin Oligodendrocyte Glycoprotein Antibody Associated Disease
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Background: The main pathogenic characteristic of neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein-associated disease (MOGAD) is the presence of autoantibodies against water channel aquaporin-4 (AQP4) and MOG, respectively. However, the underlying mechanisms in autoantibody production is largely unknown.
Objective: To establish a human culture system that could characterize the contribution of B cells in the production of serum autoantibodies against AQP4 and MOG, in NMOSD and MOGAD patients, respectively.
Methods: Unfractionated peripheral blood mononuclear cells were obtained from NMOSD (n=30) and MOGAD (n=10) patients. B cells were differentiated into plasmablasts (CD19+CD27+CD38++) in vitro with stimuli resembling the mechanism associated with NMOSD and MOGAD disease development. These include the T cell help, infections that were found to trigger these diseases, and cytokines involved in NMOSD and MOGAD. Stimulation conditions were as follows: soluble CD40L (sCD40L) only, sCD40L+ R848 (TLR7/8), sCD40L+ R848 with cytokines TNFa and IL-1B, and sCD40L+ R848 with TNFa, IL-1B, and IL-21. After 6 days of culture, a cell proliferation assay was performed and the frequency of the plasmablasts generated was determined. The culture supernatants after 13 days of culture were used to quantify total IgG levels and a live cell-based assay was used to determine the presence or absence of supernatant IgGs binding exclusively to AQP4- or MOG-expressing cells, indicating the presence of AQP4-IgG and MOG-IgG.
Results: The presence of R848, regardless of sCD40L or cytokines, resulted in proliferation of B cells in NMOSD (average: 78.2% ± 18.5) and MOGAD patients (average: 90.4% ± 5.2). In vitro generation of CD19+ CD27++CD38++ cells required sCD40L and R848 in patients with NMOSD (average: 45.6 ± 21.1) and MOGAD (average: 54.4% ± 11.5) and further culture until day 13 resulted in total IgG secretion by the plasmablasts generated from NMOSD (average: 18,150 ng/mL) and MOGAD (average: 17,959 ng/mL). For all the culture conditions that generated plasmablasts, AQP4-IgG and MOG-IgG were successfully generated and detected in the

culture supernatants in 10 of 30 NMOSD patients and 6 of 10 MOGAD patients, respectively. **Conclusion**: This in vitro model may be relevant in immunotherapy selection and feasibly applied to other antibody-mediated diseases.

P-17

Astroglial Connexin 43 is a Novel Therapeutic Target for a Chronic Multiple Sclerosis Model

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POSTER SESSION - 3

Comprehensive Clinical Care

P-18

Prevalence Of Vaccination And Its Effects On The Management Of Central Nervous System Demyelinating Diseases In Siriraj Hospital

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Background: Patients with CNS demyelinating diseases usually take at least one immunosuppressive agent or DMT. Their immunocompromise status makes them more susceptible to various infectious agents. Some infections could be prevented by vaccination. Yes, we hypothesized that our patients' vaccination prevalence would be lower than expected due to misconception.
Objective: We aimed to determine uptake of seasonal influenza vaccine and COVID-19 vaccine in our patients with central nervous system demyelinating diseases. Also, we aimed to determine lifetime uptake of other common vaccinations.
Methods: In May 2022, we surveyed patients in our CNS demyelination disease clinic at Siriraj hospital. The participating patients reported whether they had received hepatitis A, B, pneumococcal, meningococcal, MMR, Tetanus, Tdap, HIB, shingles, zoster or HPV vaccines in their lifetime. They also reported whether they had received seasonal influenza vaccine and COVID-19 vaccine. Among those who did not get the vaccines, we asked about the reasons. We summarized responses descriptively. Using multivariable logistic regression model, we are trying to evaluate participant characteristics associated with uptake of vaccines.
Results: Of 100 participants, 90% were female, with a mean (SD) age of 46.2 (12.9). Overall, all received compulsory vaccine coverage, including hepatitis B, measles-mumps-rubella, tetanus, and haemophilus influenzae B. For optional vaccines, the coverage was lower-than-expected, with rates of 3%, 4%, and 3% for human papilloma virus, pneumococcal, and zoster vaccination

coverage, respectively. Only 28% of participants received the 2021/2022 seasonal influenza vaccine. The only factor associated with the uptake of the influenza vaccination was the participants' health coverage. By asking seven questions to evaluate general vaccination knowledge, two questions related to vaccination and immuno-suppressive agents received the highest percentage of 'not sure' responses. Ninety-one percent of the participants received the COVID-19 vaccine and the ChAdOx1 nCoV-19 vaccine was the most injected COVID-19 vaccine among the participants.
Conclusion: Vaccination uptake is lower than desired in our clinic compared with existing recommendations, including for seasonal influenza.

P-19
Myelin Oligodendrocyte Glycoprotein-IgG Associated Disorder Presenting As A Relapsing-Remitting Brainstem Syndrome With Hearing Loss
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Background: Myelin oligodendrocyte glycoprotein-IgG associated disorder (MOGAD) is phenotypically heterogenous. Well-recognized clinical presentations include optic neuritis, acute disseminated encephalomyelitis or transverse myelitis. Isolated and predominant brainstem involvement is less commonly encountered in the spectrum of MOGAD.
Objective: We describe a patient with a relapsing-remitting brainstem syndrome and sensorineural hearing loss who was eventually diagnosed with MOGAD.
Methods: A 29-year-old female presented with vertigo, left-sided tongue and lip numbness, sensorineural hearing loss and tinnitus. Magnetic resonance imaging (MRI) studies revealed T2-hyperintense lesions in the left middle cerebellar peduncle and dorsolateral pons, with normal spinal cord findings. She was treated with a 5-day course of oral prednisolone. Despite initial improvement in symptoms, she developed a left facial nerve palsy a month later that was self-limiting.
Two months from her initial presentation, she developed recurrence and worsening of her previous symptoms. A repeat MRI brain revealed progression of her previous findings in the left superior and middle cerebellar peduncles and left pontomedullary region. No periventricular or juxtacortical brain lesion was observed. Cerebrospinal fluid (CSF) studies revealed lymphocytic pleocytosis (25 WBC, 90% lymphocytes) with normal protein count and absent oligoclonal bands. An infective screen, cytology and flow cytometry were unremarkable. Serum anti-aquaporin-4 antibody was negative.
Results: The patient was tested positive for serum MOG antibody (National University Hospital, Singapore, and Mayo Clinic, Rochester), with a titer of 1:20 (reference value)
Conclusion: The spectrum of MOGAD includes a recurrent, predominantly brainstem inflammatory manifestation and sensorineural hearing loss. MOG-IgG evaluation in CSF could strengthen the clinical-pathological relationship in patients with atypical presentations.
Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

P-20

A case of Susac syndrome treated with regular intravenous immunoglobulins

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Background: Wilson's disease (WD) is a classic hereditary disease in which abnormal copper metabolism is a predominant factor causing central nervous system (CNS) damage, though whether other factors besides copper toxicity contribute to neurodegeneration remains unknown. Growing evidence reveals that neuroinflammation is common in patients with WD.

Objective: In this study, we attempted to further reveal the glial-immune in the pathogenesis of WD.

Methods: A 32-year-old male with no past medical history visited our emergency department reporting transient aphasia and right facial numbness. Intermittent headache and blurry vision developed three months before his visit. His brain magnetic resonance imaging (MRI) showed multiple "snowball"-like T2 hyperintense lesions with gadolinium enhancement in his corpus callosum and periventricular white matters. Diffuse leptomeningeal enhancements were also observed. The cerebrospinal fluid (CSF) study showed elevated protein levels (171.6mg/dL) without pleocytosis. The initial clinical impression included multiple sclerosis due to the multiple periventricular lesions and the relapsing-remitting clinical pattern. Two weeks later, scotoma was developed, and the retinal fluorescein angiography revealed the branch retinal artery occlusion of his right eye. A month later, he developed vertigo and hearing impairment. Pure tone audiometry confirmed the sensorineural hearing loss. Finally, Susac syndrome was diagnosed.

Results: Due to the recurrence and progression of neurologic deterioration - including headache, hearing loss, disorientation, aphasia, and visual disturbance - within three months after diagnosis, he was treated aggressively with multiple immunotherapies: steroids including intravenous methylprednisolone (IVMP) and oral prednisolone (PL), intravenous immunoglobulin (IVIg), azathioprine (AZA), and cyclophosphamide (CPM). His neurologic symptoms were subsided immediately by IVMP, but using only steroids could not prevent relapse, even in a maintenance regimen. AZA and CPM were discontinued because of severe pancytopenia. At last, regular IVIg (1g/kg every month) successfully controlled his disease activity, and he completely recovered without any sequelae. His remission state has been sustained for a year.

Conclusion: Diagnosis and treatment of Susac syndrome are challenging. However, its pathognomonic clinical characteristics and radiographic findings might be a diagnostic key. Early and aggressive immunotherapy can prevent patients from irreversible organ damage.

P-21

CRANIAL NERVE INVOLVEMENT APART FROM OPTIC NERVE IN MOG ANTIBODY DISEASE: A CASE REPORT AND THE REVIEW OF LITERATURE

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Background: Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD) is a distinct central nervous system demyelinating disorder. Acute optic neuritis, acute disseminated encephalomyelitis, transverse myelitis, and cortical and brainstem encephalitis are commonly described clinical features. Cranial nerve involvement, apart from the optic nerve, is rarely.
Objective: We aimed to report a patient of MOGAD with cranial nerve involvement and review the literature.
Methods: We described the clinical and radiological features of a patient of MOGAD who developed cranial nerve involvement. We found four cases of cranial nerve involvement in MOGAD in a PubMed search. A chart review of all five cases (a total of eight attacks with cranial nerve involvement) was done, and the following parameters were studied: demographics, clinical syndrome, commonly involved nerves and radiologically isolated involvement.
Results: A 23-year-old female presented in 2022 with bilateral sensorineural deafness, ageusia, cerebellar dysarthria and ataxia of 2-week duration. Brain imaging showed T2/FLAIR brainstem hyperintensities with patchy enhancement. Alongside, there was an enhancement of the cisternal segments of bilateral VII-VIII and the cisternal segment of the right trigeminal nerve. She developed the index event in 2013 and later suffered six relapses. She was diagnosed with MOGAD in 2018. All attacks had brain stem involvement, out of which three showed clinical or radiological cranial nerve involvement. Chart review (5 cases/8 attacks): Mean age 43.6 years (range 16-76); M: F 1:4; Clinical presentation - Brain stem encephalitis (7/8); Commonly involved nerves - Clinical and radiological V, VII-VII; Radiologically isolated involvement – V, VII-VIII, III.
Conclusion: Cranial nerve involvement in MOGAD is rare but often seen in brain stem encephalitis. It can occur as a radiologically isolated entity.

P-22

Concomitant GABAB Receptor Antibody In A Case of Aquaporin-4 Seropositive Neuromyelitis Optica Spectrum Disorder.

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Background: Neuromyelitis optica spectrum disorder (NMOSD) can present with concomitant systemic autoimmune diseases such as Sjogren's syndrome, or coexisting anti-NMDAR encephalitis. To our knowledge, an association with gamma aminobutyric acid-b receptor antibody (GABABR-ab) has not been previously described.
Objective: We describe a case of Aquaporin-4 antibody (AQP4-ab) seropositive NMOSD with coexisting GABABR-ab.
Methods: Our patient first presented at age 15 years with fever, encephalopathy, bilateral visual loss and right hemiplegia. Magnetic resonance imaging (MRI) of the brain showed multiple white matter lesions involving the corpus callosum, midbrain, medulla, cerebellum and optic chiasm. Longitudinally extensive transverse myelitis of the cervical and thoracic regions were

seen on MRI spine. Cerebrospinal fluid (CSF) analysis revealed an inflammatory picture with pleocytosis and raised protein; oligoclonal bands were absent. She was treated with pulsed methylprednisolone, followed by oral prednisolone. AQP4-antibody seropositivity confirmed the diagnosis of NMOSD. One month later, she suffered a relapse with left hemiparesis. She was treated with steroids, intravenous immunoglobulin and cyclophosphamide, followed by mycophenolate mofetil.
She had no relapses until age 21, when she developed recurrent left optic neuritis and brainstem encephalitis. She was treated with pulsed methylprednisolone, plasmapheresis, and switched to intravenous rituximab. Five years later, she had new onset psychosis with affective features, manifesting as low mood, affective lability, agitation, behavioural changes, associated with Capgras and Fregoli delusions.
Results: In view of her neuropsychiatric symptoms, which were atypical in NMOSD, further workup was performed. Repeat MRI brain and whole spine did not show any new lesions. There was no ictal activity on electroencephalography. Serum for neural antibodies was sent for autoimmune encephalopathy analysis at the Mayo Clinic, which returned positive for GABA-B receptor antibody and negative for NMDA antibody. In view of this, a PET scan was performed, which showed no malignancy. She continued immunotherapy with intravenous rituximab, and her psychological symptoms stabilized with psychotropics.
Conclusion: Atypical clinical manifestations in NMOSD may prompt testing for other etiologies, including coexisting autoimmune encephalitis. Further studies should assess if coexisting antibodies contribute to more severe and frequent relapses of NMOSD.
Disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

P-23

Complementary and Alternative Medicine Use in Thai Patients with Idiopathic Inflammatory Demyelinating Diseases of Central Nervous System (CNS-IIDD)

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Background: Utilization of complementary and alternative medicines (CAMs) is common among patients with multiple sclerosis (MS). Vitamins, dietary supplements, herbal medicines, and relaxation practices are examples of CAMs often incorporated for physical and psychological support. Modalities of CAMs vary among different cultures and beliefs of each community.
Objective: To evaluate for prevalence and modalities of CAMs usage among patients with idiopathic inflammatory demyelinating diseases of central nervous system (CNS-IIDD) in a tertiary-care hospital in Bangkok, Thailand.
Methods: This is a cross-sectional, questionnaire-based study on CNS-IIDD patients at Siriraj

Hospital during June and December 2021. Patients with MS, neuromyelitis optica spectrum disorders (NMOSD), myelin oligodendrocyte glycoprotein-associated disease (MOGAD), optic neuritis (ON), and transverse myelitis (TM were included. Demographic data, diagnosis, duration of disease, disability status, comorbidities, current treatment, and details on CAMs use were collected. Descriptive data were expressed in frequency, percentage, mean, standard deviation. The study received approval from Siriraj Institutional Review Board.
Results: There were 107 patients. Diagnosis were MS (38), NMOSD (55), MOGAD (5), ON (2), and TM (7). Most patients were female (89.72%), and 61.68% were diagnosed for more than 5 years. The mean EDSS was 2.63 (SD, 2.38) and the median ambulation index was 0 (range 0-8.5). Patients with a history of CAMs use for at least 3 months was 63.55% while those with current use decreased to 58.49%. Vitamins and minerals are the most prevalent, with vitamin D (93.46%) and calcium (47.67%). Both treatments are mostly prescribed rather than self-administration. The main reasons for use CAMs are to strengthen their health (52%) and to relieve existing symptoms (30%).
Conclusion: This is the first study on CAMs use among Thai CNS-IIDD patients. It is a common practice. Understanding the patients' expectations and incorporating appropriate treatments should improve quality of life.

P-24
Two Cases of Neuromyelitis Optica Spectrum Disorder (NMOSD) With the Long-Term Natural History of About 30 Years Without Immunosuppressive Therapy
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Background: Recurrences of NMOSD are often severe and disabling. Aggressive immunosuppressive therapy is required to prevent recurrence. On the other hand, immunosuppressive therapy is long-term and may cause serious side effects. There are few reports on the long-term history of NMOSD without immunosuppressive therapy.
Objective: To clarify the long-term natural history of NMOSD without immunosuppressive therapy.
Methods: We studied two cases of NMOSD who were not given long-term immunosuppressive therapy because they were diagnosed with multiple sclerosis before 2000 when there was no medication in Japan.
Results: A 35 years-old woman developed brainstem encephalitis. She developed optic neuritis at the age of 42. She had a recurrence of optic neuritis at the age of 46. An asymptomatic brain lesion was revealed at the age of 54. She was diagnosed with NMOSD at the age of 56, because she was positive for anti-aquaporin 4 antibodies. She remained relapse-free for 7, 4, and 8 years without immunosuppressive therapy. A 41 years-old woman was misdiagnosed with cerebral infarction. She developed myelitis at the age of 48. She had a recurrence of myelitis at the age of 53. She had recurrent myelitis at the age of 63. She remained relapse-free for 7, 5, and 10 years without immunosuppressive therapy.

Conclusion: There are cases of NMOSD that do not relapse for years without immunosuppressive therapy. Long-term immunosuppressive therapy may cause serious side effects. Aggressive immunosuppressive therapy during relapse-free periods is controversial.

P-25

Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder developed in a Patient with Breast Cancer

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Background: Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory demyelinating disease of the central nervous system. NMOSD could be associated with other autoimmune diseases. In addition, some reports suggest that NMOSD could be one of the paraneoplastic syndromes, especially when it occurs in a relatively old age.
Objective: Herein, we report aquaporin-4 antibody-positive NMOSD that occurred in a patient with breast cancer.
Methods: A 68-year-old woman, who did not have any previous autoimmune disorders, came to the emergency room with a drowsy mentality and weakness in both lower extremities. She was diagnosed with right breast cancer (stage 1) 10 months ago and undergoing radiation therapy and chemotherapy. She had a 10-days history of intractable vomiting and a 7-days history of a painful sensation in her right arm and flank. At the time of admission, she was drowsy (Glasgow coma scale score: 12) and could not walk independently. Neurologic examination revealed the motor weakness of lower extremities (MRC grade 2) and positive pathologic reflex. Laboratory tests showed hypoosmolar hyponatremia, hypokalemia, and leukocytosis. The cerebrospinal fluid (CSF) study revealed leukocytosis (14/μL) with normal protein level. The cytology test revealed no malignant cells in CSF. Brain MRI showed multifocal T2 high signal intensity (HSI) lesions without enhancement in multiple territories. In addition, spine MRI revealed T2 HSI lesions with enhancement at multiple levels. Further laboratory tests showed that the serum aquaporin-4 antibody, which was tested by cell-based assay, was positive (3+).
Results: She was treated with steroid and antiviral agents since viral encephalitis was not excluded at the time of admission. After five days of treatment, her mental status improved. However, her weakness in both legs was not improved, so intravenous immunoglobulin (0.4g/kg/day) was administered for five consecutive days, and oral steroids were maintained. Her symptoms gradually improved, and she could walk with a walker after five months.
Conclusion: Paraneoplastic neurologic involvement is a rare condition. However, physicians need to consider not just metastasis but NMOSD in patients with cancer who presents neurologic deficits.

P-26

First Seizure And Normal Brain MRI - To Test Or Not To Test For MOG-IgG?

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Background: Unilateral cortical T2-Fluid attenuated inversion recovery (FLAIR)-hyperintense Le-

sions in Anti-Myelin Oligodendrocyte Glycoprotein (MOG)-associated Encephalitis with Seizures (FLAMES) or FLAIR-variable Unilateral Enhancement of the Leptomeninges (FUEL) have been described in patients with MOG antibody associated disease (MOGAD).
Objective:.We highlight two cases of MOGAD who presented initially with first seizure and normal brain magnetic resonance imaging (MRI), followed by development of optic neuritis with MOG-IgG seropositivity two to six weeks later.
Methods: A 21-year-old male (Mr. X) and 37-year-old male (Mr. Y) presented separately with first seizure (right upper and lower limb tonic-clonic seizure with secondary generalization). Their routine electroencephalography (EEG) and contrast-enhanced brain MRI were unremarkable. Both patients subsequently developed acute progressive painless right central scotoma and fever 2 to 6 weeks after their first seizure. Clinical examination of both patients revealed right relative afferent pupillary defect and ophthalmoscopically, optic disc oedema was visible. MRI of the anterior visual pathway (AVP) for Mr. X showed a short segment of enhancing T2 hyperintensity along the slightly thickened retrobulbar intraorbital right optic nerve. Mr. Y's AVP MRI demonstrated long segment enlargement, high T2 signal and amorphous thick enhancement involving the right optic nerve and optic nerve sheath complex, extending from the optic disc to the intracanalicur portion, associated with peri-optic fat stranding. Repeated brain MRI remained normal. Lumbar puncture demonstrated lymphocytic pleocytosis (440 and 1094 white blood cells/μL respectively) and hyperproteinnorrachia (0.74-0.78 g/L). Both received pulsed methylprednisolone and plasma exchange, followed by tapering doses of prednisolone. Serum studies for MOG-IgG returned positive for Mr. X and Mr. Y.
Results: Both patients made significant visual recovery, have had no recurrent seizure episode, or any other clinical relapse.
Conclusion: To facilitate timely diagnosis and treatment strategy, MOG-IgG testing may be considered early in young males who present with first seizure even in the presence of normal brain MRI.

P-27
Simultaneous Paraneoplastic And NMDAR antibodies In Occult Small Cell Cancer
Sarah Hasnor Binti Abu Hassan[1], Kok Pin Yong[1]
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Background: Paraneoplastic limbic encephalitis (PLE) is an immune mediated neurological syndrome caused by the remote effects of an underlying malignancy. It can manifest as memory dysfunction, behavioural issues and seizures. PLE can be the initial presentation of a variety of cancers, but is most frequently seen with small cell lung cancer.
Objective: We report a case of paraneoplastic limbic encephalitis in small cell cancer with co-occurrence of multiple paraneoplastic and N-methyl D-aspartate receptor (NMDAR) antibodies.
Methods: A previously well 73-year-old male presented with a 3-month history of progressive cognitive decline, behavioral issues, unsteady gait and diplopia. Contrast enhanced magnetic resonance imaging (MRI) of the brain was unremarkable. Electroencephalogram (EEG) recorded

periodic lateralized epileptiform discharges (PLEDs), seen independently over bilateral fronto-temporal regions, on background of severe diffuse encephalopathy. Cerebrospinal fluid (CSF) analysis demonstrated normal protein level and white cell counts as well as negative routine microbiological screen. NMDAR antibodies were detected in both CSF and serum, and anti-Hu, SOX1, Zic4 and Titin antibodies were detected in serum. Initial contrast enhanced computed tomography (CT) of the thorax, abdomen, and pelvis followed by fluorine-18-fluorodeoxyglucose-positron emission tomography-CT (FDG-PET-CT) were unremarkable. The patient did not have clinical features of a concomitant presynaptic or postsynaptic neuromuscular junction disorder despite the presence of anti-SOX1 and anti-Titin.
Results: The patient received intravenous immunoglobulin as well as pulsed methylprednisolone, followed by oral steroid taper. Antiepileptic medications were started in view of the detected PLEDs on EEG. There was marginal improvement in his cognition and functional status. A repeat FDG-PET-CT was performed 3 months after the initial scan and showed increase in size and FDG-avidity of the mediastinal lymph nodes. He underwent bronchoscopy with biopsy of mediastinal lymph nodes and histology confirmed metastatic small cell carcinoma. He was referred to medical oncology for treatment of the small cell cancer. However, the patient's cognition and behavior deteriorated further and due to his poor functional status, he was deemed unfit for chemotherapy or radiation therapy.
Conclusion: The presence of co-occurring multiple paraneoplastic and NMDAR antibodies may suggest further increased risk of malignancy. Our exemplary case emphasizes the need for prolonged repeated clinical and radiological surveillance for occult malignancy.

P-28
A case of very late-onset neuromyelitis optica spectrum disorder recurrent after discontinuation of disease-modifying therapy
Min A Lee [1], Jeong Bin Bong[1]
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Background: Neuromyelitis optica spectrum disorder (NMOSD) is an uncommon antibody-mediated disease of the central nervous system (CNS) with median onset around 40 years of age. NMOSD that begins between the ages of 50 and 70 is considered late-onset NMOSD, and those that begin after age 70 are considered very late-onset NMOSD. In very late-onset NMOSD patient
Objective: We report an elderly patient with very late-onset NMOSD who relapsed 4 months after discontinuation of disease-modifying therapy due to side effects and low compliance, and had a very poor prognosis despite active acute treatment.
Methods: A 80-year-old woman who was presented with progression of paraplegia and hypoesthesia over the course of 7 days. Neurological examination revealed muscle weakness of medical research council (MRC) grade 3/3 affecting the both lower limbs. Deep tendon reflexes were hyperactive in both lower limbs without pathological reflexes. There was loss of all sensation below T1 sensory dermatome. Longitudinally extensive transverse myelitis (T1 to T7) was seen in whole spine MRI. The cerebrospinal fluid (CSF) analysis showed negative findings for CNS infection and oligoclonal band was also negative. Her serologic test for anti-aquaporin 4 (AQP4) IgG was positive. She was diagnosed with NMOSD considering longitudinally extensive

transverse myelitis and positive for AQP4 antibody. We started steroid pulse therapy about 1g of methylprednisolone for 5 days followed by oral prednisolone 10mg daily and mycophenolate mofetil (MMF) for disease-modifying therapy. After 3 weeks of taking oral prednisolone and MMF, drugs were discontinued due to severe abdominal discomfort. And she did not want to take any other drugs.
Results: However, 4 months later, she was admitted with both extremities weakness. Neurological examination revealed muscle weakness of MRC grade 1/1 in both lower limbs and MRC grade 3/3 in both upper limbs. There was loss of all sensation below C4 sensory dermatome. The CSF analysis showed a cell count of 83/mL (60% mononuclear cells), normal glucose level, an increased protein concentration (251.4 mg/dL). Spinal MRI on T2WI revealed high signals extending from C4 to T9 in the central part of the cord. Compared with the previous spine MRI, the range of lesions was increased. She was diagnosed with NMOSD relapse and treated with high-dose steroid therapy followed by plasmapheresis. Her neurologic symptoms were not improved even after 5 cycles of plasmapheresis. After further deterioration with respiratory insufficiency and aspiration pneumonia, she was transferred to the intensive care unit for mechanical ventilation. Although antibiotics were administered, she expired on 25th day of admission.
Conclusion: Therefore, we suggest that disease-modifying therapy to prevent recurrence should be strongly recommended in patients with very late-onset NMOSD unless contraindicated.

P-29
Systemic lupus erythematosus presenting as acute transverse myelitis
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Background: Acute transverse myelitis (ATM) is an inflammatory disorder of the spinal cord associated with infectious or systemic autoimmune diseases, but its etiology remains unknown in some cases. Although myelopathy is relatively rare in systemic lupus erythematosus (SLE), ATM is the most common involvement of SLE-associated myelopathy.
Objective: We report a case of ATM as first manifestation of SLE.
Methods: A 43-year-old man with no underlying disease was admitted to the emergency department with voiding difficulty and decreased temperature sensation below his pelvis for 8 days. There was diffuse weakness of lower extremities (MRC grade 4) with sensory level at T10 on neurologic examination. And deep tendon reflexes were hypoactive in his lower extremities. His motor and sensory function of upper extremities was normal. Whole spine magnetic resonance imaging (MRI) showed abnormal intramedullary hyperintensity of cord at lower thoracic spine (T10-12) levels and the nerve conduction studies performed to rule out Guillain-Barre syndrome were normal. The cerebrospinal fluid(CSF) analysis showed lymphocytic pleocytosis (30/ul), increased protein (96mg/dL) and a normal CSF/serum glucose level. Results of CSF gram stain, viral polymerase chain reaction and fungus study for infectious causes were all negative. Initial serological test showed high titer (1:2560) of antinuclear antibody (ANA). In further evaluation, positivity for anti-ds DNA antibody (>200.0U/mL) and Anti-Sm antibody (55.8U/

mL), and decreased C3 (43.86mg/dL, normal range 65-135mg/dL), C4 (3.79mg/dL, normal range 13-35mg/dL) levels were found. A thorough examination of his past history revealed photosensitivity and alopecia for several months.
Results: Based on the clinical and laboratory findings, we made a clinical diagnosis of myelitis associated with SLE. He was treated with intravenous methyprednisolone (1g/day) for 5 days and changed to oral prednisone. A gradual improvement in paraparesis and hypesthesia at lower extremities, but urinary dysfunction were not improved after steroid treatment. So we performed 5 cycles of cyclophosphamide treatment (750mg per month) as the second-line treatment. After 1 year, he was still urinating with clean intermittent catheterization.
Conclusion: The ATM has an extensive differential diagnosis. So we emphasize that neurologists should be aware of SLE-related transverse myelitis, and that careful history taking and serologic tests should be performed.

POSTER SESSION - 4
COVID-19 and patients with MS or its related disorders

P-30
Myelin Oligodendrocyte Glycoprotein Associated Disorder presenting with longitudinally extensive transverse myelitis after BNT162b2-COVID-19 booster vaccination: a case report
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Background: After the pandemic spreading of COVID-19 infection, messenger ribonucleic acid (mRNA) or viral vector vaccinations against SARS-COV2 virus are used worldwide. Recent studies report various neurological complications after vaccination, including a new onset of central nervous system (CNS) demyelinating diseases.
Objective: MOGAD is a neurological disorder that show Myelin Oligodendrocyte Glycoprotein antibody positivity. Herein, we report a female patient diagnosed with MOGAD after mRNA based BNT162b2-COVID-19 vaccination.
Methods: A 52 years-old female visited emergency room complaining of progressing symptoms of voiding difficulty, leg weakness and paresthesia for two days. She had received a third dose of BNT162b2-COVID-19 vaccination (Pfizer) 16 days before symptom onset. She had no past medical history, including any neurologic disorder. Her neurologic examination showed a motor weakness MRC grade 3-4 in both legs with a sensory dermatome below T7. The patient showed positive Babinski and Hoffmann sign in both sides, and hyperreflexia in all limbs. Other cranial nerve examination revealed no abnormal findings. Her initial expanded disability status scale (EDSS) was assessed as 6.5. Spine MRI showed longitudinally extended (from T2 level to conus medullaris) high signal change on T2 weighted image without contrast enhancement. The cerebrospinal fluid study demonstrated pleocytosis and elevated protein levels. Routine laboratory tests and laboratory antibody tests of autoimmune disease and paraneoplastic syndrome were unremarkable. CSF laboratory tests for meningitis work up, including virus, bacteria, and fungus, were normal. Chest and abdomen computed

tomogram showed no abnormal findings. Anti-apuaporin4 (AQP4) antibody was negative, but anti-MOG antibody test was positive based on live cell assay.
Results: She was diagnosed as MOGAD presenting as LETM, and treated with high dose methylprednisolone therapy. In spite of intravenous steroid therapy, upper and lower limb weakness progressed, showing an increased EDSS score of 8.5. Follow up spine MRI showed an extended high signal on cervical spinal cord lesion with contrast enhancement. We proceeded with plasma exchange, but there was no improvement in her motor weakness. She was additional treatment with rituximab. After rituximab treatment, her neurological symptoms stabilized, and her motor weakness had been slowly improved with an improvement of EDSS of 2.5.
Conclusion: A severe LETM form of MOGAD can occur after BNT162b2-COVID-19 vaccination, and serial imaging can be helpful due to its higher possibility of progression. Lastly, a favorable outcome treating with rituximab can be achieved in these cases as well.

P-31
A Case of Neuromyelitis Optica Spectrum Disorder and Infectious Polyradiculitis after BNT161b2 Vaccination and SARS-CoV-2 Infection
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Background: Systemic complications following severe acute respiratory syndrome coronavirus (SARS-CoV-2) infection or vaccination for coronavirus disease 2019 (COVID-19) are well-known. Many cases showing single disease entity such as polyradiculitis or neuromyelitis optica spectrum disorder (NMOSD) after COVID-19 or its vaccination also were reported.
Objective: We reported the case manifested NMOSD and infectious polyradiculitis simultaneously after COVID-19 and vaccination**.**
Methods: A 37-year-old woman presented with paraparesis and paresthesia in both legs 19 and 3 days after BNT162b2 vaccination and SARS-CoV-2 infection, respectively. Cerebrospinal fluid (CSF) analysis, nerve conduction study, electromyography, magnetic resonance imaging and autoantibody tests were performed.
Results: Neurological examination showed hyperesthesia below the T7 level and markedly impaired bilateral leg weakness with absent deep tendon reflexes on the knees and ankles. CSF examination revealed polymorphonuclear dominant pleocytosis and elevated total protein levels. Enhancement of the pia mater in the lumbar spinal cord and positive sharp waves in the lumbar paraspinal muscles indicated infectious polyradiculitis. In contrast, a high signal intensity of intramedullary spinal cord on a T2-weighted image from C1 to conus medullaris and positive anti-aquaporin-4 antibody confirmed NMOSD. The patient received intravenous methylprednisolone, antiviral agents, and antibiotics, followed by a tapering dose of oral prednisolone and azathioprine. Two months after treatment, she was ambulatory without assistance.
Conclusion: The dual pathomechanism of NMOSD triggered by coronavirus disease 2019 (COVID-19) vaccination and polyradiculitis caused by SARS-CoV-2 infection may have caused atypical clinical findings in our patient.

P-32

AqP4 negative Neuromyelitis Optica Spectrum Disorder in a Healthy Female After Second Whole inactivated virus COVID-19 Vaccine

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Background: Neuromyelitis optica spectrum disorder is an autoimmune demyelinating disease with high relative prevalence in the East Asian population. Clinical manifestations include optic neuritis, longitudinally extensive transverse myelitis, area postrema syndrome, brainstem syndrome, and diencephalic syndromes.

Objective: -

Methods: A 19-year-old woman experienced visual disturbances, headaches, continous vomiting, and hiccup 2 days after receiving a whole inactivated virus COVID-19 vaccine. The patient then developed mild weakness of all four extremities with difficulty swallowing and pain radiating as if bound 2 weeks after initial symptoms. The patient is a Southeast Asian young adult, completely independent and functional at baseline. She presented with optic neuritis, area postrema syndrome, and brainstem syndrome. MRI of the head and cervical revealed demyelinating lesions on the optic nerve and medulla oblongata. Serum antibody testing revealed negative aquaporin-4 (AQP4) antibodies. The patient was diagnosed with AQP4 negative neuromyelitis optica spectrum disorder (NMOSD) and was treated with high-dose intravenous methylprednisolone and plasma exchange. The patient showed complete improvement. The patient is still being treated with azathioprine and low-dose steroids.

Results: -

Conclusion: This case report provides additional evidence that vaccination can induce NMOSD in some individuals. Administration of high-dose methylprednisolone and plasma exchange in AQP4 negative NMOSD cases triggered by COVID-19 vaccine showed optimal results.

Disclosures: There is no conflict of interest.

P-33

Risk Factors and Outcomes of COVID-19 in Patients with Neuromyelitis Optica Spectrum Disorders and Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

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Background: The bi-directional relationship between neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and COVID-19 warrants real-world data on the risks and outcomes of COVID-19 in these patients.

Objective: The aim of this study was to determine risk factors and outcomes of COVID-19 in NMOSD and MOGAD patients. A case of NMOSD relapse following COVID-19 and vaccination was also described, as one of the possible COVID-19 related outcome.

Methods: A retrospective review of NMOSD and MOGAD patients who received various types of immunotherapies in a tertiary care center in Thailand during the COVID-19 pandemic was performed. A comparison, using descriptive statistics and logistic regression models, between patients with and without COVID-19 was made to determine the risk factors.
Methods: A retrospective review of NMOSD and MOGAD patients who received various types of immunotherapies in a tertiary care center in Thailand during the COVID-19 pandemic was performed. A comparison, using descriptive statistics and logistic regression models, between patients with and without COVID-19 was made to determine the risk factors.
Results: Of the 175 NMOSD and 12 MOGAD patients in the clinic, 29 (15.5%) patients had COVID-19. The risk factors for COVID-19 were type 2 diabetes mellitus (T2DM) (OR 19.99, 95% CI 4.41-90.61), rituximab use (OR 3.71, 95% CI 1.37-10.03), and younger age (OR 0.94, 95% CI 0.90-0.98). Five patients (17.2%) had a severe-to-critical disease leading to death one. The more severe patients had comorbid T2DM, hypertension, dyslipidemia, and lymphopenia. One NMOSD patient had COVID-19 twice and had concurrent relapses with both infections, as well as after a booster vaccine.
Conclusion: The risk factors of COVID-19 in NMOSD and MOGAD patients were similar to the general population except for the additional risk from rituximab use. COVID-19 and vaccination could present with a CNS demyelinating disease relapse.

P-34
Longitudinal quantification of neutralising antibodies after SARS-CoV-2 mRNA vaccination in MS, NMOSD and other neuroimmunological diseases
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Background: Humoral responses after SARS-CoV-2 mRNA vaccination in Multiple Sclerosis (MS) patients on anti-CD20 therapies and fingolimod appear to be attenuated. However, neutralising antibodies (NAbs) against the receptor-binding domain of the spike protein are rarely measured and there is limited data in neuromyelitis optica disorder (NMOSD) patients.
Objective: To measure serum NAbs levels before and after the first (V1) and second (V2) SARS-CoV-2 mRNA vaccination in patients with neuroimmunological conditions on various immunotherapies, and, to identify the factors associated with poor humoral responses.
Methods: This was a prospective observational study performed at the National Neuroscience Institute, Singapore. Patients with MS (n=77), NMOSD (n=33), myelin oligodendrocyte glycoprotein-antibody associated disease (n=6), autoimmune encephalitis (n=3), other CNS inflammatory diseases (n=5), myasthenia gravis (n=9) and healthy controls (HCs, n=42) were recruited. No subjects had COVID-19 infection prior to V1, V2 and the sampling time points. NAbs were measured using the Genscript® cPass™ surrogate virus neutralisation test.

Results: No patients or HCs had detectable NAbs prior to V1. Two to 4 weeks after V1, patients on anti-CD20 therapies had lower NAbs levels (p=0.010) compared to HCs and untreated patients. Two to 6 weeks post V2, patients on disease-modifying anti-rheumatic drugs (DMARDs) (p=0.010),

fingolimod (p
Conclusion: Fingolimod and anti-CD20 therapies are associated with attenuated NAbs levels post-vaccination. Future studies are needed to determine whether this translates to an increased risk of COVID-19 infection.

P-35
Effects of COVID-19 vaccination on antibody responses in patients with immune-mediated neurological disorders and outcomes following infection
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Background: Patients with immune-mediated conditions are particularly vulnerable during this pandemic as they harbour increased risk of severe infection. It is unclear how well patients on immune-modulating or immunosuppressive medications respond to COVID-19 vaccination, and whether these protect them against severe infection.

Objective: This study aims to examine antibody responses in patients with immune-mediated neurological disorders compared with healthy controls. We also describe outcomes of patients who developed infection following vaccination.

Methods: We designed a case-control study to evaluate binding and non-binding antibody responses in patients with immune-mediated neurological diseases (IND) and compared these levels with age-matched healthy controls. Serum from all participants were assayed for anti-SARS-CoV-2 spike IgG (Roche, Mannheim) and total neutralizing antibodies to SARS-CoV-2 (cPass, GenScript) at different time-points over a 12-month interval: before vaccination (visit 1), a month after the first 2 doses (visit 2), before the third dose (visit 3), a month after the third dose (visit 4) and 6 months after the third dose (visit 5). We included patients with IND who received BNT162b or mRNA-1273 COVID vaccination as part of Singapore's national vaccination programme, but excluded those without IND and individuals infected prior to vaccination. Controls comprised age-matched healthy individuals with no known medical comorbidities. All participants provided written informed consent and statistical analyses were performed using IBM SPSS version 28.
Results: Forty-six patients with IND (17 MS, 12 NMO, 3 MOGAD, 9 MG and 5 others [autoimmune encephalitis with GFAP-IgG, LGI1-IgG, GABABR-IgG and CIDP]) and 65 controls were included. Median age was 41.5 years (21-74 years); 80% were female. 37 (80%) patients were on

treatment (4 interferon beta-1a, 3 cladribine, 2 fingolimod, 12 prednisolone, 4 azathioprine, 14 mycophenolate mofetil, 6 rituximab and the remaining on teriflunomide, alemtuzumab, cyclosporin and intravenous immunoglobulin, 1 each). Patients with IND had consistently lower anti-SARS-CoV-2 spike IgG and total neutralizing antibodies to SARS-CoV-2 compared with controls throughout the period of monitoring. Among those in the IND group, patients on rituximab and mycophenolate mofetil had significantly lower antibody responses following vaccination (all $p<0.05$).
Twenty IND patients developed SARS-CoV-2 infection. All had mild symptoms, 2 developed pneumonia, but none required oxygen supplementation.
Conclusion: Despite a significantly lower antibody response to COVID-19 vaccination, patients with IND develop mild symptoms following SARS-CoV-2 infection. Future studies should examine non-humoral contributions to SARS-CoV-2 immunity in patients with IND.

P-36
Central Nervous System Inflammatory Diseases after mRNA SARS-CoV-2 Vaccination
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Refer to O-5 in Plenary Oral Presentation - 1

P-37
COVID-19 Vaccination Induced Antibody Production in Immunosuppressed Patients with Autoimmune Neurological Disorders
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Background: In the Era of the COVID-19 pandemic, patients with immunosuppressants are of particular concern about lower efficacy of vaccination as well as higher risk of COVID-19 infection.
Objective:.This study is to compare the COVID-19 vaccination-induced antibody production in patients receiving immunosuppressing agent in neurological disorders with healthy controls.

Methods: Twenty-two patients (1 Optic Neuritis, 4 NMO, 10 Multiple sclerosis, 6 Myasthenia gravis and 1 Polymyositis) with neuroimmunological diseases and 58 healthy individuals were enrolled at the time of 3 months (21 patients, 42 healthy controls) or 6 months (1 patient, 16 healthy controls) after Covid-19 vaccination. The SGT anti-SARS-CoV-2 total antibody ELISA kit (Sugentech, Inc., Korea) was used to detect antibodies against nucleocapsid protein (NP) and spike protein S1 receptor-binding domain (RBD) of Covid-19 virus after vaccination. Antibody production was determined to be positive or negative based on the cut-off value of the optical density according to the manufacture's instruction.
Results: Anti-SARS-CoV-2 total antibody was negative in 3 out of 22 immunosuppressed patients (13.6%), but only 1 of 58 healthy controls at 6 months after Astra Zeneca vaccination showed borderline result (1.7%). At 3 months after vaccination, the results of all 42 healthy controls were positive. 2 NMO patients who received Rituximab within 2 weeks before or after second vaccination showed negative results while one patient who received Rituximab 4 weeks after vaccination showed positive result. A patient with MG on azathioprine was antibody negative at 3months after Astra Zeneca vaccination.
Conclusion: As in previous reports, the results of this study suggested that immunosuppressive treatment could reduce the efficacy of the Covid-19 vaccine.
Disclosures: This study was supported by a grant from the Korea Disease Control and Prevention Agency.

P-38
Central Nervous Demyelination Following COVID-19 Vaccination
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Background: COVID-19 vaccine has been deployed at an unprecedented rate as a response to the deadly COVID-19 pandemic. There have been emerging number of case reports of neurological complications associated with COVID-19 vaccination.
Objective: To describe the clinical spectrum of a cohort of patients who developed central nervous system (CNS) demyelinating disorder following exposure to COVID-19 vaccine.
Methods: We retrospectively identified patients who developed CNS demyelination within 60 days of COVID-19 vaccination from a neurology institute in Kuala Lumpur, Malaysia.
Results: We identified a total of 6 patients (4 females, 2 males) who developed CNS demyelinating events following COVID-19 vaccination. Mean age was 43.7 years. 2 patients received ChAdOx1-S, 2 received BNT162b2, while 2 other patients received CoronaVac COVID vaccine. 5 of 6 patients developed symptoms following the second dose of COVID vaccine. Mean interval between vaccination and onset of symptoms was 34.3 days. Spectrum of demyelination included 4 transverse myelitis, 1 acute disseminated encephalomyelitis, and 1 brainstem encephalitis. 5 of 6 patients presented with a demyelinating event for the first time. One patient had a background of neuromyelitis optica spectrum disorder which remained quiescent for many years on immunosuppression but presented with a relapse following COVID vaccina-

tion without other triggering factors. Only one of the patients fulfilled the diagnosis of multiple sclerosis at the time of presentation. All patients were treated with intravenous methylprednisolone.
Conclusion: There is a probable association between COVID-19 vaccine and CNS demyelination. Despite the temporal relationship, it is insufficient to prove a causal link. Further studies are required to ascertain this.
Disclosures: Chey Shin Yee, Shanthi Viswanathan and Hii Ding Wei have no disclosures.

POSTER SESSION - 5
Disease-modifying therapies

P-39
Treatment Management in Multiple Sclerosis and Psoriasis Coexistence
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Background: Multiple sclerosis (MS) is the most common immune-mediated demyelinating disease of the central nervous system.

Objective: Psoriasis is a chronic, immune-mediated, inflammatory disease. In order to give an idea about the treatment management in cases with these two immune-mediated diseases together, this case was deemed worthy to be presented.
Methods: The patient, who had been followed up for 17 years with the diagnosis of multiple sclerosis and was using interferon beta 1a treatment, was hospitalized with complaints of forgetfulness, balance disorder, drowsiness, and fatigue. It was learned that he was diagnosed with MS in 2004 with optic neuritis and left hemiparesis. The patient had a history of surgery due to psoriasis, hypertension, diabetes mellitus, asthma and cervical malignancy. There was also malignancy in the family history. In his neurological examination, the patient was conscious, oriented, and cooperative. Cranial nerve examination was normal. No loss of muscle strength was observed in the motor examination. Deep tendon reflexes were brisk. The plantar reflex was bilaterally flexor. Dysmetria, dysdiadocokinesia, and ataxia were not observed on cerebellar examination, but she had difficulty in tandem gait. Sensory examination revealed left hemihypoesthesia. EDSS was calculated as 2.5. Erythematous and scaly lesions were observed on the wrists, knees and bilateral dorsum of the feet of the patient, distal onycholysis and oil spots were observed on the toenails. The Psoriasis Area and Severity Index (PASI) value of the patient, who was evaluated by dermatology, was found to be 4.8.
Results: The patient was using methotrexate 15 mg/week and leflunomide 20 mg/day for the topical treatment of psoriasis lesions and for the treatment of psoriatic arthropathy. Laboratory examinations did not reveal any pathology other than iron deficiency anemia. On cranial and cervical magnetic resonance imaging (MRI), lesions consistent with demyelinating plaque were observed, but no contrast-enhancing active lesion was observed. Since the patient had a diagnosis of psoriasis accompanying MS, it was planned to switch to dimethyl fumarate (DMF) treatment. On the 5th day of dimethyl fumarate treatment, a significant regression was observed in the scaly lesions in the joints, PASI was calculated as 2.5, psoriatic arthritis com-

plaints regressed significantly. The patient, whose methotrexate treatment was discontinued by the rheumatology, was started on deltacortil 5 mg/day treatment.
Conclusion: Dimethyl fumarate is an effective treatment for psoriasis and MS. As in our case, monotherapy is an effective treatment option for individuals with two comorbid diseases.

P-40
Rituximab Therapy in the Treatment of Multiple Sclerosis: A Sri Lankan Experience
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Background: The availability of Disease Modifying therapies (DMTs) for Multiple Sclerosis remain limited in developing countries. While Interferon Beta-1a is the DMT of choice for patients with Relapsing Remitting Multiple Sclerosis (RRMS), Rituximab is increasingly being used for patients with a more aggressive disease course and in low-resource settings.
Objective: To highlight the option of Rituximab as a DMT for Multiple Sclerosis due to its efficacy, wide availability and relative low cost.
Methods: Five patients diagnosed with RRMS using the 2017 McDonald Criteria were selected for treatment with Rituximab at a dose of 500mg every 6-12 months. At the time, four patients were being treated with Interferon Beta-1a but had had a clinical relapse and/or new lesions seen on Magnetic Resonance Imaging (MRI) while on treatment. The remaining patient was treated with Rituximab at the first presentation due to the severity of clinical signs and the high lesion load on the MRI study, suggesting a more aggressive form of the disease.
Results: Rituximab infusions were well tolerated in all five patients. At 9 months post-treatment, all patients had not experienced any clinical relapses. The Expanded Disability Status Scale remained unchanged. Repeat MRI study of one patient showed a reduction in T2 signal intensities. Gadolinium enhancement of lesions couldn't be elicited due to the non-availability of MRI contrast at the time.
One patient suffered from an opportunistic fungal infection of the lung as a side effect of drug induced immunosuppression, 6-weeks post initial treatment. The patient responded to anti-fungal therapy and made a satisfactory recovery. No cases of severe SARS-CoV-2 infection were recorded.
Conclusion: Rituximab appears effective and safe in the treatment of MS in developing countries like Sri Lanka where affordability plays a crucial role in the choice of DMT for each patient.

P-41
PREVANZ A phase 2b Placebo Controlled Double Blind Dose Ranging Study of Vitamin D To Prevent Progression To Definite Multiple Sclerosis After a High Risk Clinically Isolated Syndrome.
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Background: Low vitamin D status as measured by serum 25(OH)D levels and low sunlight exposure are known environmental risk factors for the development of multiple sclerosis (MS). Add-on Vitamin D supplementation trials in established MS have been inconclusive. The effects of vitamin D supplementation to prevent MS development in high-risk clinically isolated
Objective: To determine if vitamin D supplementation in CIS patients with a positive MRI (at least 2 T2 brain and/or spinal cord lesions) delays time to either relapse or new MRI lesion development.
Methods: In this double-blind trial, eligible participants were randomised 1:1:1:1 to placebo, 1000, 5000, or 10000 IU of oral vitamin D3 daily within each study site (n=23) and followed for up to 48 weeks across academic MS centres in Australia & New Zealand. Between 2013 and 2020, we enrolled 204 participants. Brain MRI scans were performed at baseline, 24 and 48 weeks. Main outcome was conversion to clinically definite MS based on the 2010 McDonald criteria: new clinical event or new MRI T2 lesion. Two co-primary analyses were undertaken: 1. Outcome based on allocated dosage of vitamin D/placebo and 2. Outcome based on measured serum 25(OH)D levels during the study.
Results: In the intention-to-treat analysis based on assigned dose the ORs (95%CI) for conversion to definite MS were placebo 1.00 (reference), 1000 IU 0.94 (0.41, 2.19), 5000 IU 1.58 (0.67, 3.71) and 10000 IU 1.52 (0.64, 3.59). The as measured serum 25(OH)D analysis (co-primary outcome) was not associated with conversion. A fully adjusted model including latitude, site, smoking, age, sex, and baseline measures of: - baseline MS symptom number, presence of infratentorial lesions, and use of steroids produced ORs for conversion in the assigned dose analysis of placebo 1.00 (reference), 1000 IU 0.48 (0.18, 1.27), 5000 IU 2.49 (1.02, 6.08), and 10000 IU 1.10 (0.40, 3.04).
Conclusion: This double-blind placebo-controlled randomised study of vitamin D supplementation in high-risk CIS indicates that high dose vitamin D supplementation is not an effective treatment to prevent development of relapsing-remitting MS.
Disclosures: This study was fully funded by MS Australia, the authors have no other conflicts of interest

P-42

VISIONARY-MS Top-line Results: A Phase 2, Randomized, Double-Blind, Parallel Group, Placebo-controlled Study to Assess the Safety and Efficacy of CNM-Au8, a Catalytically Active Gold Nanocrystal Suspension in Relapsing Multiple Sclerosis

Michael Barnett[1], Heidi Beadnall[1], Alexander Klistorner[1], Robert Sergott[2], Benjamin Greenberg[3], Austin Rynders[4], Karen Ho[4], Jacob Evans[4], Jeremy Evans[4], Ryan McBride[5], Alan Hartford[4], Robert Glanzman[4], Michael Hotchkin[4]
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Refer to O-6 in Plenary Oral Presentation - 1

P-43
Five-Year Trend in Disease-Modifying Therapy Utilisation for Relapsing Multiple Sclerosis in Australia, 2017–22
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Background: In Australia, disease-modifying therapies (DMTs) for treating MS are government-funded under the Pharmaceutical Benefits Scheme (PBS). Any DMT can be selected for a patient who fulfils the PBS criteria for treatment of MS.
Objective: We aimed to characterise the patterns of DMT utilisation in Australia over the previous 5 years.
Methods: Drug utilisation was assessed for patients with relapsing MS on maintenance DMTs – platform injectables (beta-interferons, glatiramer), orals (teriflunomide, dimethyl fumarate, fingolimod, ozanimod), and high-efficacy injectables (natalizumab, daclizumab, ocrelizumab, ofatumumab). DMT utilisation was determined from monthly PBS dispensing statistics from July 2017 to June 2022. Patient numbers were estimated using World Health Organization Defined Daily Doses.
Results: At the start of the study period (July–September 2017) an estimated 13,862 patients were receiving maintenance DMTs. Fingolimod was the most widely used (36.7%), followed by natalizumab (18.3%) and beta-interferons (15.5%). By category, the utilisation was: platform injectables 21.9%, orals 59.2%, high-efficacy injectables 18.9%. By the end of the study period (March–June 2022) an estimated 17,964 patients were receiving maintenance DMTs. Ocrelizumab was the most widely used (31.6%), followed by fingolimod (20.4%) and natalizumab (15.8%). By category, the utilisation was: platform injectables 11.2%, orals 38.1%, high-efficacy injectables 50.7%. The changes observed were largely driven by declining use of beta-interferons and fingolimod, and increasing use of ocrelizumab over this period. The Covid-19 pandemic had no discernible impact on the utilisation of DMTs.
Conclusion: There is extensive utilisation of high-efficacy DMTs in Australia, which has increased over time. This is consistent with the known benefits of early high-efficacy treatment in improving outcomes in people with MS.

P-44
Efficacy of Rituximab in patients with CNS Inflammatory Demyelinating Diseases: a single institutional cohort in Singapore
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Refer to O-7 in Plenary Oral Presentation - 2

P-45

Safety and Effectiveness of Dimethyl Fumarate: an Interim Post-Marketing Surveillance Analysis of Prior DMT Subgroups

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Background: Dimethyl fumarate (DMF) has demonstrated a favourable benefit-risk profile in patients with multiple sclerosis (MS) in many studies. However, there is limited data on the non-efficacy switch to DMTs, such as data to address appropriate patient profiles and timing of switching, particularly from fingolimod (FTY) and natalizumab (NTZ) to DMF.

Objective: To investigate the safety and effectiveness of DMF in the patients with MS switched from FTY and NTZ, whose reason for switch was mainly non-efficacy, in clinical setting in Japan.

Methods: This interim analysis of post-marketing surveillance in Japan includes 1843 and 1829 DMF-treated patients in the safety and the effectiveness total population, as of March 2022, respectively. The total population, as well as subgroups stratified by prior DMT (particularly, FTY and NTZ) were analysed in this report. The estimated annual relapse rate (ARR), 95% confidence interval, and P value (Comparison of 1 year before and 1 year after the start of DMF treatment) are calculated using a negative binomial regression model.

Results: The baseline characteristics of the safety total population (n = 1843), patients switched from FTY (n=458) and NTZ (n=62) are: relapsing-remitting MS 91.3%, 84.2%, and 83.9%; no relapse 1 year before DMF initiation 50.1%, 71.6%, and 83.9%; mean EDSS 2.6, 2.8, and 2.7; reason for DMF use was (concerns about) insufficient safety/tolerability in 45.1%, 86.7%, and 87.1%, respectively. Major reason of DMF discontinuation (n=600, 216 and 28) was insufficient effectiveness/worsening of MS (12.2%, 24.0%, and 27.4%). We will report disease activity of the patients switched to DMF from FTY and NTZ stratified by age, ARR prior to DMF, baseline EDSS, washout period, and/or reason for DMF use.

Conclusion: This analysis addresses outcomes of DMF treated patients switched from FTY and NTZ. Since this is an interim report, conclusion will be made after the final analysis of the study.

Disclosures: This post-marketing surveillance is funded by Biogen.

Kazumasa Yokoyama: From Biogen Japan Ltd. and Chugai Pharmaceutical Co. Ltd. as speaker honoraria. From Ministry of Health, Labour and Welfare, Mitsubishi Tanabe Pharma Corp., Nihon

Pharmaceutical Co. Ltd., Ohara Pharmaceutical Co. Ltd., AbbVie Inc., Ono Pharmaceutical Co. Ltd. and Asahi Kasei Medical Co. Ltd. as research grant.
Hirofumi Ochi: From Novartis Pharma K.K., Mitsubishi Tanabe Pharma Corp., Chugai Pharmaceutical Co. Ltd., Biogen Japan Ltd., Takeda Pharmaceutical Co. Ltd., Alexion Pharmaceuticals Inc., Daiichi Sankyo Co. Ltd. and Nihon Pharmaceutical Co. Ltd. as speaker honoraria. From Ministry of Health, Labour and Welfare and Japan Society for the Promotion of Science as research grant.
Toshiyuki Fukazawa: From Bayer Yakuhin Ltd., Biogen Japan Ltd., Mitsubishi Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K. as consulting fees. From Biogen Japan Ltd., Mitsubishi Tanabe Pharma Corp., Takeda Pharmaceutical Co., Ltd., Novartis Pharma K.K., Chugai Pharmaceutical Co., Ltd., Kyorin Pharmaceutical Co. Ltd. and Daiichi Sankyo Co. Ltd.as speaker honoraria and/or support for travel.
Takashi Yamamura: From Biogen Japan Ltd. and Chugai Pharmaceutical Co. Ltd. as scientific advisory board. From Abbott Japan LLC, Astellas Pharma Inc., Bayer Yakuhin Ltd., Biogen Japan Ltd., Sumitomo Dainippon Pharma Co. Ltd., Eisai Co. Ltd., Mitsubishi Tanabe Pharma Corp., Nihon Pharmaceutical Co. Ltd., Novartis Pharma K.K, Santen Pharmaceutical Co. Ltd. as speaker honoraria. From Asahi Kasei Medical Co. Ltd, Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Corp., Ono Pharmaceutical Co. Ltd., Teva Takeda Pharma Ltd. Ministry of Health, Labour and Welfare and Japan Society for the Promotion of Science as research grant.
Ryusuke Sato, Haruki Makioka, Yayoi Sato, Aya Tsuchiya and Yumiko Tani are employees of Biogen Japan Ltd.

P-46

Long-Term Eculizumab in Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder: Relapse-Risk Reduction and Safety in PREVENT and its Completed Open-Label Extension

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Background: Eculizumab is well tolerated and significantly reduces relapse risk versus placebo in patients with aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD).
Objective: We report long-term relapse-risk-reduction efficacy and safety of eculizumab in AQP4+ NMOSD during PREVENT (NCT01892345) and its completed open-label extension (OLE; NCT02003144).
Methods: After receiving eculizumab or placebo during PREVENT, adults with AQP4+ NMOSD could enter the OLE (eculizumab maintenance dose, 1200 mg/2 weeks, with/without concomitant immunosuppressive therapy). Combined PREVENT and OLE (final data cut, 12 July 2021) data were analysed.
Results: During PREVENT and/or the OLE, 137 patients received eculizumab for a median (range) of 183.4 (0.1–342.0) weeks (3.5 years) and a total of 449.2 patient-years. The estimated proportion of adjudicated relapse-free patients at week 216 (4.1 years) was 92.9% (95% confidence interval [CI]: 85.9–96.5%). Nine patients experienced 10 adjudicated relapses (seven during the OLE, including one since the last interim analysis). The adjudicated annualized relapse rate was 0.022 (95% CI: 0.012–0.041). Rates of treatment-related adverse events and serious adverse events (SAEs)/100 patient-years were 165.3 and 7.0, respectively, versus 167.5 and 24.5 with placebo in PREVENT. The most common SAE was urinary tract infection (5.1% of patients). The serious infection rate was 10.5/100 patient-years, with no meningococcal infections. No patients died during the OLE.
Conclusion: The proportion of relapse-free patients remained high (92.9%) through 4.1 years' eculizumab treatment. Eculizumab was well tolerated with no new safety signals. These long-term data confirm eculizumab's sustained benefit/risk profile in AQP4+ NMOSD.
Disclosures: Funding statement: Research funding for this study was provided by Alexion, AstraZeneca Rare Disease. Medical writing support for this abstract was provided by Ana-Madalina Ion PhD of Oxford PharmaGenesis, Oxford, UK, and was funded by Alexion, AstraZeneca Rare Disease.
Author disclosures: K Fujihara has received personal fees and other support from AbbVie, Asahi Kasei Medical, Biogen, Chugai, Eisai, Merck Biopharma, Mitsubishi Tanabe Pharma, Novartis, Ono, Roche, Sumitomo Dainippon, Takeda, Teijin Pharma, UCB and Viela Bio (formerly MedImmune) and grants from the Ministry of Education, Science and Technology of Japan and the Ministry of Health, Welfare and Labour of Japan. A Berthele has received consulting and/or speaker fees from Alexion, Bayer Healthcare, Biogen, Celgene, Novartis, Roche and Sandoz/Hexal. His institution has received compensation for clinical trials from Alexion, Biogen, Merck, Novartis, Roche and Sanofi Genzyme. DM Wingerchuk has received grants from Alexion Pharmaceuticals, Inc. and personal fees from Biogen, Celgene, Genentech, MedImmune, Novartis, Reistone Biopharma, TG Therapeutics and Third Rock Ventures. J Palace has received support for scientific meetings and honoraria for advisory work from Alexion, AstraZeneca Rare Disease, Amplo, Argenx, Chugai, Janssen, MedImmune, Merck Serono, Mitsubishi, Novartis, Roche,

Sanofi and UCB, and grants from Alexion, Amplo Biotechnology, MedImmune, Roche and UCB. She holds patent ref P37347WO and licence agreement Numares multimarker MS diagnostics. She also holds shares in AstraZeneca and acknowledges partial funding by highly specialised services National Health Service England. M Levy has received research support from Alexion, Genentech and Horizon and consulting fees from Alexion, Genentech, Horizon, Sanofi and UCB. HJ Kim 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, AprilBio, Altos Biologics, 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; is a co-editor for the Multiple Sclerosis Journal and an associate editor for the Journal of Clinical Neurology. I Nakashima has received honoraria for serving on the scientific advisory board of Alexion, and for serving as speaker at a lecture meeting held by Alexion. C Oreja-Guevara 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. K-C Wang has nothing to disclose. S Shang is an employee of Alexion, AstraZeneca Rare Disease and a stockholder of AstraZeneca. M Yountz is an employee of Alexion, AstraZeneca Rare Disease and a stockholder of AstraZeneca. SJ Pittock has received personal compensation for serving as a consultant for Astellas, Genentech and Sage Therapeutics, and personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-La Roche AG, Genentech and UCB; his institution has received compensation for serving as a consultant for Alexion, Astellas and Viela Bio/MedImmune. He has received research support from Alexion, Roche/Genentech and Viela Bio/MedImmune. He has a patent, Patent# 8,889,102 (Application# 12-678350, Neuromyelitis optica autoantibodies as a marker for neoplasia), issued; another 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 patents for Kelch11, LUZP4, septin and MAP1b antibodies pending.

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Immune cell profiles as biomarkers in treatment of SPMS with Siponimod: towards precision medicine

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An Update on the Clinical use of Dimethyl Fumarate, Including as a Recently Licensed Therapy in China, Using a Modified Delphi Method: Interim Results

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Background: Dimethyl fumarate (DMF) is the most widely used oral disease-modifying multiple sclerosis (MS) therapy. There are extensive post-marketing data following approval in 2013 (USA). DMF was recently approved in China (2021), where the estimated MS prevalence is 2.39/100,000.

Objective: To evaluate evidence for DMF's current use in clinical practice and considerations relevant for its use in China.

Methods: An international Steering Committee (SC) of 14 expert MS clinicians/scientists participated. A structured literature review (DMF use as MS therapy; January 2011–February 2022) was followed by a modified DELPHI process for preparation of statements on DMF use in clinical practice, particularly in China. This process comprised ≥two voting rounds with thresholds for agreement of ≥80%, and disagreement of ≤10%, and two online SC meetings. Selected interim results are reported for: efficacy, safety, treatment sequencing, infections, haematology, effects on organ systems and DMF's impact on COVID-19 vaccination strategies.

Results: The following consensus statements were made. DMF is efficacious and early initiation is beneficial. DMF is suitable for treatment-naïve patients and those switching from another therapy; initiating DMF requires tolerability management strategies for gastrointestinal symptoms and flushing. Risk of severe opportunistic infections is very low with DMF. However, clinicians should monitor lymphocyte counts and discontinue therapy if Grade ≥3 and prolonged (≥6 months) lymphopenia occurs; it is a risk for progressive multifocal leukoencephalopathy (PML; very rare) . DMF may be a preferred treatment in patients with liver disease because of low hepatic toxicity; DMF does not increase risk of severe COVID-19 or interfere with vaccination. Limited Chinese patient data are an ongoing consideration; however, the statements remain applicable to both the global and Chinese populations.

Conclusion: DMF presents a positive efficacy and safety profile and is a valuable addition to target unmet MS treatment needs in China.

Disclosures: This Steering Committee initiative was sponsored by Biogen; writing and editorial assistance was funded by Biogen and provided by MIMS (Hong Kong) Limited.
Michael BARNETT: Dr Barnett has received institutional support for research or speaking from Alexion, Biogen, Merck, Roche, BMS and Sanofi Genzyme; is Research Director, Sydney Neuroimaging Analysis Centre; and Research Consultant, RxMx.
Andrew CHAN: Dr Chan has received speakers'/board honoraria from Actelion (Janssen/Johnson & Johnson), Alexion, Almirall, Bayer, Biogen, Bristol Myers Squibb (Celgene), Genzyme,

Merck KGaA (Darmstadt, Germany), Novartis, Roche, and Teva, all for hospital research funds.
Huiyu FENG: Beyond this project, Dr Feng has no further disclosures.
Kazuo FUJIHARA: Dr Fujihara serves as an advisor or on scientific advisory boards for Biogen, Mitsubishi Tanabe, Novartis, Chugai/Roche, Alexion, VielaBio/Horizon Therapeutics, UCB, Merck Biopharma, Japan Tobacco and AbbVie; has received funding for travel and speaker honoraria from Biogen, Eisai, Mitsubishi Tanabe, Novartis, Chugai, Roche, Alexion, VielaBio, Teijin, Asahi Kasei Medical, Merck, and Takeda; and has received the Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan and the Grants-in-Aid for Scientific Research from the Ministry of Health, Welfare and Labor of Japan.
Gavin GIOVANNONI: In the last 2 years, Dr Giovannoni has received compensation for serving as a consultant or speaker for, or has received research support from AbbVie, Aslan, Atara Bio, Biogen, BMS-Celgene, GlaxoSmithKline, Janssens/J&J, Japanese Tobacco, Jazz Pharmaceuticals, LifNano, Merck & Co, Merck KGaA/EMD Serono, Moderna, Novartis, Sanofi and Roche/Genentech. In the last 5 years GG has received grant support for research from Biogen, Merck KGaA/EMD Serono, Novartis, Sanofi, Roche/Genentech and Takeda.
Ralf GOLD: Dr Gold has received research support and speaker's honoraria from Bayer Schering, Biogen, Bristol Myers Squibb, Chugai, Eisai, Janssen, Merck Serono, Nikkiso Pharma, Novartis, Roche, Sanofi-Genzyme and TEVA, and consulting honoraria from ZLB Behring, Baxter, Merck, MIMS, and Talecris. He holds personal stock options in Bayer, Merck, Novartis and Roche.
Xavier MONTALBÁN: Dr Montalban has received speaking honoraria and travel expenses for participation in scientific meetings, has been a Steering Committee Member of clinical trials or participated in advisory boards of clinical trials in the past years with AbbVie, Actelion, Alexion, Biogen, Bristol Myers Squibb (Celgene), EMD Serono, Genzyme, Hoffmann-La Roche, Immunic Therapeutics, Janssen, MedDay, Merck, Mylan, Nervgen, Novartis, Sandoz, Sanofi-Genzyme, Teva Pharmaceuticals, TG Therapeutics, Excemed, Multiple Sclerosis International Federation and National Multiple Sclerosis Society .
Fu-Dong SHI: Beyond this project, Dr Shi has no further disclosures.
María TINTORÉ: Dr Tintore has received compensation for consulting services, speaking honoraria and research support from Almirall, Bayer Schering Pharma, Biogen-Idec, Genzyme, Janssen, Merck-Serono, Novartis, Roche, Sanofi-Aventis, Viela Bio and Teva Pharmaceuticals.
Qun XUE: Beyond this project, Dr Xue has no further disclosures.
Chunsheng YANG: Beyond this project, Dr Yang has no further disclosures.
Hongyu ZHOU: Beyond this project, Dr Zhou has no further disclosures.

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Oral cladribine modulates the transendothelial migration of leukocytes long after its direct effect on the immune system

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Background: Oral cladribine induces a long-term immunomodulatory effect well beyond direct drug immune system interactions. The trans-endothelial migration of lymphocytes across the blood-brain barrier (BBB) represents a critical step in MS pathogenesis. Although cladribine's inhibition of this step has been proposed,few studies have been performed
Objective: To determine if peripheral blood mononuclear cells (PBMC) of oral cladribine-treated people with MS (PwMS) have defective transendothelial migration using a well-established in vitro BBB model
Methods: We enrolled a subset of our oral cladribine treated patients in a prospective study to characterise its immunomodulatory effect using high dimensional mass cytometry, spectral flow cytometry and in a transmigration assay. PBMC were sequentially drawn prior to and at regular time-points after course 1 and course 2 of oral cladribine. In this study we focused on blood drawn 0, 4 (C4M) and 24 (C24M) months post cladribine treatment and from healthy controls (HC). PBMC were cryopreserved within 4 hours of the blood sampling and also used immediately in a well characterised model of the BBB, in which PBMC are allowed to migrate or not across collagen-coated polycarbonate filters on which activated human brain endothelial cells had been grown to confluence. After 14-18 hours, lower chamber migrated cells, top chamber unmigrated cells and a sample of unmanipulated PBMC were analysed using spectral flow cytometry. Results were presented as the logarithm of 2-fold change of the ratio of migrated to non-migrated cells. Within group statistical analysis was performed using a one sample nonparametric Wilcoxon signed-rank test with Pratt method, comparing the median of test groups to a hypothetical value of 0. To compare more than two groups, a Kruskal-Wallis nonparametric one-way ANOVA with a Dunn's multiple comparisons test was performed
Results: We have treated 58 people with MS (PwMS) with oral cladribine in our rural Australian practice 40% of whom were not previously on disease modifying therapy (DMT). 31.6% of patients are now in year 3 and 33.3% of PWMS are in year 4 after treatment. Only two patients have been switched to higher efficacy treatment because of treatment failure and two patients have been given a third course of oral cladribine. In our prospective immunological study we found that peripheral blood CD4+ TEM cells were significantly reduced in C4M compared to untreated PwMS (C0M) and CD8high TCM cells were significantly reduced in C4M compared to HC. Furthermore, CD8low TCM cells were significantly reduced in C4M compared to both HC and C0M. The migration of CD4+ effector memory T (TEM) and CD8+ central memory T (TCM) cells was reduced in cladribine-treated PwMS. CD28 expression was decreased on both CD4+ TEM and CD8+ TCM cells. These cells have likely reconstituted following cladribine treatment
Conclusion: Two courses of oral cladribine induced MRI and clinical stability in the majority

of our cladribine-treated PwMS. Not only are substantial phenotypic changes induced by this treatment, the drug induces prolonged effects on lymphocyte migration
Disclosures: This work is part funded by an ISS grant and an Educational grant from Merck.

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Safety and Effectiveness of Eculizumab in Japanese Patients with Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder (AQP4+ NMOSD): Interim Analysis of a Post-Marketing Surveillance Study
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Background: Eculizumab (ecu) is approved in Japan for the prevention of aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD) relapse and is undergoing mandatory post-marketing surveillance (PMS) of real-world use.
Objective: To assess the long-term safety and effectiveness of the terminal complement C5 inhibitor ecu in Japanese patients (pts) with AQP4+ NMOSD using PMS data.
Methods: This PMS interim analysis assessed the safety and effectiveness of ecu in Japanese pts with AQP4+ NMOSD from approval (November 2019) to interim data cut-off (April 2022).
Results: Of 147 ecu-treated pts, 71 consented and formed the safety set and 68 pts formed the effectiveness set (3 were excluded due to phase 3 PREVENT study participation). Twelve pts discontinued (physician decision, n=6; patient decision, n=5; adverse events [AEs], n=3; other, n=1). In the effectiveness set, 64/68 pts (94.1%) were female, mean (standard deviation [SD]) illness duration was 6.9 (6.3) years (range, 0.1–25.0 years) and mean (SD) age at ecu initiation was 50.6 (13.2) years (range, 19.0–84.0 years). In the 2 years before ecu, 51/68 pts (75%) had 1 relapse; 29/68 pts (42.6%) had ≥2 relapses. In the effectiveness set, relapse rate (RR) was 0.02/patient-year (PY) (1 relapse; 57 PY of treatment) vs a 0.74/PY RR in the 2 years before treatment (136.0 PY). In the safety set, 31 AEs and 18 serious AEs (SAEs) were observed in 19 and 11 pts, respectively; 16 AEs and 10 SAEs were deemed treatment-related. No meningococcal infections occurred; the safety profile was consistent with PREVENT.
Conclusion: In a real-world setting, ecu was effective in preventing relapses and was well tolerated in Japanese pts with AQP4+ NMOSD, consistent with its efficacy and safety profile in the global phase 3 PREVENT study.

Disclosures: Funding statement: Funding for this study was provided by Alexion Pharma GK. Medical writing support for this abstract was provided by Ana-Madalina Ion PhD of Oxford PharmaGenesis, Oxford, UK, and was funded by Alexion, AstraZeneca Rare Disease.
Author disclosures: J Nakahara has received personal fees from AbbVie, Alexion Pharma GK, Asahi Kasei Medical, Biogen, Bristol Myers Squibb, Chugai Pharmaceutical, CSL Behring, Daiichi Sankyo, Eisai, Kyorin, Mitsubishi Tanabe Pharma, Novartis, Otsuka, Roche, Takeda and Teijin Pharma; research scholarships from AbbVie, Boehringer Ingelheim, Chugai Pharmaceutical, Daiichi Sankyo, EA Pharma, Eisai, Japan Blood Products Organization, Mitsubishi Tanabe Pharma, Otsuka, Shionogi, Sumitomo Pharma, Teijin Pharma and Tsumura; and grants from Biogen, the Ministry of Education, Science and Technology of Japan and the Ministry of Health, Welfare and Labour of Japan. I Nakashima has received personal fees from Biogen Japan, Mitsubishi Tanabe Pharma, Novartis and Takeda, and grants from LSI Medience, the Ministry of Education, Science and Technology of Japan and the Ministry of Health, Welfare and Labour of Japan. H Yokote has received personal fees from Alexion Pharma GK, Biogen Japan, Chugai Pharmaceutical, Mitsubishi Tanabe Pharma and Novartis, and grants from the Ministry of Health, Welfare and Labour of Japan. Y Manabe, K Okamura and K Hasegawa are employees of, and hold stock in, Alexion Pharma GK, AstraZeneca Rare Disease. K Fujihara has received personal fees and other support from AbbVie, Asahi Kasei Medical, Biogen, Chugai Pharmaceutical, Eisai, Merck Biopharma, Mitsubishi Tanabe Pharma, Novartis, Ono, Roche, Sumitomo Dainippon, Takeda, Teijin Pharma, UCB and Viela Bio (formerly MedImmune) and grants from the Ministry of Education, Science and Technology of Japan and the Ministry of Health, Welfare and Labour of Japan.

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METEOROID: A Randomised, Double-Blind, Placebo-controlled, Multicentre Phase 3 Study of Satralizumab in Patients with Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD).

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Background: MOGAD is a rare, demyelinating, autoimmune disease of the central nervous system. Interleukin-6 (IL-6) may play a key role in MOGAD pathogenesis. Satralizumab, an antibody targeting the IL-6 receptor, reduced relapse risk with a favourable safety profile in two phase 3 trials in neuromyelitis optica spectrum disorder (NCT02028884/NCT02073279).

Objective: METEOROID (NCT05271409) is a randomised, double-blind (DB), placebo-controlled study evaluating the efficacy, safety, pharmacokinetics (PK) and pharmacodynamics (PD) of satralizumab ± background immunosuppressive therapy (IST) in patients with MOGAD.

Methods: METEOROID will enrol approximately 152 participants from 10 countries globally. Eligible participants are aged ≥12 years with a diagnosis of relapsing MOGAD (≥2 attacks in the last 24 months, consistent with optic neuritis, transverse myelitis, acute disseminated encephalomyelitis, or other brain, brainstem, or cerebellar syndrome compatible with demyelination), confirmed by MOG-IgG cell-based assay.

The study comprises an event-driven DB period, followed by an open-label extension (OLE) period. Patients will be randomized 1:1 to receive either satralizumab or placebo as monotherapy or in addition to background IST(s), administered subcutaneously at Weeks 0, 2, 4 and Q4W thereafter. Patients who continue to relapse despite ongoing treatment with azathioprine (AZA) or mycophenolate mofetil (MMF) may maintain a stable dose of AZA or MMF throughout. Patients receiving oral corticosteroids at screening may enter the trial, but steroids must be discontinued by Week 16. Patients can enter the OLE and receive satralizumab after completing the DB period or if they experience an adjudicated relapse during the DB period.

Results: The primary endpoint is time to first MOGAD relapse in the DB period, adjudicated by an independent committee. Key secondary endpoints are annualised relapse rate, annualised rate of active lesions on MRI of the neuroaxis, proportion of participants receiving rescue therapy, and the annualised rate of all inpatient hospitalisations.

To evaluate the safety of satralizumab, the frequency, seriousness, and severity of adverse events will be investigated, as well as changes from baseline in targeted ECG, vital signs, laboratory parameters, physical examination, and body weight.

Exploratory endpoints include changes in disability, quality of life, low contrast visual acuity, change in retinal layer thickness by optical coherence tomography, PK (satralizumab serum concentration at specified time points) and PD profile, and longitudinal biomarker assessments.

Conclusion: METEOROID is the first study of satralizumab in MOGAD, providing efficacy, safety, and PK/PD data for satralizumab (as monotherapy or in combination with IST) in adolescents and adults with relapsing MOGAD.

Disclosures: K. Fujihara: Received grants from Ministry of Education of Japan, Ministry of Health, Welfare and Labor of Japan; received personal fees from Roche/Chugai, Alexion, Viela Bio, Biogen, Eisai, Mitsubishi Tanabe, Novartis, Astellas, Takeda, UCB, Merck Biopharma, Abbvie and Asahi Kasei.

F. Paul: Served on advisory boards for Novartis, MedImmune and Viela Bio, has speaker

honoraria and travel grants from Bayer, Novartis, Biogen Idec, Teva, Sanofi-Aventis / Genzyme, Janssen, Merck Serono, Alexion, Chugai, MedImmune, Shire, Roche, Actelion, and Celgene. He serves as the academic editor for PLoS ONE and associate editor for Neurology, Neuroimmunology and Neuroinflammation. He has consultancies for SanofiGenzyme, BiogenIdec, MedImmune, Shire,and Alexion. He has Research support from from Bayer, Novartis, Biogen Idec, Teva, Sanofi-Aventis / Genzyme, Alexion and Merck Serono. Receives research support from German Research Council (DFG Exc 257), Werth Stiftung of the City of Cologne, German Ministry of Education and Research (BMBF Competence Network Multiple Sclerosis), Arthur Arnstein Stiftung Berlin, EU FP7 Framework Program (combims.eu) and Arthur Arnstein Foundation Berlin, Guthy Jackson Charitable Foundation, National Multiple Sclerosis Society of the USA.
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C. Hemingway: Received honoraria from Novartis and consulting fees from UCB, Novartis, Biogen, Roche and VielaBio.
I. Vodopivec, D. Stokmaier, and K. Weber: Employees of F. Hoffmann-La Roche Ltd.
M. Levy: Receives research support from: National Institutes of Health and has previously received research support from Genzyme, Alexion, Alnylam, and Shire. He also received personal compensation for consultation with Alexion, Acorda, Genentech/Roche, Horizon, Quest Diagnostics, UCB and Sanofi and he serves on the scientific advisory boards for Alexion, Horizon, Genentech/Roche.
This study is funded by F. Hoffmann-La Roche Ltd. Writing and editorial assistance was provided by Reece Bracewell, MBiolSci, and David Mayes, MChem, of ApotheCom, London.

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Efficacy Subgroup Analyses From the Phase 3 CHAMPION-NMOSD Trial in Adults With Anti-Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder.

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Background: CHAMPION-NMOSD (NCT04201262) is a phase 3 study of ravulizumab in adults with anti-aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder. Ravulizumab binds to the same complement component 5 epitope as eculizumab; however, its longer elimination half-life than eculizumab extends the dosing interval (every 8 vs 2 weeks).

Objective: The objective of this pre-specified analysis of the CHAMPION-NMOSD global, open-label, multicentre, phase 3, externally controlled study was to evaluate the efficacy of ravulizumab in clinically relevant patient subgroups.

Methods: Patients aged ≥18 years received a weight-based intravenous loading dose of ravulizumab (2400–3000 mg) on day 1) followed by maintenance doses (3000–3600 mg) on day 15 and once every 8 weeks thereafter. Concurrent placebo treatment was precluded owing to the availability of eculizumab and other treatments; thus, the placebo arm from PREVENT (NCT01892345) was used as an external comparator. Pre-specified efficacy subgroup analyses of time to first adjudicated on-trial relapse (the primary endpoint) were conducted and safety outcomes were analysed across subgroups.

Results: Of 58 ravulizumab-treated patients, at baseline, 30 were receiving monotherapy and 28 concomitant immunosuppressive therapy (IST): steroids (n=12), azathioprine (n=7), mycophenolate mofetil (n=6) or other (n=3). No ravulizumab-treated patient experienced a positively adjudicated on-trial relapse. Based on time to first adjudicated on-trial relapse, ravulizumab was superior to placebo in preventing on-trial relapse in monotherapy (hazard ratio [HR], 0.021; 95% confidence interval [CI]: 0–0.176; relapse risk reduction [RRR], 97.9%; p

Conclusion: T he robust treatment effect of ravulizumab on RRR was observed across all pre-specified subgroups, including ravulizumab monotherapy as well as concomitant IST use, age, sex and geographic region.

Disclosures: Funding statement:

The study was funded by Alexion, AstraZeneca Rare Disease. Medical writing support for this abstract was provided by Alan Storey PhD of Oxford PharmaGenesis, Oxford, UK, and was funded by Alexion, AstraZeneca Rare Disease.

Author disclosures:

M Barnett has received institutional support for research or speaking from Alexion, Biogen, Bristol Myers Squibb, Merck, Roche, and Sanofi Genzyme; is Research Director, Sydney Neuroimaging Analysis Centre and Research Consultant, RxMx. SJ Pittock has received personal compensation for serving as a consultant for Genentech, Sage Therapeutics and Astellas and personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffmann-La Roche AG, Genentech and UCB; his institution has received compensation for serving as a consultant for Astellas, Alexion and Viela Bio/MedImmune. He has received research support from Alexion, Viela Bio/MedImmune and Roche/Genentech. He has a patent, Patent# 8,889,102 (Application# 12-678350, Neuromyelitis optica autoantibodies as a marker for neoplasia), issued; another 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 patents for Kelch11, LUZP4, Septin and MAP1b antibodies pending. JL Bennett has received personal fees from AbbVie, Alexion, BeiGene, Clene Nanomedicine, Genentech and F. Hoffmann-La Roche Ltd, Mitsubishi Tanabe, Reistone Biopharma and Viela Bio and grants from Alexion, Mallinckrodt, the US National Institutes of Health and Novartis. He has a patent ‘Compositions and methods for the treatment of neuromyelitis optica’ – issued. A Berthele has received consulting and/or speaker fees from Alexion, Bayer Healthcare, Biogen, Celgene, Novartis, Roche and Sandoz/Hexal. His institution has received compensation for clinical trials from Alexion, Biogen, Mer-

ck, Novartis, Roche and Sanofi Genzyme. J de Sèze has served on the scientific advisory board and as a consultant for Alexion. M Levy has received research support from Alexion, Genentech and Horizon Therapeutics and consulting fees from Alexion, Genentech, Horizon Therapeutics, Sanofi and UCB. I Nakashima has received honoraria for serving on the scientific advisory board of Alexion, and by serving as speaker at a lecture meeting held by Alexion. C Oreja-Guevara 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. J Palace 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; and grants from Alexion, Amplo Biotechnology, MedImmune, Roche and UCB. She holds patent ref P37347WO and a licence agreement Numares multimarker MS diagnostics. She also holds shares in AstraZeneca and acknowledges partial funding by highly specialised services of National Health Service England. F Paul has received honoraria and research support from Alexion; 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, Roche and Parexel; received honoraria for lectures, presentations, speakers bureaus and support for attending meeting from Alexion, Bayer, Biogen, Celgene, the Guthy-Jackson Foundation, Merck Serono, Mitsubishi Tanabe, Novartis, Sanofi Genzyme, Roche, UCB and Viela Bio; served as an advisory board member for Celgene, Merck, Roche and UCB; and served as an editor for PLOS One and as an associate editor for Neurology Neuroimmunology & Neuroinflammation. C Pozzilli 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. K Allen, Y Mashhoon and M Yountz are employees of Alexion, AstraZeneca Rare Disease. HJ Kim 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-53

Sensitivity Analysis Using Propensity Score Methods for Primary Efficacy Outcome in the CHAMPION-NMOSD Trial

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Background: Eculizumab, a complement component 5 (C5) inhibitor, was approved to treat anti-aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD) following the PREVENT trial (NCT01892345). Ravulizumab also binds C5 but has a longer elimination half-life than eculizumab, allowing an extended dosing interval.
Objective: We report the results of pre-specified sensitivity analyses used to account for the external placebo comparator in the global, open-label, phase 3 CHAMPION-NMOSD trial (NCT04201262) in adults with AQP4+ NMOSD.
Methods: In the CHAMPION-NMOSD trial, ravulizumab reduced the risk of relapse by 98.6% vs the PREVENT placebo arm, the external comparator used. Propensity scores were used to account for potential differences in patient characteristics between the ravulizumab and PREVENT placebo groups and were estimated with a logistic regression using as predictors age at first dose, sex, region, use of immunosuppressive therapy (IST), baseline Expanded Disability Status Scale (EDSS) score and historical annualized relapse rate (ARR). Time to first adjudicated relapse and relapse risk reduction (RRR) were analysed using a stabilized inverse probability of treatment weighting (SIPTW) approach. A tipping point analysis (E-value) was used to assess how much unaccounted-for confounding would be needed to mitigate the treatment effect. The lowest E-value possible (E-value, 1) means no confounding is needed; the higher the E-value, the more confounding is needed to account for the treatment effect.
Results: Baseline characteristics in the ravulizumab group (n=58) and PREVENT placebo group (n=47), respectively, were as follows: mean age, 47.4 vs 45.0 years; female, 90% vs 89%; Americas, 36% vs 32%; Europe, 29% vs 40%; Asia-Pacific, 34% vs 28%; IST use, 48% vs 72%; median EDSS, 3.25 vs 4.00; median historical ARR, 1.4 vs 1.9. In CHAMPION-NMOSD, no adjudicated on-trial relapses occurred (median follow-up, 73.5 weeks) compared with 20 patients having a relapse in the PREVENT placebo group (median follow-up, 36.0 weeks); hazard

ratio (HR), 0.014 (95% confidence interval [CI]: 0.000–0.103); percentage reduction, 98.6% (CI: 89.7%–100.0%; p

Conclusion: The treatment effect of ravulizumab was not affected by differences in baseline characteristics between groups. High E-values indicate considerable unmeasured confounding would be needed to account for the ravulizumab RRR.

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meeting from Alexion, Bayer, Biogen, Celgene, the Guthy-Jackson Foundation, Merck Serono, Mitsubishi Tanabe, Novartis, Sanofi Genzyme, Roche, UCB and Viela Bio; served as an advisory board member for Celgene, Merck, Roche and UCB; and served as an editor for PLOS One and as an associate editor for Neurology Neuroimmunology & Neuroinflammation. C Pozzilli 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. Y Mashhoon and M Yountz are employees of Alexion, AstraZeneca Rare Disease. SJ Pittock has received personal compensation for serving as a consultant for Genentech, Sage Therapeutics and Astellas and personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffmann-La Roche AG, Genentech and UCB; his institution has received compensation for serving as a consultant for Astellas, Alexion and Viela Bio/MedImmune. He has received research support from Alexion, Viela Bio/MedImmune and Roche/Genentech. He has a patent, Patent# 8,889,102 (Application# 12-678350, Neuromyelitis optica autoantibodies as a marker for neoplasia), issued; another 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 patents for Kelch11, LUZP4, Septin and MAP1b antibodies pending.

P-54

B cells Deletion in HTLV-1-Associated Myelopathy

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Background: Human T-cell Lymphotropic Virus Type 1 (HTLV-1) is a retrovirus, resulting in HTLV-1-Associated Myelopathy/Tropical Spastic Paraplegia (HAM/TSP). HAM/TSP is a chronic neurodegenerative disease similar to multiple sclerosis (MS). Effect of B cells in this disease is still unknown.

Objective: To investigate the efficacy of B cell deletion in HAM

Methods: Peripheral blood mononuclear cells from HAM patients were collected and the proliferation of T cells was detected using CFSE after deleting B cells in vitro. Eligible participants received intravenous infusion of Rituximab at a dose of 375 mg/m2 body surface area, administered twice at baseline and 24-week follow-up period. The improvement of pyramidal or bowel-bladder function score in EDSS was looked on as the primary outcome. Secondary outcomes included the change of HTLV-I proviral load in PBMCs and CD4+ CADM1+ cell counts at 48 weeks post-therapy. Each follow-up visit required the collection of clinical data, neurological function assessment, HTLV-1 Proviral Load (PVL), and immune cell count measurements. In addition, the patients' proviral load and immune cell levels were measured by digital PCR and flow cytometry.

Results: The proliferation of T cells was suppressed after deleting B cells in vitro. The study met the primary endpoint, with a significant remission with Rituximab. During the 48weeks study period, 85.7% of 14 participants receiving Rituximab got remission. Improvement in bowel-blad-

der function was more noticeable than that in pyramidal function. In PBMCs, CD4+ CADM1+ cell count and the HTLV-1 proviral load both had a slight downward trend during 48 weeks of treatment. No severe adverse events occurred during the course of the study.
Conclusion: The initial significant clinical efficacy of rituximab treatment provides new ideas for the treatment of HAM, new clues to broaden the B-cell mechanism of CNS injury after HTLV-1 infection.

P-55
A Multi-Country Comparative Effectiveness Study of Dimethyl Fumarate and Non-Specific Immunosuppressants in a Real-World Setting: Evidence from MSBase
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Background: Non-specific immunosuppressants (NSIS) remain frequently used for the treatment of relapsing-remitting multiple sclerosis (RRMS) in many countries despite limited data on comparative efficacy.
Objective: This study investigated patient outcomes of dimethyl fumarate (DMF) versus NSIS in a real-world setting using the MSBase registry database.

Methods: We conducted a propensity score (PS) adjusted analysis of DMF and NSIS by using MSBase registry data. NSIS in this study included azathioprine, cyclosporine, methotrexate, mitoxantrone, mycophenolate mofetil, and cyclophosphamide. RRMS patients age >18 initiating DMF or NSIS as monotherapy after 2014 were included. To ensure sufficient exposure, each cohort had to be on therapy for at least 6 months. Major outcome variables were time to discontinuation, annualized relapse rate (ARR), time to disability progression and time to disability improvement.
Results: We identified 2707 patients in DMF cohort and 516 patients in NSIS cohort from more than 15 countries. Both cohorts were balanced after PS adjustment. PS weighted analysis shows that annualised relapse rate (ARR) for the DMF cohort was 0.14 [95% confidence interval (CI) 0.13-0.15] vs 0.15 [95% CI 0.13-0.17] for the NSIS cohort (p=0.29). For time to discontinuation, time to 24-week confirmed disability progression, and time to 24-week confirmed improvement, the hazard ratios (HR) were 0.75 [95% CI 0.64-0.89, p=0.001], 0.53 [95% CI 0.39-0.73, p
Conclusion: In this multi-country real-world study of DMF vs NSIS, ARR was comparable, but DMF treatment was associated with better results in time to discontinuation, time to disability progression, and time to confirmed improvement.
Disclosures: Supported by Biogen

P-56
Rituximab For Maintenance Of Remission In IgG4-related Pachymeningitis
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Background: IgG4-related disease (IgG4-RD) is recently recognized as one of the leading causes of hypertrophic pachymeningitis. There is currently no consensus about treatment for IgG4-RD but steroid is recommended as the first-line treatment.
Objective: We report a favorable response to rituximab and low-dose steroids in a patient with IgG4 -related pachymeningitis who was resistant to steroid monotherapy.
Methods: A 59-year-old female was admitted to our hospital following the onset of acute visual and auditory hallucinations. Two months before her admission, she had a throbbing headache. The pain persisted in the right frontal temporal area. Brain MRI revealed pachymeningeal thickening with enhancement in the right hemisphere. An examination of the CSF revealed elevation of the WBC count (80/μL, lymphocyte-dominant 90%) and protein (158 mg/dL). CSF glucose level was 48mg/dL, and serum glucose level was 88mg/dL. Viral PCR testing, AFB stain, and CSF cytology were not informative. Plasma IgG4 levels were normal (82.3mg/dL, reference range: 3.9–86.4 mg/dL). Anti-NMDAR antibodies and paraneoplastic antibodies (anti-Hu, anti-Yo, and anti-Ri) were negative. At first, with a possibility of autoimmune or tuberculosis or viral encephalitis, she was treated with intravenous methylprednisolone (IVMP, 1,000 mg/day for 5 days) with anti-viral and anti-tuberculosis agents.
Results: Treatment resulted in partial regression of neurologic symptoms. Two weeks later, a meningeal biopsy revealed storiform fibrosis, phlebitis, and numerous IgG4+ plasma cells

(>10) in a high-power field. Based on the clinical, radiological, and pathological findings, the patient was diagnosed with IgG4-RD. Oral prednisolone (60mg) after IVMP was introduced and reduced by 5mg every week. However, her headaches worsened 1 month later. IV Rituximab (375 mg/m2) weekly for four doses was started with a low dose of prednisolone (10mg). Six months later, clinical and radiologic improvement was observed with complete regression of headaches.
Conclusion: A histopathologic study is essential for diagnosing IgG4-RD and ruling out mimickers as the normal range of IgG4 serum levels does not rule out IgG4-RD. Rituximab may be a treatment option in patients with IgG4-related pachymeningitis.

P-57
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
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Background: CHAMPION-NMOSD (NCT04201262) is a global, open-label, phase 3 study of

ravulizumab in adults with anti-aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD). Ravulizumab binds the same complement component 5 epitope as eculizumab, but its longer elimination half-life enables an extended dosing interval (8 vs 2 weeks).

Objective: We report the efficacy and safety profiles of ravulizumab in adults with AQP4+ NMOSD.

Methods: Patients aged ≥18 years received a weight-based intravenous loading dose of ravulizumab (2400–3000 mg) on day 1, then weight-based maintenance doses (3000–3600 mg) on day 15 and once every 8 weeks thereafter. Concurrent placebo treatment was precluded owing to the availability of eculizumab and other treatments; thus, the placebo arm from PREVENT (NCT01892345) was used as an external comparator. The primary endpoint was time to first adjudicated on-trial relapse and relapse risk reduction (RRR). Key secondary efficacy endpoints included adjudicated on-trial annualized relapse rate (ARR) and clinically important worsening from baseline in Hauser Ambulation Index (HAI) score.

Results: Median (range) follow-up was 73.5 (11.0–117.7) weeks for ravulizumab (n=58). The study met its primary endpoint; there were no patients with adjudicated relapses in the ravulizumab arm vs 20 patients in the placebo arm (RRR, 98.6%; p

Conclusion: In patients with AQP4+ NMOSD, ravulizumab significantly lowered risk of relapse and HAI worsening compared with placebo and was well tolerated, with a safety profile consistent with that of eculizumab and ravulizumab in other indications.

Disclosures: Funding statement: This study was funded by Alexion, AstraZeneca Rare Disease. Medical writing support for this abstract was provided by Ana-Madalina Ion PhD of Oxford PharmaGenesis, Oxford, UK, and was funded by Alexion, AstraZeneca Rare Disease.
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P-58

Changes in treatment to prevent relapse of NMOSD with the emergence of biologics in Japan

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Background: Since December 2019, a series of biologics have been launched in Japan as relapse prevention for neuromyelitis optica spectrum disorders (NMOSD), with an increasing number of cases introduced. Biologics are effective in cases that cannot be controlled with previous drugs, and they are expected to greatly improve the prognosis of NMOSD.

Objective: In this report, we present the transition of relapse prevention treatment for NMOSD before and after the launch of biologics and discuss future prospects and challenges.

Methods: Patients with NMOSD with a history of attending our hospital were retrospectively sur-

veyed for medical information from their medical charts before (2018-2019) and after (2020-2021) the launch of the biologics. The diagnosis of NMOSD was made using the "International Panel for the Diagnosis of NMOSD". This study was approved by the ethics committee of our university.
Results: Prior to the launch of biologics (2018-2019), there were 18 NMOSD patients (14 women, 4 men) with a mean age of 58.3 years, mean disease duration of 7.7 years, mean EDSS 4.8, and mean number of relapses per year 0.4. The preventive treatment for relapse was oral steroids (PSL) in 13 patients (72.2%, mean dose 10.7 mg/day) and immunosuppressive drugs in 11 patients (61.1%).
After market launch of biologics (2020-2021), there were 27 NMOSD patients (21 women and 6 men) with a mean age of 54.9 years, mean disease duration of 6.8 years, mean EDSS of 4.2, and mean number of relapses per year of 0.3. The preventive treatment for recurrence was PSL in 23 patients (85.2%, mean dose 9.1 mg/day), immunosuppressive drugs in 12 patients (44.4%), and biological agents in 7 patients (25.9%).
Conclusion: Biologics were accompanied by a decrease in PSL dosage and immunosuppressive drug use; EDSS and annual recurrence rates also tended to decrease, suggesting that biologics improve prognosis.
Disclosures: Speaker honoraria: Alexion and Chugai Pharmaceutical

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Efficacy of Early Ofatumumab versus Late-Switch from Teriflunomide: Subgroup Analysis of the ALITHIOS Open-Label Extension Study by Prior Disease Modifying Therapy Exposure and Age
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Background: Ofatumumab (OMB), reduced annualized relapse rate (ARR) and MRI lesion activity, and delayed disability worsening vs teriflunomide (TER) in relapsing multiple sclerosis patients in the Phase 3 ASCLEPIOS I/II trials. Patients entering the ALITHIOS open-label extension study

continued OMB or switched from TER to OMB.
Objective: To compare clinical and MRI outcomes in patients initiating OMB in ASCLEPIOS (core) vs switching from TER to OMB in ALITHIOS (extension), according to the number of prior DMTs and age.
Methods: Cumulative clinical and MRI outcomes from ASCLEPIOS and ALITHIOS (ARR, time to 3- or 6-month-confirmed disability worsening [3/6mCDW],number of gadolinium enhancing [Gd+] T1 lesions, and annualized T2 lesion rate) were analysed in patients who received OMB during the core and extension (OMB- OMB) and patients who switched from TER to OMB in the extension (TER-OMB) according to number of DMTs prior to enrolment in ASCLEPIOS I/II (0,1, 2, >2, any) and age at baseline (≤40, >40).
Results: Of the 1882 patients randomized in the core, 946/936 received OMB/TER and 690/677 continued/were switched to OMB in the extension. Switching from TER to OMB in the extension significantly reduced the ARR by 68.3–76.6%; continuing OMB in the extension further reduced ARR by 39.9–65.1%. Within the prior DMT subgroups, the lowest mean ARR was achieved in patients in the OMB-OMB group with ≤1 DMT (0.046–0.049). Switching to, or continuing OMB was associated with a consistent numerical reduction in the risk of 3/6mCDW with the greatest benefit observed in patients on continuous OMB with ≤1 DMT or ≤40 years old. The almost complete suppression of T1 Gd+ activity and new/enlarging T2lesions (though delayed) seen in those randomised to OMB in the core was mirrored in the TER-OMB groups in the extension (90.00–100% across all prior DMT and age subgroups) and sustained in the OMB-OMB group. Incidence of adverse events was consistent with the ASCLEPIOS I/II studies.
Conclusion: Switching from TER to OMB reduced clinical and MRI disease activity across all prior DMT and age subgroups. However, younger patients and those treated with ≤1 DMT at baseline appear to experience the greatest benefit.
Disclosures: Funding: This study was funded by Novartis Pharma AG (Basel, Switzerland).
Jeffrey A. Cohen received personal compensation for consulting for Biogen, Bristol-Myers Squibb, Convelo, Genentech, Janssen, NervGen, Novartis, and PSI; speaking for H3 Communications; and serving as an Editor of Multiple Sclerosis Journal.
Ralf Gold has received compensation for serving as a consultant or speaker from Bayer HealthCare, Biogen Idec, Merck Serono, Novartis and Teva Neuroscience. He, or the institution he works for, has received research support from Bayer HealthCare, Biogen Idec, Merck Serono, Novartis and Teva Neuroscience. He has also received honoraria as a Journal Editor from SAGE and Thieme Verlag.
Jérôme de Seze received personal compensation from Alexion, Allergan, Almirall, Bayer, Biogen, Chugai, CSL Behring, F. Hoffmann-La Roche Ltd., Genzyme, LFB, Merck, Novartis and Teva.
Derrick Robertson has received fees for consulting, contracted research and speaker's bureau from Biogen, Celgene, EMD Serono, Genentech, Sanofi Genzyme, Janssen, TG therapeutics, Mallinckrodt; consulting fees and speakers bureau for Bristol Myers Squibb, Horizon, and Alexion; consulting fees and contracted research for Novartis; consulting fees for Greenwich biosciences; contracted research for GW Pharmaceuticals, PCORI, Atara Biotherapeutics, CorEvitas, MedDay Pharmaceuticals, PRIME CME, and Actelion.
Heinz Wiendl has received honoraria for acting as a member of scientific advisory boards for

Biogen, Evgen, Genzyme, MedDay Pharmaceuticals, Merck Serono, Novartis, Roche Pharma AG, and Sanofi-Aventis, as well as speaker honoraria and travel support from Alexion, Biogen, Cognomed, F. Hoffmann-La Roche Ltd., Gemeinnützige Hertie-Stiftung, Merck Serono, Novartis, Roche Pharma AG, Genzyme, Teva, and WebMD Global. Heinz Wiendl is acting as a paid consultant for AbbVie, Actelion, Biogen, IGES, Johnson & Johnson, Novartis, Roche, Sanofi-Aventis, and the Swiss Multiple Sclerosis Society. His research is funded by the German Ministry for Education and Research (BMBF), Deutsche Forschungsgemeinschaft (DFG), Else Kröner Fresenius Foundation, Fresenius Foundation, the European Union, Hertie Foundation, NRW Ministry of Education and Research, Interdisciplinary Center for Clinical Studies (IZKF) Muenster and RE Children's Foundation, Biogen, GlaxoSmithKline GmbH, Roche Pharma AG, and Sanofi-Genzyme.
Sibyl Wray received consulting fees from and advisory boards for Biogen, Celgene, and EMO Serano; speaker bureaus for Biogen, Celgene, EMO Serano, Genentech-Roche, and Sanofi-Genzyme; research support from Biogen, Celgene, EMO Sereno, Genentech-Roche, Novartis, Receptos, Sanofi- Genzyme, and TG Therapeutics.
Francesco Saccà served on advisory boards for Almirall, Argenx, Avexis, Biogen, Forward Pharma, Merck, Novartis, Pomona, Roche, Sanofi, Alexion, and Takeda. He received public speaking or travel honoraria from Biogen, Mylan, Novartis, Roche, Sanofi, and Teva. He received honoraria from Almirall, Novartis, and Sanofi for educational editorial work. He received consultancy fees from Argenx, Forward Pharma, Novartis, and Novatek.
Maggie Lieu is an employee of Novartis Pharmaceuticals Australia.

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Longer-term safety and efficacy of ofatumumab in recently diagnosed and treatment naïve patients is consistent with the overall population in the ALITHIOS open-label extension study

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Background: Ofatumumab (OMB) showed superior efficacy and similar safety vs teriflunomide in the Phase 3 ASCLEPIOS I/II trials in patients with relapsing MS (RMS) and a subgroup of patients recently diagnosed (≤3 years) and treatment-naïve (RDTN). In the open-label extension study, OMB showed well-tolerated safety and longer-term efficacy up to 4 years.
Objective: To assess the longer-term safety and efficacy of OMB for up to 4 years (data cut-off: 25-Sep-2021) in a subgroup of RDTN RMS patients.
Methods: Efficacy outcomes (annualized relapse rate (ARR), time-to-3/6-month confirmed disability worsening [3m/6mCDW], number of Gd+T1 lesions, annualized T2 lesion rate) up to 4 years were analyzed in two groups: 1) RDTN patients randomized to OMB in ASCLEPIOS I/II and continuing OMB in ALITHIOS (continuous; n=314) and 2) RDTN patients randomized to TER in ASCLEPIOS I/II, switched to OMB in ALITHIOS (switch; n=301). Safety outcomes were analyzed in overall (RDTN patients enrolled in ASCLEPIOS I/II and ALITHIOS, n=546), continuous (OMB in core studies+ALITHIOS; n=314) and switch groups (TER in ASCLEPIOS I/II and OMB in ALITHIOS; n=232).
Results: Mean age at baseline was 36.8/35.7 years, 69.1%/65.8% were female, and the mean EDSS was 2.30/2.22 in the continuous/switch groups. Over ASCLEPIOS I/II+ALITHIOS, the ARR in the continuous group remained low up to 4 years and the cumulative number of confirmed relapses was 42% lower in continuous vs switch group. Within group (ASCLEPIOS I/II vs ALITHIOS) analysis showed that continuous use of OMB was associated with a significant reduction in ARR by 43.1%; switching to OMB resulted in a pronounced reduction in ARR (76.6%). The difference in KM estimates at Month 36 for 3m/6mCDW indicates that risk of events was similar in both the treatment groups after switching to OMB. Treatment emergent adverse events (AEs) occurred in 93.6%/83.2% of the continuous/switch groups and serious AEs were reported in 16.2%/7.8%, respectively. Detailed safety (severity of AEs, treatment discontinuation) and efficacy data will be presented at the congress.
Conclusion: Consistent with up to 4 years of safety and efficacy findings in the overall ALITHIOS study population, these analyses show the favorable benefit–risk profile of OMB in RDTN RMS patients, supporting its use as a first-line therapy in MS.

Disclosures: This study was funded by Novartis Pharma A.G., Basel, Switzerland.
Jutta Gartner in the past 3 years, has received fees for lectures and consultancy fees from Bayer, Biogen, Merck, Novartis and Sanofi, as well as funding for a research project from Novartis. Stephen L. Hauser has received personal compensation from Annexon, Alector, Accure, and Neurona; he has also received travel reimbursement from F. Hoffmann-La Roche Ltd and Novartis for CD20-related meetings and presentations. Amit Bar-Or has participated as a speaker in meetings sponsored by and received consulting fees and/or grant support from: Accure, Atara Biotherapeutics, Biogen, BMS/Celgene/Receptos, GlaxoSmithKline, Gossamer, Janssen/Actelion, Medimmune, Merck/EMD Serono, Novartis, Roche/Genentech, Sanofi- Genzyme. Xavier Montalban has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with Actelion, Alexion, Bayer, Biogen, Celgene, EMD Serono, Genzyme, Immunic, Medday, Merck, Mylan, Nervgen, Novartis, Roche, Sanofi-enzyme, Teva Pharmaceutical, TG Therapeutics, Excemed, MSIF and NMSS. Jeffrey A. Cohen received personal compensation for consulting for Biogen, Bristol-Myers Squibb, Convelo, Genentech, Janssen, NervGen, Novartis, and PSI; speaking for H3 Communications; and serving as an Editor of Multiple Sclerosis Journal. Derrick Robertson has received fees for consulting, contracted research and speaker's bureau from Biogen, Celgene, EMD Serono, Genentech, Sanofi Genzyme, Janssen, TG therapeutics; consulting fees and speakers bureau for Bristol Myers Squibb, Horizon, and Alexion; consulting fees and contracted research for Novartis; consulting fees for Greenwich biosciences; contracted research for GW Pharmaceuticals, PCORI, Atara Biotherapeutics and CorEvitas. Anne H. Cross has received consulting fees, support, and honoraria from Biogen, Celgene, Bristol Myers Squibb, EMD Serono, Merck, Genentech, Roche, Greenwich Biosciences (Jazz Pharmaceuticals), Horizon Therapeutics, Janssen (subsidiary of Johnson & Johnson), Novartis, TG Therapeutics, Academic CME, Projects In Knowledge, CME Outfitters, WebMD, Conrad N. Hilton Foundation, Potomac Center for Medical Education, The Consortium of Multiple Sclerosis Centers, and ACTRIMS; has received a grant from the Departmen of Defense, USA; has been the secretary (elected) of The Consortium of Multiple Sclerosis Centers, member of the scientific advisory board of Race to Erase MS, program committee (chair) of ACTRIMS, member of the COVID-19 advisory committee of the National Multiple Sclerosis Society and National Multiple Sclerosis Society representative on the Progressive MS Alliance; has participated on the data safety monitoring board or advisory board for Race to Erase MS (charity), National Multiple Sclerosis Society, Novartis, EMD Serono, Biogen, Celgene/Bristol Myers Squibb, and TG Therapeutics; has received patent for "Yablonskiy DA, Sukstansky AL, Wen J, Cross AH. Methods for simultaneous multi-angular relaxometry of tissue using magnetic resonance imaging. Patent 15060-630 (015875)." Carrie M. Hersh has received speaking and consulting fees from Genentech, Genzyme, Biogen, Novartis, and EMD-Serono. She has received research support paid to her institution by PCORI, Biogen, and Genentech. Kumaran Deiva has received personal compensation for speaker activities from Novartis and Sanofi. Karlsson

Goeril, Ayan Das Gupta, Ronald Zielman, Soudeh Ansari, Bernd Kieseierare employees of Novartis. Ludwig Kappos' institution (University Hospital Basel) has received the following exclusively for research support: steering committee, advisory board, and consultancy fees (Actelion, Addex, Bayer HealthCare, Biogen Idec, Biotica, Genzyme, Lilly, Merck, Mitsubishi, Novartis, Ono Pharma, Pfizer, Receptos, Sanofi, Santhera, Siemens, Teva, UCB, and Xenoport); speaker fees (Bayer HealthCare, Biogen Idec, Merck, Novartis, Sanofi, and Teva); and support for educational activities (Bayer HealthCare, Biogen, CSL Behring, 43). Rozhin Asghari is an employee of Novartis Pharmaceuticals Australia.

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Tracking the immune response to SARS-CoV-2 mRNA vaccines in ofatumumab treated RMS patients in a multicenter study

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Background: Recently developed SARS-CoV-2 mRNA vaccines have been shown to efficiently protect healthy individuals against COVID-19 and contribute greatly towards fighting the COVID-19 pandemic. There is only limited data available for Multiple Sclerosis (MS) patients with immunosuppressive treatment.
Objective: This study aims to understand the impact of ofatumumab treatment on the development of cellular and humoral immune responses to initial and booster SARS-CoV-2 mRNA vaccines.
Methods: KYRIOS is a prospective, open-label, two-cohort study including 34 MS patients at 8 sites in Germany. Patients receive initial or booster SARS-CoV-2 mRNA vaccination either before (cohort 1) or at least 4 weeks after starting ofatumumab treatment (cohort 2). As primary endpoint, the impact of ofatumumab treatment on development of SARS-CoV-2 reactive T-cells will be evaluated. Additionally, neutralizing antibodies will be assessed, and the immune responses will be monitored and phenotypically described for up to 18 months.
Results: Interim analysis will show the complete primary endpoint results of the KYRIOS study. All patients vaccinated during continuous ofatumumab treatment (5/5) developed an immune response as soon as one week after initial vaccination cycle. While the extent of T-cell response was not affected in ofatumumab treated patients, neutralizing antibodies titers were lower compared to the control group. After the first booster vaccine, the majority of ofatumumab patients (n=15) showed an increase in neutralizing antibodies to a comparable extend as the control group (n=8). Data show that seroconversion during continuous ofatumumab treatment is possible. In general, this analysis confirms first positive interim analysis data presented at AAN 2022.
Conclusion: This data demonstrates that ofatumumab treated patients can mount specific immune responses towards SARS-CoV-2 mRNA vaccines and emphasize the importance of booster vaccines in immunocompromised patients.

Disclosures: TZ has received research support, consulting fee and honoraria for lectures from Alexion, Biogen, Celgene, Merck, Novartis, Roche, Sanofi, Teva.
TB has received consulting fee and honoraria for lectures from Biogen, Celgene, Merck, Novartis, Pathos Therapeutics, Roche, Sanofi, Teva.
BE and MG are employees of Novartis. Sponsor of this study is the Novartis Pharma Vertriebs GmbH.
ML is an employee of Novartis Australia.

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Factors Associated with Glatiramer Acetate Efficacy in Japanese Multiple Sclerosis

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Background: Glatiramer acetate (GA) is widely used as a disease-modifying drug in multiple sclerosis (MS). However, some patients experience relapses during GA treatment and little is known about factors associated with the efficacy of GA in Asians, especially in Japanese MS patients.
Objective:.To identify the factors related to the efficacy of GA in Japanese MS patients, we conducted a single-centre, retrospective, observational study.
Methods: We retrospectively enrolled 21 MS patients (19 relapsing-remitting MS and two secondary progressive MS), who received GA in Kyushu University Hospital between November 2015 and December 2020. Clinical data from GA initiation to the end of December 2021 were obtained. HLA-DRB1 alleles were typed for 19 out of 21 patients. The patients were divided into two groups according to the presence or absence of clinical relapses during GA treatment, and factors associated with relapses were assessed. We conducted survival curve analysis by the log-rank test, for relapses during GA treatment by dividing the participants by the factors of interest.
Results: All patients were female and six experienced clinical relapses. Relapsed patients demonstrated higher proportions of HLA-DRB1*04:05 carriers (3/5 vs 1/14, $p = 0.037$), and HLA-DRB1*15:01 carriers (3/5 vs 2/14, $p = 0.084$) than non-carriers of respective alleles. There was no difference in annualized relapse rates before GA initiation by the carrying status of these two alleles. Relapsed patients also tended to show lower IgG index (0.65 vs 0.86, $p = 0.081$). Time from initiation of GA to the relapse was significantly shorter in these allele carriers than non-carriers (HLA-DRB1*04:05: $p < 0.001$, HLA-DRB1*15:01: $p = 0.002$). There was no difference in time to relapses between the patients with higher or lower IgG index ($p = 0.313$).
Conclusion: Japanese MS patients with HLA-DRB1*04:05 allele or HLA-DRB1*15:01 allele may be resistant to the efficacy of GA treatment to prevent relapses.
Disclosures: E.T. received speech honoraria payments from Novartis Pharma.
M.W. received speaker honoraria and consultant fee from Novartis Pharma, Biogen Japan, Chugai Pharmaceutical, Alexion Pharmaceuticals, Mitsubishi Tanabe Pharma, and Argenx

Japan and a grant from JSPS KAKENHI (Grant No. 22K07351).
S.F. has nothing to declare.
K.S. has nothing to declare.
K.M. received speaker honoraria from Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, Alexion Pharmaceuticals, Novartis Pharma, and Takeda Pharmaceutical Company.
T.M. received speech honoraria payments from Biogen Japan, Chugai Pharmaceutical, Alexion Pharmaceuticals, Novartis Pharma, and Takeda Pharmaceutical Company.
N.I. received grant support from Mitsubishi Tanabe Pharma, Novartis Pharma, Biogen Japan, Chugai Pharmaceutical, Teijin Pharma, Eisai and speaker honoraria from Novartis Pharma, Biogen Japan, Alexion, Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, Teijin Pharma, Japan Blood Products Organization, Takeda Pharmaceutical, and Eisai.

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Compliance and Persistence With Ofatumumab Treatment in Patients with Relapsing Multiple Sclerosis in Clinical Trials for Up to 4 Years

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Background: Ofatumumab (OMB) demonstrated superior efficacy and a similar safety profile to teriflunomide in the ASCLEPIOS I/II trials in relapsing multiple sclerosis (RMS) patients. Sustained efficacy and a consistent safety profile have also been observed in the long term ALITHIOS open-label extension study for up to 4 years.
Objective:.To evaluate compliance and persistence with OMB treatment in RMS patients for up to 4 years across the OMB core studies and ALITHIOS extension study.
Methods: Patients completing the core ASCLEPIOS I/II, APOLITOS and APLIOS trials could enter ALITHIOS. Compliance was analyzed for up to 4 years (cut-off: 25-Sep-2021) in overall, continuous (OMB in core) and newly switched (teriflunomide core and OMB extension) groups. Compliance was calculated as the duration of exposure to study drug/duration of on-treatment period×100%, with =80% defined as the threshold to indicate patients were compliant. The number of patients continuing OMB (as a measure of treatment persistence) and discontinuing treatment in ALITHIOS, and reasons for discontinuations are also presented.

Results: As of 25-Sep-2021, in the overall (N=1969), continuous (N=1292), and newly switch groups (N=677), 94.9%, 95.1%, and 94.4% of patients were compliant with OMB therapy, respectively. In total, 1715 patients entered the ALITHIOS study; 12 (0.7%) of these were screening failures, and 1703 patients were enrolled in the study and received study treatment; 1508 (87.9%) were ongoing in the study at the time of data cut-off, and 195 (11.4%) discontinued study treatment. The primary reasons for discontinuation in the ALITHIOS study were patient/guardian decision (n=75 [4.4%]); adverse event (n=66 [3.8%]); pregnancy (n=12 [0.7%]); physician decision (n=12 [0.7%]); lack of efficacy (n=12 [0.7%]); lost to follow-up (n=8 [0.5%]); death (n=6 [0.3%]); non-compliance (n=2 [0.1%]); and protocol deviation (n=2 [0.1%]).
Conclusion: Overall ~95% of patients were compliant with OMB treatment across core studies and the open-label extension study, indicating high compliance with monthly subcutaneous OMB therapy.
Disclosures: This study was funded by Novartis Pharma AG Basel, Switzerland.
Karen Thomas received educational sponsorship or remuneration for contributing to pharmaceutical-led project development from Sanofi-Genzyme, Roche, Novartis, Biogen and Merck. Enrique Alvarez received compensation for consulting from Actelion/Janssen, Alexion, Bayer, Biogen, Celgene/BMS, EMD Serono/Merck, Genentech/Roche, Genzyme, Novartis, Sanofi, and TG Therapeutics and for research from Biogen, Genentech/Roche, Novartis, TG Therapeutics, Patient-Centered Outcomes Research Initiative, National Multiple Sclerosis Society, National Institutes of Health, and Rocky Mountain MS Center.Sibyl Wray received consulting fees from and advisory boards for Biogen, Celgene, and EMO Serano; speaker bureaus for Biogen, Celgene, EMO Serano, Genentech-Roche, and Sanofi-Genzyme; research support from Biogen, Celgene, EMO Sereno, Genentech-Roche, Novartis, Receptos, Sanofi- Genzyme, and TG Therapeutics.Carrie M. Hersh has received compensation for consulting and research from Novartis, Biogen and Genentech and for consulting from EMD Serono and consulting and speaker bureau from Genzyme. Derrick Robertson has received fees for consulting, contracted research and speaker's bureau from Biogen, Celgene, EMD Serono, Genentech, Sanofi Genzyme, Janssen, TG therapeutics; consulting fees and speakers bureau for Bristol Myers Squibb, Horizon, and Alexion; consulting fees and contracted research for Novartis; consulting fees for Greenwich biosciences; contracted research for GW Pharmaceuticals, PCORI, Atara Biotherapeutics and CorEvitas. Ayan Das Gupta, Xixi Hu, Ronald Zielman, Ibolya Boer, Andy Cheadle are employees of Novartis. Jeffrey A. Cohen received personal compensation for consulting for Biogen, Bristol-Myers Squibb, Convelo, Genentech, Janssen, NervGen, Novartis, and PSI; speaking for H3 Communications; and serving as an Editor of Multiple Sclerosis Journal.

POSTER SESSION - 6
Epidemiology, Genetics, and Epigenetics

P-64
Promotor Polymorphisms in susceptibility and progression to Multiple Sclerosis: Are there synergistic interactions of MMP-9 C-1562T, MMP-2 C-735T and MMP-7A-181G?
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Background: Gene gene interactions are effective in susceptibility to MS formation and disease progression.
Objective: The aim of this study is to investigate the synergistic effects of MMP-2 C-735T, MMP-9 C-1562T, and MMP-7 A-181G functional polymorphisms in the susceptibility to Multiple sclerosis (MS).
Methods: Materials and Methods: In this cross-sectional study, 149 patients who were diagnosed with Multiple Sclerosis between January 2017-December 2018 in the department of Neurology, Medical Faculty, Trakya University (Edirne, Turkey) and 152 healthy controls were included. Following DNA isolation from patient and control peripheral blood, allelic discrimination of MMP-7a-181G (rs11568818) polymorphisms was performed with real-time PCR using TaqMan® SNP Genotyping Assay kit for MMP-2 C-735T (rs2285053), MMP-9 C-1562T (rs3918242) and MMP-7A-181G (rs11568818). Thus, genotype, allele, and haplotype analyses of the patient and control groups were performed.
Results: A statistically significant difference was found between CC, CT, and CC genotypes in the Expanded Disability Status Scale (EDSS) score. MMP-9 C-1562T functional polymorphism was found in MS patients in terms of transition of C to T ($p = 0.021$). A statistically significant difference was found between men and women in terms of transition of C to T in the MMP-9 C -1562T functional polymorphism ($p = 0.014$). A statistically significant difference was found between CC, CT and CC genotypes in terms of C to T in disease duration and MMP-9 C-1562T functional polymorphism ($p = 0.040$). For the MMP-2 C-735T functional polymorphism, a statistically significant difference was found when the TT genotype and the C allele were compared between the patient and control groups ($p = 0.070$; $p = 0.04$, respectively). When both MMP-9 C and MMP-7 G alleles were present, the risk of MS increased 1.5 times ($p = 0.035$).
Conclusion: The presence of both MMP-9 C and MMP-2 C alleles has an even greater risk of MS. Therefore, gene-gene interactions and variants of more than one gene may be better predictors for the susceptibility to MS.
Disclosures: No potential conflict of interest was reported by the authors.

P-65
The First Multiple Sclerosis Study in Mongolia; Predictors of Disability and Depression in Mongolian MS Patients
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P-66
The Risk of Dementia in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder: a Nationwide Cohort Study in South Korea
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Refer to O-10 in Plenary Oral Presentation - 2

P-67
Breast Cancer Occurrence In Multiple Sclerosis And Neuromyelitis Optica
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Background: The association of autoimmune disease with cancer has been attributed to chronic inflammation, reduced self-tolerance or cross-reactivity with tumour antigens. This predilection to malignancy is further potentiated by individual risk including concomitant immunomodulatory treatment.
Objective: We describe two patients with MS and one with NMOSD who had developed breast cancer during the course of their disease.
Methods: Case series
Results: Case 1-A 49-year-old postmenopausal lady who had recently undergone mastectomy for right breast carcinoma presented with right hemiparesis associated with hypoaesthesia. She was diagnosed to have seropositive NMOSD and recovered well after plasma exchange.
Case 2-A 50-year-old lady presented with recurrent right optic neuritis and left hemiparesis. She was diagnosed with RRMS and started on Interferon-Beta. Despite treatment, her disease evolved into secondary progression. She was later diagnosed with left breast carcinoma at the age of 67.
Case 3-A 22-year-old lady presented with left hemiparesis and diplopia. A diagnosis of RRMS

was made with subsequent commencement of Interferon-Beta. This was interrupted during her unplanned pregnancy with subsequent switch to Azathioprine and then Teriflunomide. She experienced frequent relapses with secondary progression needing change to Cladribine. However, it was stopped 2 months later when she was diagnosed with right breast carcinoma.
Conclusion: Breast cancer in MS and NMOSD appears to be due to immune dysregulation with a complex interplay of genetic and environmental factors. Further studies examining this causal interrelation would be impactful on immunomodulatory therapy development.

P-68
COVID-19 infection after at least two doses of SARS-CoV-2 mRNA vaccine in Multiple Sclerosis, AQP4-antibody NMOSD and MOGAD during the Omicron BA.1/2 wave in Singapore
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P-69
Clinical Characteristics of Multiple Sclerosis, Neuromyelitis Optica Spectrum Disorders and MOG Associated Diseases in Korea; Analysis of 302 Patients in the National Research Network Registry
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Background: A new registration system for Korean CNS demyelinating diseases has been developed since 2020.
Objective:.Here we described the clinical features of MS, NMOSD, and MOGAD in Korea based on an expanded clinical registry.
Methods: We collected clinical data using an internet based clinical research and trial management system(iCReaT). We compared baseline characteristics in the patients with MS, NMOSD, and MOGAD, and analyzed the risk of relapses.
Results: Total 302 patients were registered from May 2020 to July 2022. The proportion of MS, seropositive NMOSD(SP-NMOSD), and MOGAD was 33.2%, 21.9%, and 11.6%, respectively. Disease duration was shorter in MOGAD than MS or SP-NMOSD(p=0.009). ARR and baseline EDSS were lower in MS than in SP-NMOSD or MOGAD(p=0.093, p 60 years)(adjusted HR 0.09 95% CI 0.01-0.97), and higher with elevated CSF protein(adjusted HR 5.21, 95% CI 1.47-

18.54).
Conclusion: Here we described the distinctive clinical features of MS, NMOSD, and MOGAD based on the newly expanded registry system in Korea. It was found that elevated CSF protein were associated with higher risk of relapse in these diseases.
Disclosures: This study was supported by a grant from the Korea Disease Control and Prevention Agency.

POSTER SESSION - 7
Mental Health and Psychosocial issues

P-70
Evaluation of Psychiatric Characteristics İn Children Of Parents With Multiple Sclerosis
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Background: Most affected individuals have children under the age of 18 at the time of their diagnosis with MS. Disease and physical disabilities in the person may adversely affect their children. There is a limited number of data on psychiatric disorders in children of MS patients in the literature.
Objective: This study aims to investigate the psychiatric disorders in children with parental multiple sclerosis (MS) and to research the differences between without parental chronic disease.
Methods: The children of the parents with MS diagnosis in the neurology department and the children of parents without chronic medical and psychiatric diseases were included in the study. Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children Present and Lifetime Version (K-SADS-PL) was applied to the children. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinical Version (SCID-I-CV) was applied to parents with MS. Psychiatric characteristics of the parents and children were determined. The accompanying psychiatric disorders in children and adolescents with paternal MS and the clinical features affecting these disorders were analyzed.
Results: Fifty children and adolescents with parental MS were included in the study group and 75 children and adolescents without a chronic disease in the parents were included in the control group. The mean age of children in the study group was 12.7±2.9 years and 58% were girls. 52% of the parents with MS were diagnosed with a psychiatric disorder. As a result of the evaluation, 54% of the children with parental MS were diagnosed with psychiatric disorder. The most common psychiatric diagnoses were anxiety disorders (30%), attention deficit and hyperactivity disorder (ADHD) (22%), and tic disorders (16%), respectively. The Expanded Disability Status Scale scores of the parents of children with psychi-atric diagnoses were significantly higher than those of the children with no diagnosis.
Conclusion: Children of MS patients have a high rate of psychiatric disorder. As the severity of MS increases, it is more common for children to be affected psychosocially.
Disclosures: No potential conflict of interest was reported by the authors

P-71

Depression And Gender In People With Multiple Sclerosis

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Background: Multiple sclerosis (MS) is an autoimmune disease of the central nervous system. In addition to physical symptoms, complaints of depression are very common.
Objective: To verify and analyze the relationship between symptoms of depression and gender in people with MS.
Methods: A quantitative study was performed with 52 people diagnosed with multiple sclerosis (41 relapsing-remitting, 4 primary-progressive and 7 secondary-progressive), aged between 23 and 59 years (Mean = 43.75, SD = 10.51 years), 18 men (34.6%) and 34 women (65.4%), with EDSS score from 0 to 7.5 (Mean = 3.56, SD = 2.19), time of diagnostic between 0.7 and 26 years (Mean = 9.96, SD = 6.39 years). For evaluation, an interview was conducted to collect data and applied the BDI (Beck Depressions Inventory). It was used the chi-squared test for statistical hypothesis test.
Results: It was observed that 28.8% of the patients presented depression, being 17.3% mild, 9.6% moderate and 1.9% severe. Among people with depression, 60.0% had a mild outcome, 33.3% moderate and 6.7 severe. The men were aged between 25 and 57 years (Mean = 39.94, SD = 8.97 years), with EDSS score from 0 to 6.5 (Mean = 3.14, SD = 2.15), time of diagnostic between 0.7 and 18 years (Mean = 7.65, SD = 4.71 years). The women were aged between 23 and 59 years (Mean = 45.76, SD = 10.83 years), with EDSS score from 0 to 7.5 (Mean = 3.78, SD = 2.22), time of diagnostic between 1 and 26 years (Mean = 11.18, SD = 6.88 years). With regard to men, 27.8% had depression, being 16.7% mild, 5.6% moderate and 5.6% severe. With regard to women, 29.4% had depression, being 17.6% mild and 11.8% moderate). There was no significant difference between the results of men and women (p=0.901).
Conclusion: Observou-se que, entre os pacientes com depressão, a maioria apresentou nível leve. Sugere-se que não há diferença significativa na depressão entre os sexos.
Disclosures: There is no conflict of interest between the authors.

POSTER SESSION - 8
Neuroimaging and Neurophysiology

P-72

A case of MRI-negative Encephalomyelitis in a patient with long-term stable MOG antibody-associated disease

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Background: Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) is a central nervous system inflammatory disease that has various symptoms, such as optic neuritis, acute disseminated encephalomyelitis, and myelitis. Since MOG antibodies were found in some seronegative neuromyelitis optica (NMOSD) patients, MOGAD has been reported to have

a phenotype different from that of NMOSD and is classified as a disease different from NMOSD. Recently, there have been cases in which MRI lesions were not observed in patients with myelitis or myelopathy among individuals with MOG antibody-related diseases.
Objective: We report a case of MRI-negative encephalomyelitis in a MOGAD patient who had not relapsed for several years, which was accompanied by MRI-negative myelopathy and cognitive impairment.
Methods: A 37-year-old woman presented with an acute memory disturbance and excessive sleepiness (12~15 hours) 2 weeks prior to assessment. A neurological examination revealed memory deterioration, attention deficit, decreased word fluency, and time disorientation. Cranial nerve examination was normal, and there was no limb weakness, but sensory examination showed hypesthesia below the T2~T2 level. Brain and spinal cord MRI with gadolinium enhancement revealed normal findings.
Results: Six years ago, the patient had a history of hospitalization for quadriparesis and fever. At that time, cerebrospinal fluid showed pleocytosis (WBC 490/mm3 (lymphocyte 90%) and protein 109 mg/dl). Brain MRI showed multifocal hyperintense lesions involving the bilateral thalamus, midbrain, and periaqueductal area without definite contrast enhancement, and spinal cord MRI showed increased signal intensity from the C4 to C7 level, showing no definite enhancement. Anti-AQP4 IgG antibody was normal, and the infectious etiology test was confirmed to be normal. Initially, viral encephalitis or aseptic meningoencephalitis (ADEM) was suspected, and the symptoms improved after treatment with antiviral drugs and steroid pulses.
Most of the symptoms improved over several months, after which the brain MR and spine MR lesions disappeared. Brain MRI taken several years later remained normal. Approximately three years later, the patient was confirmed as positive for serum anti-MOG IgG antibody, which b
Conclusion: Although MRI-negative myelitis rarely occurs in MOGAD, it can be assumed that MRI-negative myelitis is expressed as a rare phenotype of MOGAD through response to acute steroid treatment.
Since the patient, in this case, had accompanying MRI-negative
Disclosures: Disclosure Statement
The authors report no financial disclosures.
Acknowledgments: This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIT) (No. 2020R1G1A1008446).

P-73
Clinical, imaging features and treatment response of idiopathic hypertrophic pachymeningitis
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Background: Idiopathic hypertrophic pachymeningitis (IHP) is a rare inflammatory disease that causes focal or diffuse thickening of the dura mater. However, longitudinal follow up studies are still lacking for these patients.
Objective: To investigate the clinical characteristics, neuroimaging findings, treatment response and outcome of IHP.

Methods: A retrospective case series of 30 patients admitted Beijing Tiantan Hospital were screened via Hospital Information System from January 1st, 2011, to January 31st, 2021. All patients' clinical symptoms, imaging, and treatment response were collected via a standardized form. We compared the effects of high-dose and low-dose corticosteroids on headache, impaired vision, and MRI remission during acute onset. The effects of different immunosuppressants on preventing relapses were also compared.
Results: Headache (93.3%) and multiple cranial neuropathy (66.7%) were the most common symptoms of IHP. Cerebral spinal fluid test showed that protein levels were elevated in 17 (56.7%) patients, and white blood cells were increased in seven patients. MRI demonstrated that diffuse (60%) and focal (40%) enhancement occurred in the dura mater, especially in the tentorium cerebellum (80%). High-dose and low-dose corticosteroids reduced headache and dural enhancement during the acute phase. The high dose corticosteroid significantly relieved the headache than the low dose group ($p = 0.041$). Patients treated with mycophenolate mofetil and cyclophosphamide might achieve longer remission (months, $p = 0.428$).
Conclusion: Headache and multiple cranial neuropathy are the most common clinical manifestations of IHP. In this study, almost all patients had a good initial response to corticosteroid therapy during the acute phase.

P-74
The difference of the retinal structural and microvascular characteristics in patients with MOGAD-ON and AQP4-ON
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Background: Antibodies against myelin-oligodendrocyte-glycoprotein (MOG-Abs) associated disorders (MOGAD) has been recognized as a disease entity. Optic neuritis (ON) is the most common symptom in MOGAD.
Objective: To demonstrate the differences in retinal microvascular characteristics between patients with MOGAD-ON and aquaporin-4 antibody (AQP4-Ab) positive ON.
Methods: In a prospective study, optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) were used to measure retinal and microvascular parameters.
Results: 26 MOGAD-ON eyes, 40 AQP4-ON eyes, and 60 control eyes were included in the study. The thickness of RNFL and GCC in MOGAD-ON eyes is significantly lower than that of HC (p
Conclusion: The retinal neuro-axonal damages between MOGAD-ON and AQP4-ON were comparable. Unlike AQP4-ON eyes, microvascular densities were significantly reduced in MOGAD-ON and were positively correlated with the deterioration of visual acuity in MOGAD-ON.

P-75
A Case of Primary Progressive Multiple Sclerosis Showing Multiple Iron Rim Lesions
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Background: Iron rim lesions (IRLs), which reflect the chronic active inflammation and ongoing tissue destruction, are considered as a specific imaging marker of multiple sclerosis (MS) that is distinct from other MS-mimicking diseases. Recent data suggested that patients with IRLs have a propensity to develop primary progressive MS (PPMS).
Objective: We report a case of PPMS with multiple IRLs on susceptibility-weighted image (SWI).
Methods: A 63-year-old woman complained progressive gait disturbance, cognitive impairment and recurrent dizziness from 30 months earlier. She had no previous underlying diseases and family history of neurological diseases. In neurological examination, saccadic hypometria on left side, hyperactive deep tendon reflexes, Romberg test positive, and impaired Tandem gait were observed. In brain magnetic resonance imaging (MRI), multifocal T2/fluid attenuated inversion recovery (FLAIR) high signal intensities observed in periventricular, juxtacortical, deep white matters, and cerebellum. In addition to multifocal white matter lesions, there was a 2.4*2.1*2.4 cm sized meningioma in left retro-cerebellar convexity. Some of the T2/FLAIR lesions showing high signal intense appeared as multiple IRLs on SWI. Laboratory tests for central nervous system (CNS) demyelinating diseases revealed no abnormalities including aquaporin 4, myelin oligodendrocyte glycoprotein (MOG), and other rheumatological autoimmune antibodies. In cerebrospinal fluid (CSF) analysis, CSF immunoglobulin G index was elevated to 0.73. She showed moderate cognitive dysfunction with 16 points in the Mini-Mental State Examination (MMSE).
Results: She was initially treated with intravenous corticosteroid at other hospital suspected CNS demyelinating disease such as multiple sclerosis, but it had been getting worse. Because it worsened despite high-dose steroid treatment, we suspected PPMS and attempted treatment with rituximab 8 months after the initial high-dose steroid treatment. With the induction and maintenance treatment of rituximab, her gait disturbance and memory impairment were partially improved. She is currently able to walk with an assistant device, and latest MMSE score is 20 points, which is better than before. In brain MRI, there was no interval changes in T2/FLAIR white matter lesions, but IRLs were slightly decreased than before.
Conclusion: Multiple white matter lesions in old age are required to be distinguished for various CNS involving disease in addition to MS, and IRLs can help diagnose MS.

P-76
Neuromyelitis Optica Spectrum Disorder Presenting With Symptomatic Narcolepsy Due To Involvement Of The Bilateral Hypothalamus
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Background: Neuromyelitis Optica spectrum disorder (NMOSD) is an inflammatory demyelinating central nervous system (CNS) disorder associated with antibodies to aquaporin-4(AQP4). Narcolepsy is a sleep disorder characterized by excessive daytime sleepiness, cataplexy, and other rapid eye movement sleep abnormalities.
Objective: It can be either primary or symptomatic due to other neurologic disorders. NMOSD is a CNS disorder in which symptomatic narcolepsy is described as one of the core clinical fea-

tures.
Methods: The patient was a 45-year-old woman who had been suffering from repeated excessive daytime sleepiness and transient confusion for 21 days. These symptoms were repeated several times a day and lasted about 10 minutes. At the beginning of these symptoms, confusion occurred, and the conversation was impossible. She was hospitalized for uncontrolled vomiting, dizziness, and bulbar palsy two years ago. At that time, there was a lesion in the right dorsal medulla oblongata, and the anti-AQP4-IgG antibody was negative. Investigations revealed normal hematological and biochemical parameters in the blood. A brain MRI showed symmetrical diffusion restriction and T2 HSI in the bilateral medial hypothalamus and left hippocampal head with no contrast enhancement. The retest for anti-AQP4-IgG antibody by cell-based assay gave a positive result.
Results: We diagnosed the patient as having NMOSD with AQP4 antibody, and we administered high-dose methylprednisolone (1000 mg/day, five days) followed by oral prednisolone and azathioprine. Her repeated hypersomnia and confusion improved within a month, and she has been symptom-free for over 1 year. Since the circumventricular organs around the third and fourth ventricles are enriched with AQP4, NMOSD can present with hypersomnia due to secondary damage to orexin neurons in the hypothalamus.
Conclusion: In conclusion, hypersomnia or symptomatic narcolepsy might be an initial and major clinical manifestation of NMOSD.

P-77
ADEM – A Continuum Of The MS Spectrum?
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Background: MS and ADEM are both CNS inflammatory diseases with overlapping clinical characteristics but with distinctive radiological features. Observations of imaging features resembling ADEM in MS raises questions on the corresponding clinical phenotype and course of disease evolution.
Objective: We present 3 cases of confirmed RRMS with atypical MRI features.
Methods: Case series
Results: Case 1: A 43-year-old lady presented with cerebellar ataxia and diplopia. MRI revealed poorly demarcated lesions at temporal, parietal and medullary-pontine regions. A diagnosis of RRMS was made with positive CSF oligoclonal bands and follow up MRI showing new lesions.
Case 2: A 34-year-old lady presented one month post COVID-19 vaccination with left sided hemiparesis and diplopia. MRI showed diffuse and poorly marginated lesions at bilateral hemispheres, cerebellum and pons. She was initially diagnosed as vaccine-induced ADEM but later met the diagnosis of RRMS.
Case 3: A 23-year-old lady was intubated after presenting with diplopia, dysarthria, and vomiting. MRI showed fluffy lesions at supra- and infratentorial regions with enhancement at midbrain and medulla. CSF oligoclonal band positivity and the callosal-septal interface involvement was diagnostic of MS. Despite the aggressive lesion load, she responded well to methylprednisolone and IV immunoglobulin.

Conclusion: These cases illustrate the clinicoradiologic heterogeneity in the spectrum of MS phenotypes.Larger studies are needed to characterise its clinical course and other atypical phenotypes as this may offer new insight to treatment approaches and outcomes.

P-78

An Unusual MOG-IgG-Associated Optic Neuritis Radiological Phenotype

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Background: MOGAD is a distinct CNS inflammatory disease with clinical and radiological characteristics that overlap with other neuroinflammatory disorders. Optic neuritis (ON) in MOGAD is typically bilateral with perineuritis, involving the anterior segment, characteristically sparing the optic chiasm and retrochiasmatic pathways.
Objective: We illustrate a case of relapsing adolescent-onset MOGAD with atypical ON characteristics on MRI imaging.
Method: Case Report
Results: A 14-year-old boy presented with right hemiparesis and unsteady gait. His first MRI was suggestive of acute disseminated encephalomyelitis with multifocal T2 hyperintense lesions at the grey-white matter junction in frontoparietal lobes, adjacent to head of right caudate nucleus with cortical edema and peripheral contrast enhancement. Lumbar puncture showed pleocytosis with raised CSF protein and unmatched CSF oligoclonal bands. MOG antibody was positive in CSF and serum. Despite initial good response to IV methylprednisolone, he relapsed with bilateral optic neuritis and right upper limb monoparesis. MRI showed new lesions in bilateral optic nerves with involvement of chiasm and post-chiasmatic optic tracts, bilateral cerebellar peduncles, pons and internal capsules. He subsequently underwent plasma exchange followed by IV immunoglobulin prior to Rituximab commencement.
Conclusion: The pattern of chiasmal and retrochiasmal involvement has been described to be a discriminating feature of NMO rather than MOGAD. More studies are needed to examine the expanding MOGAD phenotypes as there are prognostic and therapeutic implications.

P-79

Chi-Separation Imaging for Diagnosis of Multiple Sclerosis versus Neuromyelitis Optica Spectrum Disorder

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P-80

Transorbital Ultrasonography to Differentiate Optic Neuritis from Ischemic Optic Neuropathy

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Background: Optic neuritis (ON) is one of the common clinical features in the inflammatory demyelinating disease of the central nervous system. ON and ischemic optic neuropathy has similar clinical manifestations, including acute visual loss. Transorbital ultrasound (TOUS) has recently been considered a valuable tool for evaluating optic nerves.
Objective: This study aimed to investigate whether TOUS could be distinguishing between optic neuritis and ischemic optic neuropathy.
Methods: We reviewed the medical records of 18 patients who visited our hospital for the first attack of unilateral optic neuropathy (both optic neuritis and ischemic optic neuritis) between January 2020 and December 2021. Demographic data, visual acuity (VA), visual evoked potential, and optical coherence tomography (OCT) results were collected. TOUS was performed using B-mode US equipment and scanned bilateral optic nerves. The correlation analysis between TOUS and clinical variables was performed. The Mann-Whitney test was performed to compare TOUS variables between ON and ischemic optic neuropathy.
Results: Among 18 patients, ten patients with ON (4 men and 6 women) and eight with ischemic optic neuropathy (4 men and 4 women) were enrolled. The median age is younger in the ON group than in the ischemic optic neuropathy group, but there was no statistical difference between the two groups (56.5-year-old vs. 64.0-year-old; p=0.122). There were no statistical differences in mean thickness of optic nerve diameter (OND) without sheath, OND with sheath, and optic nerve sheath (ONS) on the affected eye between ON and ischemic optic neuropathy groups. The correlation analysis revealed that retinal nerve fiber layer (RNFL) thickness in the affected eye was negatively correlated with the duration between symptom onset and evaluation (ρ=-0.572, p=0.026). In addition, partial correlation analysis with covariates (age and the duration between symptom onset and evaluation) revealed that RNFL thickness in the affected eye was negatively correlated with ONS thickness (r=-0.570, p=0.042).
Conclusion: TOUS could be an effective tool for evaluating the optic nerve. However, TOUS has limited value and evidence as a tool to differentiate ON from ischemic optic neuropathy. Further studies with a large number of patients would be needed to clarify this.

P-81
MOG antibody-positive myelopathy as a paraneoplastic manifestation of lymphoma
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Background: Although myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an autoimmune demyelinating disease, it may occur as a paraneoplastic syndrome in rare instances.
Objective: Herein, we reported a case of MOG-positive paraneoplastic myelopathy with lymphoma.
Methods: A 80-year-old woman presented with paresthesia and weakness of four extremities for ten days.

Results: Spine magnetic resonance image showed longitudinally extensive transverse myelitis. Laboratory tests revealed positive MOG antibodies. Both high-dose intravenous methylprednisolone and plasma exchange were not effective and further evaluation showed lymphoma.
Conclusion: Considering that the average age of onset of MOGAD was in the early to mid-30s, the patient in this case developed at an unusually late age, and malignant lymphoma was identified as a concomitant tumor. Even in MOGAD, careful attention and screening.

P-82
7T-MRI Features Of Chinese Multiple Sclerosis Patients: A CNRIDD Based Cohort Study
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Background: 7T MRI can provide exceptional detection rate of multiple sclerosis (MS) lesions. However, 7T-MRI features of Chinese multiple sclerosis patients are unknown.
Objective: To investigate the distribution characteristics of MS lesions, the incidence of central vein sign and iron rim sign in Chinese patients by 7T-MRI.
Methods: A 7T-MRI cohort was established, based on China National Registry of CNS Inflammatory Demyelinating Diseases (CNRIDD). T1-MPRAGE, T2-FLAIR, T2*WI and SWI were used to identify lesions, central vein sign, and iron rim sign. Lesions were classified as cortical, juxtacortical, periventricular, infratentorial and others. Images were segmented using the 3D Slicer, and lesion volume were calculated
Results: One hundred MS patients were enrolled from April 2021. The age of the patients was 34.59 ± 9.42 years. The female to male ratio was 1.86. Patients had a mean disease duration of 5.7 ± 5.6 years. The median EDSS score was 2 [range, 0-6.5]. A total of 5885 lesions were detected, and total lesion volume were 671 cm3, including 243 (4.1%) cortical lesions, 1415 (24.0%) juxtacortical lesions, 1560 (26.5%) periventricular lesions, 429 (7.4%) infratentorial lesions and 2238 (37.9%) other lesions. A total of 4297 (73.02%) lesions had central vein sign, 1503 (25.54%) lesions had iron rim sign, and 1386 (23.55%) lesions had both central vein sign and iron rim sign. Central vein sign developed in 100 (100%) patients and iron rim sign in 88 (88%) patients.
Conclusion: We obtain 7T-MRI features of Chinese multiple sclerosis patients for the first time. Comparison with the lesion characteristics between different races helps to further explain the pathogenesis of MS.

P-83

Deep Gray Matter Iron Deposition in NMOSD and MOGAD: a Comparative Study With MS

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Background: NMOSD, MOGAD and MS are inflammatory demyelinating diseases of CNS with shared clinical manifestations, but harboring distinct pathological mechanisms and optimal treatment. Iron deposition in deep gray matter associated with disability was observed in MS, while iron deposition and its clinical significance in NMOSD and MOGAD are not well studied.

Objective: To investigate deep gray matter (DGM) iron deposition in NMOSD and MOGAD by quantitative susceptibility mapping (QSM), compared to MS and HC, and assess their associations with structural MRI measures and clinical variables.

Methods: We prospectively recruited 81 NMOSD (62 aquaporin 4 [AQP4] antibody seropositive [AQP4+] and 19 AQP4 antibody seronegative [AQP4-]), 20 MOGAD, 71 MS and age- and sex-matched 28 HC with QSM images to measure the brain magnetic susceptibility from December 2018 to December 2021. Voxel-wise analysis was used to compare the difference of susceptibility in DGM including bilateral caudate, putamen, pallidum, thalamus, hippocampus, and amygdala between groups. Linear regression analysis was performed to relate susceptibility with volumes of white matter hyperintensity (WMH) and DGM, and clinical variables including number of relapses, disease duration and cognitive scores. Patients were further divided into subgroups with low and high Expanded Disability Status Scale (EDSS) scores and their DGM susceptibility was compared using Student's t-test.

Results: Compared to HC, AQP4+ NMOSD showed higher susceptibility in bilateral putamen, pallidum, hippocampus, and amygdala, MOGAD demonstrated higher susceptibility in right putamen, left thalamus, right hippocampus and amygdala (voxel-wise Gaussian random filed [GRF] corrected p300), while AQP4- NMOSD showed no susceptibility alterations. Compared to MS, only AQP4+ NMOSD showed lower susceptibility in bilateral putamen, left caudate and thalamus. Susceptibility in several DGM subregions (e.g. right putamen, hippocampus and amygdala) in AQP4+ NMOSD and MOGAD negatively correlated with DGM volume (p

Conclusion: Distinct patterns of DGM iron deposition reflected by increased magnetic susceptibility were identified in AQP4+ NMOSD and MOGAD, and associated with clinical disability especially in MOGAD.

P-84

A Deep Learning Classification Model for Predicting Brain Atrophy in Multiple Sclerosis

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Background: Predicting disease progression in MS is critical for developing an individualised treatment strategy to prevent the accrual of irreversible disability. Despite the exploration of

clinical factors and MRI biomarkers, studies that apply deep learning techniques to baseline MRI scans to predict future disease prediction are limited.
Objective: To predict the severity of annualised brain volume change (ABVC) in MS patients with a binary classification deep learning model, based on a single baseline MRI scan.
Methods: An in-house dataset of 733 MS subjects was used for the study. The inclusion criterion was the availability of both baseline and follow-up T1-w scans with an interval of 1 to 3 years. We used SIENA to obtain the ABVC for each baseline and follow-up pair and assigned cut-offs for mild (ABVC >-0.24%) or severe (ABVC)
Results: 1. For the testing set, our classification model achieved an AUC of 0.83, 0.74 specificity and 0.84 sensitivity with selected hyper-parameters. To further assess the predictive ability of the model, we performed a 5-fold cross-validation by changing train-test splits, and the model achieve an AUC of 0.74±0.08, 0.63±0.11 in specificity and 0.71±0.06 in sensitivity.
Conclusion: We describe a deep learning model that predicts the severity of brain atrophy in patients with MS using baseline T1-w MRI only. Its application may help inform therapeutic strategies in newly diagnosed patients at high risk of severe brain atrophy.
Disclosures: Geng Zhan is a part-time research engineer at Sydney Neuroimaging Analysis Centre.
Dongang Wang is a part-time research engineer at Sydney Neuroimaging Analysis Centre.
Michael Barnett has received institutional support for research, speaking and/or participation in advisory boards for Biogen, Merck, Novartis, Roche and Sanofi Genzyme, and is a research consultant at Medical Safety Systems and research director for the Sydney Neuroimaging Analysis Centre. Chenyu Wang is a part-time employee at the Sydney Neuroimaging Analysis Centre.

P-85
Incorporating Cumulative Damage Along White Matter Tracts in Structural Connectomes in MS
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[2]Sunshine Coast University Hospital
[3]Buffalo Neuroimaging Analysis Centre
Background: Multiple sclerosis (MS) can be modelled as a disconnection syndrome. Modelling the MS 'disconnectome' based on known pathophysiological features will improve the accuracy of predictions of the model. Cumulative and incomplete damage along white matter tracts in the brain is a feature of MS that can be incorporated into models of disconnection.
Objective: Model cumulative damage of white matter MS lesions along tracts represented by MR diffusion-based tractography streamlines. Test the model against electrophysiological parameters of latency and amplitude of white matter tracts of the visual pathways.
Methods: Healthy control (HC) models of both optic radiations (OR) were constructed from probabilistic tractography with MrTrix from the Human Connectome Project. Streamlines included weighting calculated with SIFT2.
33 pwMS underwent 3D T2/FLAIR and T1 MR brain imaging, as well as multifocal visual evoked potentials (mfVEPs). No patients had a clinical history of optic neuritis (ON). Binocular average

hemifield latency and amplitude values from the mfVEPs were used as electrophysiological parameters of comparison. T2 lesions were segmented and graded for damage based on average T1 signal intensity within the lesion from 0 to 1, representing normal appearing white matter to CSF signal intensity. A lesion mask of damage was transformed on to the HC ORs by warping T1 sequences using ANTs.
To model cumulative damage the sum of damage to voxels along each streamline was calculated and transformed with a logistic function and the SIFT weighting of the streamline was adjusted. Several values of constant (k), the steepness of the logistic function, were evaluated. The strength of the connection of each OR for each constant was correlated with the hemifield amplitude and latency of the mfVEP on the contralateral side, to find the best fit. This was compared to models of complete lesion damage and single highest damage value along the streamline.
Results: 33 pwMS were analysed. No patients had contrast enhancing lesions. k values between 0.09 and 10 were trialled. The value of k with the highest R2 value corresponding to the amplitude and latency to both left and right ORs were: Left OR amplitude k=10 (R2=0.5110); left OR latency k=1 (R2=0.5168); right OR amplitude k=10 (R2=0.4859); right OR latency k=2 (R2=0.4919).
A k value of 4 performed second best in three of the ORs and 4th in left OR latency and was taken as the best performing value across all four correlations.
The k value of 4 outperformed the models of complete (binary) lesion damage and single maximum damage value in all four situations: Left OR amplitude k=4 (R2=0.5079), binary (R2=0.4834), max (R2=0.4286); left OR latency k=4 (R2=0.4867), binary (R2=0.3728), max (R2=0.3947); right OR amplitude k=4 (R2=0.4744) binary (R2=0.3922), max (R2=0.2985); right OR latency k=4 (R2=0.4807), binary (R2=0.3012), max (R2=0.4358).
Conclusion: Modelling cumulative damage along tractography streamlines better explains the electrophysiological function of the underlying white matter tract compared to single measurements of complete or worst damage and should be included in connectome models.

P-86

MSBase Imaging Repository – Phase II – Automated Quantitative Magnetic Resonance Imaging (MRI) Analyses in Multiple Sclerosis (MS)

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Background: MSBase is a global registry containing over 80,000 MS patient records. Phase I of the MSBase Imaging Repository (MSBIR), enabling storage and retrieval of matched MRI datasets, was completed in 2021. Access to routine, automated quantitative imaging metrics would significantly enhance the research data available to the MS research community.

Objective: To facilitate routine quantitative analysis of compatible brain MRI scans uploaded to MSBIR using an automated AI-based software platform; and to populate brain lesion and brain volume metrics into MSBase and the MSBase Data entry Software (MDS).

Methods: Automated, AI-based imaging pipelines that measure brain lesion metrics and brain volumes from compatible clinically acquired MS MRI brain scans were developed and refined by the Sydney Neuroimaging Analysis Centre (SNAC). These tools provide both cross-sectional and longitudinal lesions metrics, including measures of new and enlarging lesion volume; and brain and brain substructure volume, and their change over time, referenced to a healthy control population. De-identified images uploaded to MSBIR are automatically checked for quality and compatibility, routed to a dedicated cloud-based MSBIR server for analysis and the results returned to MSBase. Data is not retained on the analysis server. The quantitative brain metric results are securely transmitted to and displayed within the corresponding patient record within MDS via the unique MSBase ID. Pre-requisite MRI sequences include 3D Fluid Attenuated Inversion Recovery and pre-contrast 3D T1-weighted sequences. Longitudinal compatibility requires acquisition on the same scanner, parameter compatibility and an affine similarity index of >0.2.

Results: A fully automated quantitative analysis pipeline has been successfully developed and implemented by SNAC, MSBase and the University of Sydney (USYD) MSBIR team. USYD has been granted a perpetual free licence to use all proprietary algorithms for MSBIR. Quantitative MRI (QMRI) brain metrics now available in MSBIR/MSBase include; T2 lesion number & volume, new T2 lesion number & volume, enlarging T2 lesion number & volume, T2 lesion volume change, whole brain volume & volume change, thalamic volume & volume change, and, cortical grey matter volume & volume change. All metrics are stored in MSBIR/MSBase, in a de-identified manner, for the purpose of future MSBase studies.

Conclusion: Compatible MRI brain scans entering MSBIR are quantitatively analysed by an automated AI-based software platform. The derived quantitative MRI data is stored in MSBIR; and displayed in patient records through successful integration with MSBase/MDS.

Disclosures:

-Andy Shieh and Chenyu Wang are employees of the Sydney Neuroimaging Analysis Centre. Michael Barnett is a consultant for the Sydney Neuroimaging Analysis Centre.

-Funding for the development and build of the MSBIR platform have been provided by the following industry sponsors: Biogen, Bristol Myers Squibb, Merck, Novartis and Roche.

POSTER SESSION - 9

Patient Reported Outcomes and Programs that Support Quality of Life

P-87

Professional Skills Development Project For People With Multiple Sclerosis

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[1]*Brazilian Association of Multiple Sclerosis (ABEM)*
Background: Multiple Sclerosis (MS) is a disabling disease that affects people of working age and impacts employability.
Objective: To present a professional skills development project for people with MS.
Methods: The Brazilian Multiple Sclerosis Association (ABEM) entered into a partnership with the Brazilian Support Service for Micro and Small Enterprises (SEBRAE), a private entity for training and promoting development. Subsequently, the free training program was disseminated throughout the Brazilian territory. The program consisted of seven remote meetings that addressed the topics of emotional intelligence, marketing, entrepreneurship, finance, business idea and company formalization.
Results: 755 registrations were obtained from people with MS, residing in 22 Brazilian states. Of these, 418 (55.36%) regularly participated in the meetings, completed the program and received a Certificate of Participation. All received didactic material and had a technical team for the application of classes, lives and calls. The Training Program promoted entrepreneurship, increased self-knowledge, enabled a greater network of contacts, awakened competitiveness in business and guided financial credit.
Conclusion: The project to develop professional skills for people with MS is a pioneer in Brazil. Participants acquired knowledge, tips and information that optimized their personal skills and instrumented their ideas to decide the professional future.
Disclosures: There is no conflict of interest between the authors.

P-88
Impact of body mass index on fatigue in multiple sclerosis, neuromyelitis optica spectrum disorder and myelin-oligodendrocyte glycoprotein associated disease
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[1]*Department of Neurology, Samsung Medical Center, Sunkyunkwan University School of Medicine*
Background: Obesity is a risk factor for multiple sclerosis (MS) and overweight patients with MS experience worse self-reported health status. Still, the association between fatigue and obesity in MS is not precisely known, as is the case in neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein (MOG)-associated disease (MOGAD).
Objective: We tried to investigate the effect of body mass index (BMI) on fatigue and self-reported health statuses such as sleep, depression, pain, and quality of life in Korean patients with MS, NMOSD, and MOGAD.
Methods: In a prospective cohort of CNS demyelinating disease, we collected BMIs of patients and surveys of the modified fatigue impact scale (MFIS), Pittsburgh Sleep Quality Index (PSQI), Short Form-36 (SF-36), Beck Depression Index-II (BDI-II), and Brief pain inventory (BPI). We also collected patient clinical information such as gender, age, number of attacks, and duration of disease. Patients who performed the surveys at least once were analyzed, and the BMI at the time of the survey and the BMI at the time of disease onset were compared with survey scales.
Results: A total of 75 patients with MS (age, 30.9±11.2 y, F:M=58:17), 54 patients with NMOSD (age, 40.0±14.0 y, F:M=49: 5), and 35 patients with MOGAD (age, 40.3±17.0 y, F:M= 16:19)

were analyzed. BMI at the time of survey and BMI at onset of disease was significantly higher in MOGAD (25.7±3.9, 25.4±5.8), compared to MS (23.8±4.1, 23.3±3.6) and NMOSD (23.1±4.6, 22.4±3.9) patients, whereas there were no significant differences between MFISs of three groups. A significant negative association between BMI and MFIS was observed in patients with MS (B=-0.960, p=0.005), while a positive association between BMI and MFIS was found in patients with MOGAD (B=1.781, p=0.015). In addition, there was a significant positive association between BMI and PSQI (B=0.353, p
Conclusion: This study suggests that BMI is higher in patients with MOGAD, compared to MS and NMOSD and that higher BMI is associated with less fatigue in patients with MS, but more fatigue in patients with MOGAD. Further large-scale prospective studies are war
Disclosures: JHM has lectured, consulted, and received Honoria from Bayer Schering Pharma, Merck Serono, Biogen Idec, Sanofi Genzyme, Teva-Handok, UCB, Samsung Bioepis, Mitsubishi Tanabe Pharma, Kolon Life Science, and Roche; received a grant from the National Research Foundation of Korea and SMC Research and Development Grant.
HJ and YHJ have nothing to disclose.

P-89
The Association of Cognition and Gait Disturbance in CNS demyelinating Disorder with Minimal Disability
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Background: Gait disturbance is one of the most troublesome problems which has a direct impact to life quality in CNS demyelinating disorder; multiple sclerosis (MS) and neuromyelitis optica (NMO). However, the associations with gait disturbance and other clinical variables in these two diseases have not been fully elucidated.
Objective: This study aimed to evaluate the gait disturbance using a computerized gait-analysis system, and its association with various clinical variables in patients with MS and MNO.
Methods: Total of thirty-three patients (fourteen of MS and nineteen of NMO) with minor disabilities (who were able to walk independently) and who had passed their acute phase were enrolled. The clinical variables such as disease duration, medication, BMI, hand grip power, and muscle mass were recorded. The Montreal Cognitive Assessment (MOCA), Beck Depression Inventory score-II (BDI), and fatigue scale were measured with self-questionnaires. Expanded Disability Status Scale (EDSS) was scored by a trained neurologist.
Results: Gait speed was the single parameter that showed a significantly positive correlation with MOCA (P
Conclusion: Our findings suggest that the gait disturbance in MS/NMO patients and cognitive deficit are closely correlated. We think that the care for cognitive function of MS/NMO patients might be helpful to maintain their good walking ability.

P-90
Quality of Life Study among Multiple Sclerosis Patients in Japan
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Background: Improvement of quality of life (QOL) is an important goal in the treatment of multiple sclerosis (MS), but there are limited data in Japanese MS patients. Recently, highly effective disease-modifying drugs for MS have been approved in Japan, and it is thought that there are changes in QOL and treatment satisfaction in MS patients in Japan.
Objective: To evaluate QOL and patient-reported outcomes (PROs) of MS patients in the current treatment environment in Japan.
Methods: The subjects were adult MS patients in Japan who had been treated for more than 6 months. EQ-5D-5L was evaluated as the primary endpoint. PROs including TSQM-9, WPAI-GH, FSS, QIDS-SR, and economic burden were measured as the secondary endpoints and its relationship with QOL was explored. The survey was conducted via the Internet for MS patients enrolled in several patient panels.
Results: 124 MS patients were enrolled The patient background are as follows; age (mean ± SD) was 45.9 ± 9.0 years, 74 females (60%) was included, the PDDS (Median and Q1, Q3) was 1 (0, 4), and the annualized relapse rate (mean ± SD) was 0.4 ± 0.9. EQ-5D-5L was 0.73 ± 0.22 (mean ± SD), which was similar to the value reported in western countries . As for TSQM-9 (mean ± SD), the effectiveness was 54.9 ± 21.0, the convenience was 74.1 ± 19.9, and the global satisfaction was 60.5 ± 21.5, showing that the effectiveness and global satisfaction tended to be lower than those reported previously in overseas. Absenteeism in WPAI-GH was 6.7% and Presenteeism was 23.3%.
Conclusion: QOL in Japanese MS patients was similar to the previously reported in overseas, though treatment satisfaction rate was lower. Therefore, factors related to lower treatment satisfaction should be considered to improve QOL.

P-91
A Preliminary Study of The Validity of The MSWS-12 Indigenization in MS
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Background: There is no sinicized subjective evaluation scales for Chinese Multiple Sclerosis(MS) patients to undergo self-evaluation in walking ability for now.
Objective: To sinicize MSWS-12 walking scale and analyze its validity in evaluating the disability of MS patients.
Methods: Authorized by the original author, we translated the original English MSWS-12 walking scale into a simplified Chinese version, making some indigenization and cross-cultural modification.
Ten patients diagnosed with MS were invited to finish the MSWS-12 walking scale in simplified Chinese version. The EDSS scores were collected for each patient during routine clinical visits.
Results: After indigenizing the MSWS-12 walking scale, the professional committee evaluated the Chinese version and made no major revises. The content, structure and semantic rules of the Chinese version correspond to the original version. Ten MS patients finished the MSWS-12 walk-

ing scale in simplified Chinese, Male: Female 3:7, average age 35.6±7.5 years old, median disease course 1.86(0.31, 15.1) years, the median EDSS score was 0.0(0.0,3.1) points. The average time of completing the scale was 2.0(1.0, 3.0) minutes. All the patients found the scale intelligible. The score of the scale is well consistent with the EDSS, of which the Pearson correlation coefficient is 0.976(P=0.000).
Conclusion: The MSWS-12 walking scale in simplified Chinese showed excellent semantic equivalence and acceptability, which may serve as a good complement to evaluate the walking ability of Chinese MS patients.

P-92
A Preliminary Study of The Validity of The MSWS-12 Indigenization in NMOSD
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[1]*Department of Neurology, Peking Union Medical College Hospital*
Background: There is no sinicized subjective evaluation scales for Chinese Neuromyelitis Optica Spectrum Disorders(NMOSD) patients to undergo self-evaluation in walking ability for now.
Objective: To sinicize MSWS-12 walking scale and analyze its validity in evaluating the disability of NMOSD patients.
Methods: Authorized by the original author, we translated the original English MSWS-12 walking scale into a simplified Chinese version, making some indigenization and cross-cultural modification. Ten patients diagnosed with NMOSD were invited to finish the MSWS-12 walking scale in simplified Chinese version. The EDSS scores were collected for each patient during routine clinical visits.
Results: After indigenizing the MSWS-12 walking scale, the professional committee evaluated the Chinese version and made no major revises. The content, structure and semantic rules of the Chinese version correspond to the original version. Ten NMOSD patients finished the MSWS-12 walking scale in simplified Chinese, Male: Female=1: 9, average age 37.8±10.2 years old, median disease course 7.2 (1.5, 12.9) years, the median EDSS score was 2.0 (1.0, 3.0) points. The average time of completing the scale was 1.2(0.7, 1.9) minutes. All the patients found the scale intelligible. However, the consistency of the MSWS-12 walking scale and EDSS scores of NMOSD patients was not very good. The reason might be that NMOSD patients with isolated optic neuritis (ON) obtained high EDSS scores from high visual function scores (FS) instead of ambulation restriction, which was mainly reflected by the pyramidal and/or cerebellar FS. We found that MSWS-12 walking scale tended to be consistent with pyramidal FS scores.
Conclusion: Isolated optic neuritis might be a confounding factor when applying the MSWS-12 for NMOSD patients. MSWS-12 might be consistent with pyramidal FS scores in NMOSD patients.

P-93
Novel Real World Evidence from MSGo, a Digital Support Program for Secondary Progressive Multiple Sclerosis Patients in Australia using Siponimod
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Background: Siponimod is approved in Australia for adults with secondary progressive multiple sclerosis (SPMS). Prescreen requirements for siponimod include a CYP2C9 genotype test to determine maintenance dosing. An integrated digital platform, 'MSGo', was developed by Novartis and RxMx to support Healthcare Professionals and their multiple sclerosis patients.
Objective: Data derived exclusively from MSGo was utilised to explore the onboarding experience of siponimod patients in Australia.
Methods: The study enrolled >350 adults with SPMS registered in MSGo for siponimod in Australia. Primary endpoint is the average time for onboarding with key secondary endpoints addressing adherence and variables that influence onboarding and adherence.
Results: Final data extraction on April 20, 2022 included 368 patients (median age 59y). CYP2C9 genotype testing took a median of 19 days (95%CI 17-21) from registration and maintenance doses of 2mg (n=166) or 1mg (n=27) were initiated as per label recommendations. Mixture-cure modelling estimated 58% of patients will ever initiate siponimod, with median time to initiation of 56d (95%CI 47-59) from registration. Self-reporting of daily

treatment had a drop-off of ~25% after the first week of initiation; a continued decline in reporting over time limited assessment of adherence. The study uncovered the important role of care partners, with Cox regression analyses showing that SPMS patients who nominated a care partner were more likely to initiate (HR:2.1, 95%CI 1.5-3.0) and to continue self-reporting their daily medication (HR:2.2, 95%CI 1.3-3.7). A total of 90 patients discontinued the study; 48 prior to and 42 after siponimod exposure.

Conclusion: This study provides insights into siponimod onboarding for adults living with SPMS in Australia and demonstrates the impact of MSGo and care partner support during a period challenged by the COVID-19 pandemic.

Disclosures: Todd Hardy has received speaking fees or received honoraria for serving on advisory boards for Biogen, Merck, Teva, Novartis, Roche, Bristol-Myers Squibb and Sanofi-Genzyme and is Co-Editor of Advances in Clinical Neurosciences and Rehabilitation.

Patrick Aouad has received honoraria for research, speaking engagements, advisory board contributions and academic travel from Biogen, Sanofi Genzyme, Novartis, Merck, Roche and Teva and has received honoraria for research, speaking engagements, advisory board contributions and academic travel from Biogen, Sanofi Genzyme, Novartis, Merck, Roche and Teva.

Michael Barnett reports research grants from Genzyme-Sanofi, Novartis, Biogen, and Merck outside the submitted work and is a co-founder of RxMx and Research Director for the Sydney Neuroimaging Analysis Centre.

Stefan Blum has received speaking fees, travel assistance or received honoraria for serving on advisory boards from Merck, Biogen, Novartis, Bayer, Sanofi Genzyme, CSL, Roche.

Simon Broadley has accepted honoraria for attendance at advisory boards, speaker fees and sponsorship to attend scientific meetings from Novartis, Biogen-Idec, Sanofi-Genzyme, Roche, Bayer-Schering, Teva, CSL and Merck Serono and has been a principle investigator for clinical trials sponsored by Biogen-Idec, Novartis, Sanofi-Genzyme and ATARA.

Professor Carroll has been the recipient of travel assistance and honoraria for participation in industry sponsored meetings from, and has provided advice to Bayer Schering Pharma, Biogen-Idec, Novartis, Genzyme, Sanofi-Aventis, CSL,Teva, Merck and Celgene.

Denis Crimmins: nothing to disclose

Dayna Griffiths has received speaking fees or honoraria for serving on advisory boards for Merck, Novartis and Roche

Prof Suzanne Hodgkinson has received honoraria and support for conference travel and advisory board attendance from Merck, Biogen, Novartis, Atara, Roche and Sanofi.

Jeannette Lechner-Scott has received travel compensation from Biogen, Merck, Novartis; has been involved in clinical trials with Biogen, Novartis, Roche; her institution has received honoraria for talks and advisory board service from Biogen, Merck, Novartis, Roche

Andrew Lee: nothing to disclose

Ram Malhotra: nothing to disclose

Pamela McCombe has received sponsorship from Novartis, Teva, Sanofi and Biogen

John Parratt has received personal compensation for speaking engagements and conference travel from Biogen, Sanofi/Genzyme, Merck Serono and Roche and served on advisory boards

for Sanofi/Genzyme, Novartis, Biogen and Roche and is also a recipient of the Multiple sclerosis research Australia Neil and Norma Hill inaugural junior practitioner fellowship.
Chris Plummer and his Neurology Department have each been paid $AUD 1000 for setting up ethics and enrolment in the study for patients in the private and public clinic, respectively.
Anneke van der Walt served on advisory boards and receives unrestricted research grants from Novartis, Biogen, Merck and Roche She has received speaker's honoraria and travel support from Novartis, Roche, and Merck and receives grant support from the National Health and Medical Research Council of Australia and MS Research Australia.
Kate Martel and Rob Walker are employees of Novartis Pharmaceuticals Australia.

P-94

Characterizing the use of ofatumumab in a real world setting (EAFToS). Secondary Use of Data Study characterizing ofatumumab onboarding and utilization in relapsing multiple sclerosis patients using MSGo

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Background: Ofatumumab is approved in Australia for the treatment of adults with relapsing forms of multiple sclerosis (RMS). This study will analyze onboarding data, determine impact of baseline factors on compliance to treatment and identify the ofatumumab patient profile, through secondary use of data from the integrated digital patient support program MSGo
Objective: The primary objective is to characterise onboarding experience and utilization of ofatumumab of RMS patients in Australia. Secondary objectives are to describe profile of the patients initiating ofatumumab and evaluate demographics and prior therapy.
Methods: The data available in the MSGo patient support program was utilized to conduct a retrospective, longitudinal secondary use of data analysis. Key inclusion criteria include; adult patients diagnosed with RMS with Expanded Disability Status Scale of 5.5 or lower, treatment with ofatumumab and enrolment in the study via the MSGo digital support platform. The primary endpoint is the proportion of doses not completed within three days of the expected date during initiation and +/- 14 days during the first three months of maintenance. Key secondary endpoints will assess the profile of the patients initiating ofatumumab and evaluate patient demographics, prior therapy and whether treatment administrator influences compliance to treatment.
Results: Interim analysis was triggered on the 29th Jun 2022 and detailed study design and results will be presented at PACTRIMS 2022. Between 01April2021 and 29Jun2022, 235 de-identified patient MSGo platform data were extracted for analysis under the secondary use of data study protocol. Out of these 235, 18 patients discontinued therapy (8%). The design is novel, allowing any health care practitioner across Australia to participate in the study, thereby reflect-

ing the real-world prescribing setting for ofatumumab. This study has been approved by Ethics Committees in the public and private clinic settings, and will provide the first RWE for ofatumumab in Australia, giving local physicians insights into onboarding and adherence.
Conclusion: This study will use data derived exclusively from a digital support platform, and represents a novel approach for understanding quality use of medicines for MS in the real-world and is of value to both local and international medical community.
Disclsoures: TH- Todd Hardy has received speaking fees or received honoraria for serving on advisory boards for Biogen, Merck, Teva, Novartis, Roche, Bristol Myers Squibb and Sanofi
AVDW- Anneke van der Walt served on advisory boards for Novartis, Biogen, Merck and Roche and NervGen. She received unrestricted research grants from Novartis, Biogen, Merck and Roche. She is currently a co-Principal investigator on a co-sponsored observational study with Roche, evaluating a Roche-developed smartphone app, Floodlight-MS. She has received speaker's honoraria and travel support from Novartis, Roche, Biogen and Merck. She serves as the Chief operating Officer of the MSBase Foundation (not for profit). Her primary research support is from the National Health and Medical Research Council of Australia and MS Research Australia.
JB- have received speaker honoraria, scientific advisory board fees from Bayer, Biogen-Idec, Novartis, Sanofi-Aventis, Merck, Merck, Sanofi-Genzyme and Roche
RA- Works at Novartis Pharmaceuticals

POSTER SESSION - 10
Symptom Management; Rehabilitation Research and Strategies

P-95
Reflexology For Anxiety And Pain In Multiple Sclerosis
Alice Dias[1], Evanda Oliveira[1]
[1]Brazilian Association of Multiple Sclerosis (ABEM)
Background: Devastating symptoms adversely affect the daily lives of people with Multiple Sclerosis (MS). Reflexology is used for physical and mental relaxation.
Objective: The aim of this study was to show and analyze the perception of people with MS about the effects of reflexology on anxiety and pain.
Methods: Participated fourteen people with MS and complains of anxiety and pain, ten women and four men, aged 40 to 57 years, relapsing-remitting MS (n=8/57%), primary-progressive MS (n=5/36%), secondary-progressive MS (n=1/7%), and Kurtze Expanded Disability Status Scale (EDSS) between 1 and 5.5. Participants underwent ten Reflexology sessions held once a week. Reflexology was applied for 60 minutes and conducted on an ergonomic bed that could be positioned in a special room with controlled temperature and light. The technique promoted manual stimuli in specific points of the body, known as nerve plexuses, located in the hands, legs, feet, nose, skull and ears. Before and after the therapy period, all answered a structured questionnaire containing open questions about sociodemographic and physical and mental sensations.
Results: Eight participants had already undergone Reflexology before and were in maintenance therapy, six were beginners in the approach. They reported that conventional treatment did not

always alleviate anxiety and pain satisfactorily. Therefore, everyone turned to reflexology to help them with on physical, emotional and spiritual well-being. As a reason for seeking Reflexology, five (36%) mentioned anxiety and pain, three (21%) reported pain and one (7%) sought therapy to relax. All stated improvement after the sessions.
Conclusion: Reflexology, as a complementary health approach, has been shown to be effective as an anxiolytic and analgesic effect in the opinion of this group of people with MS, promoting relaxation and increasing well-being. There is a need for evidence.
Disclosures: There is no conflict of interest between the authors.

P-96
Effects of a Novel Probiotic Mixture Plus Vitamin D Supplementation on Patients with Multiple Sclerosis by Altering the Level of Serum Neurofilament Light and Modulation of T Helper Cytokines Profile
Saba Sadeghi Rashed[1], Nahid Beladi Moghadam[1], Mehran Ghaffari[1], Maryam Tajabadi Ebrahimi[2]
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[2]*Islamic Azad University Central Tehran Branch*
Background: Multiple sclerosis (MS) is a chronic inflammatory and immune-mediated disease. Numerous studies have shown that probiotics could synergize with current MS therapies. Probiotics can reduce inflammation by integrating the gastrointestinal tract barrier and reducing the leaking ability of endotoxins into the bloodstream.
Objective: This study was conducted to assess the effects of probiotic supplementation on the Level of Serum Neurofilament Light and T Helper Cytokines Profile.
Methods: This randomized, double-blind, placebo-controlled clinical trial was performed among 37 patients with MS. Participants were randomly assigned into two groups to receive either a probiotic capsule containing Bacillus coagulans, Lactobacillus acidophilus, Lactobacillus pracasei, Lactobacillus rhamnosus, Lactobacillus reuteri, and Bifidobacterium longum (2×109 colony-forming units/g each) or placebo for 12 weeks. we conducted ELISA to assess the effects of probiotic supplementation on the level of Neurofilament Light (NFL) and T Helper Cytokines Profile in the serum of MS patients.
Results: We found that in the Treatment group levels of IFN-g, IL-17, and TGF-b inflammatory cytokines were significantly reduced, and there was a gradual increase in the level of IL-10 cytokine compared to the placebo group. Furthermore, there is a significant reduction in the level of NFL in the Treatment group compared to the placebo control group.
Conclusion: Overall, probiotic supplementation for 12 weeks in patients with MS modulates the T helper cytokines profile and significantly reduced the NFL serum level.

PHARMA EDUCATIONAL SYMPOSIA

NOVARTIS SYMPOSIUM
Wednesday, 24 November 2022, 17:15 – 18:45
Transforming treatment strategy and B cell therapy in MS
Chairperson: Jin Nakahara (Keio University, Japan)

Evolving treatment strategy and role of B cells
Speaker: Yusei Miyazaki (Hokkaido Medical Center, Japan)

Practical aspects of using B cell therapy
Speaker: Michael Barnett (University of Sydney, Australia)
Early intervention with high efficacy therapy for relapsing forms of multiple sclerosis (MS) has gained increasing traction in the last 5 years, based upon a combination of clinical trial evidence, observational and registry-based data, and reassuring longer-term safety data. Indeed, the majority of patients with multiple sclerosis in Australia are now treated with high efficacy injectables or infusions. Of these, B cell depleting therapies are the most widely used. A structured approach to patient selection, pre-immunosuppression screening, treatment initiation, monitoring and compliance is required to optimise clinical outcomes for patients commencing these agents. While generally a smooth process, the patient treatment journey may be punctuated by inflexion points related to life events such as pregnancy and breastfeeding, vaccination requirements, treatment-related adverse events and change in disease status. Illustrated by relevant case histories, this presentation seeks to provide a framework for optimal care of patients commencing B cell depleting therapy, with a focus on ofatumumab.

MITSUBISHI TANABE SYMPOSIUM
Friday, 25 November 2022, 08:00 - 09:30
Chairperson: Ho Jin Kim (Department of Neurology, National Cancer Center, Goyang, Republic of Korea)

The role of B-lineage cells and the therapeutic mechanism of inebilizumab in NMOSD
Speaker: Yusei Miyazaki (Hokkaido Medical Center, Japan)
Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory disease of the central nervous system (CNS) clinically characterized by recurrent attacks of neurological symptoms. Most patients have anti-aquaporin (AQP)-4 autoantibody in their circulation, which upon breakdown of the blood-brain barrier, penetrate the CNS and mediate destructive inflammation. The precise mechanism of anti-AQP4 antibody production remains unknown, but the major role of circulating plasmablasts has been highlighted in recent studies as the

source of this autoantibody.
Inebilizumab is a humanized monoclonal antibody specific to CD19, which is expressed specifically on B-lineage cells including plasmablasts. In the N-MOmentum study, inebilizumab significantly suppressed NMOSD relapses compared with placebo, and the result has led to the approval of this drug in several countries. Interestingly, in addition to removing autoantibody-producing plasmablasts, paraclinical data obtained through the N-MOmentum study suggested therapeutic mechanisms that are independent of reducing anti-AQP4 antibody. In this lecture, I would like to discuss the antibody-dependent as well as -independent roles of B-lineage cells and the therapeutic mechanism of inebilizumab in NMOSD

Emerging therapies for AQP4-NMOSD: State of the Art
Speaker: Jin Nakahara (Keio Univ. in Japan)
Neuromyelitis optica-spectrum disorders (NMOSD) is an autoimmune disorder of the central nervous system medicated by pathogenic anti-aquaporin 4 (AQP4) antibodies, affecting approximately 1 to 5 per 100,000 people around the world. Once relapsed, only 20% of patients will recover fully, resulting in neurological sequelae in the vast majority. Therefore, it is no exaggeration to say that the relapse prevention determines the long-term prognosis and quality of life of NMOSD patients. For the purpose, immunosuppressive therapies (IST) and corticosteroids mainstayed until recently, albeit the fact that not a few patients still experienced relapses especially during the “cluster” period or the first 1-2 years after the last attack. Thankful to better understanding of pathophysiology underlying NMOSD, three molecular-targeted therapies were approved one after another since 2019, namely eculizumab, satralizumab and inebilizumab, targeting complement C5, IL-6 receptors and CD19+ B cells, respectively. While the efficacy of all three therapies appears to be reaching another dimension when compared to ordinal treatment options, different pros and cons exist for each of three therapies. In the lecture, State-of-the-Art of emerging therapies for AQP4-NMOSD will be reviewed, with a particular focus on ineblizumab.

ALEXION SYMPOSIUM
Friday, 25 November 2022, 16:30 – 18:00
Targeting complement in neuroimmunological diseases during the coronavirus pandemic
Generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD) are rare, disabling, autoimmune neuroinflammatory diseases in which uncontrolled activation of complement can lead to substantial neurodegeneration. The first approved therapies for anti-acetylcholine receptor antibody-positive (AChR+) gMG and anti-aquaporin-4 antibody-positive (AQP4+) NMOSD target the complement system and have proven efficacy in randomized controlled trials. Their approvals broaden the array of therapeutic options for these diseases. This symposium will provide an opportunity to engage in discussion with our expert faculty, who will consider the latest clinical data for the management of AChR+ gMG and AQP4+ NMOSD.

The terminal complement component 5 inhibitor, eculizumab, will be highlighted; real-world use of eculizumab will be discussed in addition to phase 3 clinical data, and valuable insights into the treatment journey of a Japanese patient with AQP4+ NMOSD will be shared.
Findings from large registries of patients with multiple sclerosis (MS) during the COVID-19 pandemic, including risk factors for poor COVID-19 outcomes and the effect of therapies on COVID-19 vaccine response, will also be presented. Similarities with findings from smaller studies in NMOSD and gMG will be discussed, and consideration will be given as to how learnings from MS treatment can be applied to the clinical management of NMOSD.
Throughout the session, the faculty will review the merits and limitations of broad immunosuppression and complement-system inhibition as therapeutic approaches in light of the experience gained during the global coronavirus pandemic. They will also discuss how complement-based therapies may be used to improve outcomes in patients with AChR+ gMG or AQP4+ NMOSD.
Chairperson: Jin Nakahara (Department of Neurology, Keio University School of Medicine, Tokyo, Japan)
Speakers:
Heinz Wiendl (Department of Neurology, University of Münster, Münster, Germany)
John Vissing (University of Copenhagen, Copenhagen, Denmark)

CHUGAI-ROCHE SYMPOSIUM
Saturday, 26 November 2022, 08:00 – 09:30
Right Treatment at the Right Time: Slowing Multiple Sclerosis Disease Progression and Improving Patient Outcomes
The treatment landscape for multiple sclerosis has rapidly evolved — offering the ability to improve outcomes and quality of life in patients with multiple sclerosis. This symposium aims to bring together a panel of leading experts to discuss the current landscape and unmet needs in multiple sclerosis in Asia and evaluate strategies for integrating the latest clinical and scientific updates into clinical practice.
Chairperson: Kazuo Fujihara
Speakers:
Kevin Tan (National Neuroscience Institute, Singapore)
Jason Burton (Perron Institute, Australia)