10th Congress of the Pan-Asian Committee for Treatment and Research in Multiple Sclerosis

November 23-25, 2017  Ho Chi Minh City, Vietnam
At Merck, we have a steadfast commitment to partnering with the healthcare community to improve the lives of the more than 2.3 million people around the world who have multiple sclerosis (MS).

Welcome Note 5
PACTRIMS Committee 6
Programme Overview 7
Invited Lecture 12
Ordinary Submission Abstracts 21
European Charcot Foundation Symposium 71
Pharma Educational Seminar Abstracts 72

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2018

BERLIN, GERMANY

34TH Congress of the European Committee for Treatment and Research in Multiple Sclerosis

www.ectrims-congress.eu
WELCOME NOTE

Dear Friends and Colleagues,

This year, PACTRIMS welcomes you to Ho Chi Minh City in Vietnam. We are excited to host our tenth PACTRIMS Congress in Vietnam. Ho Chi Minh City is Vietnam’s largest city and an important economic, trade, cultural and research centre, both within the country and in South-East Asia. We are even more excited to have the Vietnam neurological fraternity support PACTRIMS and we very much hope that it will be mutually beneficial. For those of you who have attended past PACTRIMS congresses, we welcome you again and for those of you who will be joining us for the first time, we hope you will find the experience enjoyable rewarding and informative.

For two decades there has been continuing significant advances in the understanding and treatment of MS and other inflammatory demyelinating diseases of the CNS. There has been much progress in imaging and understanding even though the cause and prevention remain elusive. Furthermore the accessibility of the communities in our region to many of the treatments remains excessively inequitable. As has been the situation in the past we still have much to learn and to attain for those who are affected and those who provide the care. PACTRIMS has also played a significant role in the education of healthcare professionals who provide care and advice to those with MS and related disorders in the region. The annual PACTRIMS meeting provides the opportunity for world class researchers and keynote speakers to address and update all those who participate.

Each PACTRIMS meeting is characterised by high quality science and teaching and facilitated delegate interaction which ensures delegates are brought up-to-date with the current information and practice. This year, we are pleased to present one of the most informative programmes developed by Prof Jun-ichi Kira and his Scientific Programme committee.

Some of the key lectures are from guests speakers such as Hanne Flinstad Harbo, Vanda A. Lennon, Jan Hillert, Noriko Isobe, Riwanti Estiasari, Fu-Dong Shi, Su-Hyun Kim, Ha Young Shin, Olga Ciccarelli, Jin Nakahara, Yaou Liu, Alan S. Verkman, Ichiro Nakashima and Ryo Yamasaki.

Also highly valued in previous PACTRIMS congresses is the opportunity afforded to delegates to be able to interact socially and informally in both evenings and at the day two lunch. Together with the Local Organising Committee we have an appropriate social programme for you to complement the Scientific sessions as well as the industry sponsored educational symposia. We know you will enjoy your stay in Ho Chi Minh City and the educational value of the tenth PACTRIMS meeting.

Finally, we offer our heartfelt thanks to those who have strived to prepare this meeting for us, especially Kays Asia, Pharma and industry and the PACTRIMS subcommittees. On behalf of them all, we wish you a most enjoyable, satisfying and memorable meeting.

Takahiko Saida                 William Carroll        Nguyen Thi Hung
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Dr Nguyen Thi Hoang Mai
Dr Nguyen Dinh Toan
Dr Tran Trung Thanh
## PROGRAMME OVERVIEW

**Thursday, 23 November 2017**

### Grand Ballroom

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:30-14:00</td>
<td>European Charcot Foundation Symposium&lt;br&gt;How to Improve Recovery in MS&lt;br&gt;Chairpersons: William Carroll (Australia)&lt;br&gt;1. Remyelination Strategy: Its Basic Science and Clinical Application - Hans-Peter Hartung (Germany)&lt;br&gt;2. Symptomatic Treatment - Kazuo Fujihara (Japan)&lt;br&gt;3. New Strategies for Rehabilitation - Giancarlo Comi (Italy)&lt;br&gt;4. Neuromodulation to Enhance Recovery in MS - Letizia Leocani (Italy)</td>
</tr>
<tr>
<td>14:00-14:30</td>
<td>Coffee Break</td>
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<tr>
<td>14:30-14:45</td>
<td>Opening Ceremony&lt;br&gt;1. Welcome Address by the Chairman, 2017 Local Organising Committee - Nguyen Thi Hung (Vietnam)&lt;br&gt;2. Opening Address by the President, PACTRIMS - Takahiko Saida (Japan)&lt;br&gt;3. Special Remarks by the Vice Minister of Health, Ministry of Health (Vietnam) - Le Quang Cuong (Vietnam)</td>
</tr>
<tr>
<td>15:55-16:05</td>
<td>Coffee Break</td>
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<tr>
<td>17:15-17:30</td>
<td>Coffee Break</td>
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<tr>
<td>17:30-19:00</td>
<td>Merck Sponsored Symposium&lt;br&gt;Changing the Paradigm in the Treatment of MS in Asia Pacific</td>
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<tr>
<td>19:30-21:00</td>
<td>Welcome Reception @ Purple Jade, 1F, InterContinental Asiana Saigon</td>
</tr>
</tbody>
</table>
# PROGRAMME OVERVIEW

## Friday, 24 November 2017

### Grand Ballroom

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:30-10:00</td>
<td><strong>Sanofi Genzyme Sponsored Symposium</strong>&lt;br&gt;New Treatment Options for Multiple Sclerosis – How to Find the Right Approach for Each Patient?</td>
</tr>
<tr>
<td>10:00-10:30</td>
<td><strong>Coffee Break</strong></td>
</tr>
<tr>
<td>10:30-12:30</td>
<td><strong>Oral Presentation-1 (10:30-11:15)</strong>&lt;br&gt;Chairperson: Alvin Seah (Singapore)&lt;br&gt;(O-1) Contribution of Cortical Lesions to Cognitive Dysfunction in Japanese Patients with Multiple Sclerosis&lt;br&gt;- Koji Shinoda (Japan)&lt;br&gt;(O-2) Narrowband UVB Phototherapy for Clinically Isolated Syndrome: Delivering the Benefits of All UVB-Induced Molecules&lt;br&gt;- Marzena Fabis-Pedrini (Australia)&lt;br&gt;(O-3) Restoration of Regulatory B Cell Deficiency Following Alemtuzumab Therapy in Patients with Active Multiple Sclerosis&lt;br&gt;- Yeseul Kim (Republic of Korea)</td>
</tr>
<tr>
<td>11:15-12:00</td>
<td><strong>Oral Presentation-2 (11:15-12:00)</strong>&lt;br&gt;Chairperson: Byung-Jo Kim (Republic of Korea)&lt;br&gt;(O-4) Nationwide Epidemiological Study of Neuromyelitis Optica in Japan&lt;br&gt;- Katsuichi Miyamoto (Japan)&lt;br&gt;(O-5) Intestinal Microbiota Distinguish Neuromyelitis Optica Patients from Healthy Individuals in a Chinese Pilot Study&lt;br&gt;- Jun Li Gong (China)&lt;br&gt;(O-6) Bidirectional Degeneration in The Visual Pathway in Neuromyelitis Optica Spectrum Disorder (NMOSD)&lt;br&gt;- Decai Tian (China)</td>
</tr>
<tr>
<td>12:00-12:30</td>
<td><strong>Two Minute Oral Presentation of Selected Posters (12:00-12:30)</strong>&lt;br&gt;Chairperson: Makoto Matsui (Japan)&lt;br&gt;(O-7) Brain Volume Loss Is Present in Japanese Patients with Multiple Sclerosis with No Evidence of Disease Activity&lt;br&gt;- Hiroaki Yokote (Japan)&lt;br&gt;(O-8) Dynamic Expression of Circulating MicroRNA-155 in Plasma of Patients with Multiple Sclerosis&lt;br&gt;- Qin Bing (China)&lt;br&gt;(O-9) Deviated Repertoire of γδ T Cells is Associated with Disease Severity of Multiple Sclerosis&lt;br&gt;- Maimaitijiang Guazhi (China)&lt;br&gt;(O-10) De Novo Trigeminal Neuralgia Induced by Dalfampridine (4-aminopyridine) - 3 Cases&lt;br&gt;- Mehmet Ozmenoglu (Turkey)&lt;br&gt;(O-11) Neuromyelitis Optica: An 18-case Experience at Ho Chi Minh City University Medical Center in Vietnam&lt;br&gt;- Thi Vu Thuy (Vietnam)&lt;br&gt;(O-12) Ethnic Differences in Clinical Manifestation of Neuromyelitis Optica Spectrum Disorder&lt;br&gt;- Su-Hyun Kim (Republic of Korea)&lt;br&gt;(O-13) Discrimination of Spinal Cord Sarcoidosis from Neuromyelitis Optica Spectrum Disorder or Spondylotic Myelopathy&lt;br&gt;- Hiroshi Kuroda (Japan)&lt;br&gt;(O-14) Different Features between Pediatric-Onset and Adult-Onset Patients Who Are Seropositive For MOG-IgG: A Multicenter Study in South China&lt;br&gt;- Lu Chen (China)&lt;br&gt;(O-15) Cerebrospinal Fluid-Actin Related Protein 2/3 Complex Subunit 4 as an Astrocytic Foot Process Damage Marker of Aquaporin-4-IgG Positive Neuromyelitis Optica Spectrum Disorders&lt;br&gt;- Shuhei Nishiyama (Japan)&lt;br&gt;(O-16) Choroidal Plexitis in Neuromyelitis Optica Spectrum Disorder&lt;br&gt;- YeoJin Oh (Republic of Korea)&lt;br&gt;(O-17) Oligodendroglia-Specific Connexin 47 Deletion Induced Relapse-Remitting EAE Model Mice&lt;br&gt;- Ryo Yamasaki (Japan)</td>
</tr>
<tr>
<td>12:30-13:30</td>
<td><strong>Lunch at Market 39, Lobby &amp; Purple Jade, 1F, InterContinental Asiana Saigon &amp; Poster Viewing</strong></td>
</tr>
</tbody>
</table>
### 10th PACTRIMS Anniversary Lecture
Chairperson: Helmut Butzkueven (Australia)
The Impact of Registries for MS and NMOSD Research and Care
- Jan Hillert (Sweden)

### 14:10-14:20
**Coffee Break**

### 14:20-15:20
**Presidential Symposium: Main Symposium-2**  
Therapeutics and Health Care Policies for MS and NMOSD in Asia: Present Status and Road Blocks to Change  
Chairpersons: Le Van Tuan (Vietnam) and Ching-Piao Tsai (Taiwan)
1. Multiple Sclerosis: Challenge on Diagnostic and Management in Vietnam  
   - Nguyen Thi Hung (Vietnam)
2. Therapeutics and Health Care Policies for MS and NMOSD in Indonesia  
   - Riwanti Estiasari (Indonesia)
3. Therapeutics and Health Care Policies for MS and NMOSD in Malaysia  
   - Shanithi Viswanathan (Malaysia)
4. Therapeutics and Health Care Policies for MS and NMOSD in Asia: Present Status and Road Blocks to Change - From China  
   - Fu-Dong Shi (China)

### 15:20-15:50
**Coffee Break & Poster Viewing**

### 15:50-17:20
**PACTRIMS Teaching Session-1: Main Symposium-4**  
Differential Diagnosis for MS/NMOSD/Autoimmune Encephalitis/Other Mimickers: An Interactive Case Discussion  
Chairpersons: Ho Jin Kim (Republic of Korea) and Naraporn Prayoonwiwat (Thailand)
1. Autoimmune Encephalitis  
   - Lekha Pandit (India)
2. Neuro-Behcet Disease  
   - Ha Young Shin (Republic of Korea)
3. Anti-MOG Antibody Syndrome in Thai Patients  
   - Sasitorn Siritho (Thailand)
4. **(O-18)** Case Presentation from The Ordinary Submissions-1: Susac’s Syndrome in A Patient Misdiagnosed with Multiple Sclerosis  
   - Jong Sze Chin (Singapore)
5. **(O-19)** Case Presentation from The Ordinary Submissions-2: Fingolimod-Associated PML with Mild Immune Reconstitution Inflammatory Syndrome in Multiple Sclerosis  
   - Tatsuro Misu (Japan)

### 18:30-22:00
**Presidential Dinner @ Cham Charm**
### Friday, 24 November 2017

**Phu Quoc (Breakout Session)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 14:20-15:20| **Main Symposium-3**  
**Imaging MS and NMO Lesions by Conventional MRI and Novel Methodologies**  
**Part 1. Imaging MS and NMO Lesions by Conventional MRI**  
Chairpersons: Ernest Willoughby (New Zealand) and Jen-Jen Su (Taiwan)  
1. Keynote Lecture: Imaging MS Lesions and Treatment Effects by Conventional MRI  
   - Ernst-Wilhelm Radue (Switzerland)  
2. Imaging NMO Lesions and Treatment Effects by Conventional MRI  
   - Su-Hyun Kim (Republic of Korea) |
| 15:20-15:50| **Coffee Break & Poster Viewing**                                      |
| 15:50-17:20| **Main Symposium-3**  
**Imaging MS and NMO Lesions by Conventional MRI and Novel Methodologies**  
**Part 2. Imaging Tissue Damage and Repair in MS and NMO by Novel Methodologies**  
Chairpersons: Michael Barnett (Australia) and Yaou Liu (China)  
3. Keynote Lecture: Imaging Tissue Damage and Degeneration in MS and NMO  
   - Olga Ciccarelli (UK)  
4. Imaging Remyelination by q-Space Myelin Map in MS and NMO  
   - Jin Nakahara (Japan)  
5. Imaging Plasticity in MS and NMO  
   - Yaou Liu (China) |
## PROGRAMME OVERVIEW

### Saturday 25 November 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 8:30-10:00 | **PACTRIMS Teaching Session-2: Main Symposium-5**  
**Neuroimaging Teaching Course: How to Make Good Use of MRI in Clinical Practice for CNS Demyelinating Disease**  
Chairpersons: Anthony Traboulsee (Canada) and Joyce Joseph (Malaysia)  
1. How to Use MRI Diagnostic Criteria for MS and NMOSD  
   - Frederik Barkhof (The Netherlands)  
2. How to Use MRI for Differential Diagnosis of MS and NMOSD  
   - Olga Ciccarelli (UK)  
3. How to Use MRI For Monitoring Treatment Effects in MS and NMOSD  
   - Ernst-Wilhelm Radue (Switzerland) |
| 10:00-10:30 | Coffee Break & Poster Viewing                                                                 |
| 10:30-11:40 | **Main Symposium-6**  
**Understanding Autoantibody-mediated Neuro-inflammation**  
**Part 1. Autoimmunity Against Astrocytes**  
Chairpersons: Akio Suzumura (Japan) and Trevor Kilpatrick (Australia)  
1. Keynote Lecture: A Novel Mechanism of AQP4 Antibody-mediated Demyelination  
   - Alan S. Verkman (USA)  
2. Mechanism and Spectrum of Autoimmune GFAP Meningoencephalomyelitis  
   - Vanda A. Lennon (USA) |
| 11:40-12:00 | Coffee Break                                                                                     |
| 12:00-13:00 | **Main Symposium-6**  
**Understanding Autoantibody-mediated Neuro-inflammation**  
**Part 2. Autoimmunity Against Myelinating Cells**  
Chairpersons: Byoung Joon Kim (Republic of Korea) and Kevin Tan (Singapore)  
1. Mechanism and Spectrum of MOG Antibody-mediated Encephalomyelitis  
2. IgG4 Anti-neurofascin 155 Antibody in Peripheral and Central Demyelination  
   - Ichiro Nakashima (Japan)  
3. Closing and Award Ceremony  
   1. Award Ceremony  
      - Jun-ichi Kira (Japan)  
   2. Closing Remarks by the Vice President, PACTRIMS  
      - William Carroll (Australia) |
How Genes and Germs Influence CNS Inflammation?

Part 1. How Genetic Factors Influence Neuroinflammation?

L-1
From Genetic Association to Functional Studies in MS
Hanne Flinstad Harbo (Norway)
Oslo University Hospital and University of Oslo, Oslo, Norway

Multiple Sclerosis (MS) is a complex, inflammatory and demyelinating disease of the central nervous system (CNS), and both genetic and environmental factors are implicated in disease development. Associations with susceptibility loci in the Human Leukocyte Antigen (HLA) region were identified already in the 1970's, and more recently, large-scale genome screens have revealed that more than 200 non-HLA single nucleotide polymorphisms (SNPs) are also associated with MS risk. An overrepresentation of immunologically relevant genes, in particular genes important for T helper cell differentiation, has been observed. Still, there is sparse knowledge about the functional mechanisms that underlie the associations with the genetic risk variants in MS. Further studies need to consider the genetic architecture of the region surrounding the most highly associated SNPs, the molecular pathways and cell types that are involved and the epigenetic factors which might trigger MS onset or be of importance for development of different MS phenotypes. This includes MS phenotypes identified by MRI scanning of CNS and biomarkers in body fluids, as well as treatment responses to the growing number of effective immune-modulatory treatments. Through such studies, methods for personalized treatment and follow-up of MS patients can probably soon be established.

L-2
Genetic Risk Factors for MS in Non-Caucasian Populations
Noriko Isobe (Japan)
Department of Neurological Therapeutics, Kyushu University, Fukuoka, Japan

Multiple sclerosis (MS) pathogenesis is known to result from both genetic and environmental factors. Genome-wide association studies (GWAS) have contributed considerably to the understanding of MS susceptibility through the identification of genetic variants influencing risk and quantification of their effects. Immunologically relevant genes, including epistatic signals across the major histocompatibility complex (MHC) region, dominate the genomic signature of MS. Although most of the GWAS have been conducted in populations of European origin, it is also important to assess in other populations the risk factors for MS susceptibility, due to the following reasons. First, an increase of MS incidence has been reported not only in European populations but also in populations of African origin and in Asians including Japanese. Studies on common risk factors of genetics, environment or interactions between genetics and environment are crucial to reveal the contributing factors for increasing MS incidence in females. Second, taking advantages of different haplotype block patterns across populations, we could narrow down the genetic regions with possible causal variants for the common susceptibility loci across populations. Finally, it is well-known that MS severity is different by populations or genetic backgrounds. Multi-populational studies will provide us some clues which genetic loci, environmental factors, or both combinations may contribute for the distinct disease phenotypes. In this talk, I will describe important genetic studies of MS in non-Caucasian populations, such as African Americans and Asians, including the latest results of an ongoing GWAS in Japanese population, and discuss the implication for disease incidence and future directions.

Part 2. How Environmental Factors Influence Neuroinflammation?

L-3
The Microbiota and MS
Allan Kermode (Australia)
Centre for Neuromuscular and Neurological Disorders, Pemom Institute, University of WA, Australia; Institute of Immunology and Infectious Diseases, Murdoch University, Australia; Department of Neurology, Sir Charles Gairdner Hospital, Perth, Australia; Sun Yat Sen University, China

All humans are colonized by a diverse range of commensal, symbiotic and pathogenic micro-organisms, termed the microbiota. These include bacteria, fungi, archaea and viruses. The human microbiome refers to their genomes. Multiple lines of evidence implicate the gastrointestinal microbiota as playing an important role in the development and modulation of the human immune system as well as a variety of metabolic roles. In parallel with the basic science exploring potential mechanisms whereby the microbiota could be implicated in disease causation, accumulating epidemiological research has demonstrated unequivocal associations between a wide spectrum of human illnesses and variations in the microbiota. This lecture will explain the function and nature of the microbiota, the biological pathways by which the microbiota fundamentally influence the development and regulation of the immune system, provide a broad overview of the emerging technologies used to study the microbiome, and emphasise their existing and growing evidence for the role of the microbiome in MS and the potentials for therapeutic manipulation.

L-4
Underlying Mechanisms for How Environmental Allergens Modulate Neuroinflammation
Jun-ichi Kira (Japan)
Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Allergy or atopy is defined as a condition with exaggerated IgE responses to universal environmental allergens. Allergy is mediated by T helper type 2 (Th2) cells. In contrast, multiple sclerosis (MS) is postulated to be produced by autoreactive Th1 and/or Th17 cells. As Th1/Th2 cells are mutually suppressive, allergy is not considered to aggravate MS, despite the rapid parallel increases in the prevalences of MS and allergy in advanced countries. Although allergy in peripheral tissues is not considered to induce inflammation in tissues of the central nervous system (CNS), which is closed to the external environment, we previously
reported the emergence of a peculiar form of myelitis presenting with persistent dysesthesia and neuropathic pain (NeP) as cardinal symptoms in patients with atopic disorders, such as atopic dermatitis, allergic rhinitis, and atopic asthma. Nationwide surveys repeatedly revealed widespread occurrence of this form of myelitis in Japan, and similar cases were reported worldwide, including in Western countries. Neuropathological studies on biopsied and autopsied spinal cord lesions from patients with atopy and persistent myelitis revealed active inflammation with loss of myelin and axons, accompanied by varying degrees of eosinophil infiltration and microglial and astroglial activation. Thus, the term “atopic myelitis” (AM) was introduced, together with appropriate diagnostic criteria. However, the precise mechanisms for how allergy induces CNS inflammation remain to be established.

We recently reported that atopic mice exhibited widespread activation of microglia and astroglia in their spinal cord compared with non-atopic mice, and displayed NeP. In atopic mice, the blood–brain barrier also became leaky. Microarray analysis of isolated microglia revealed marked upregulation of endothelin receptor type B (EDNRB) in atopic mice. EDNRB expression was enhanced in microglia and astroglia of atopic mice, while endothelin-1, an EDNRB ligand, was increased in their serum, lungs, and epidemis. EDNRB antagonist BQ788 abolished glial activation and allodynia. We also found increased serum endothelin-1 and activation of spinal microglia and astroglia with EDNRB upregulation in AM patients with NeP. Therefore, allergic/atopic inflammation induces diffuse glial activation, and influences the nociceptive system via the EDNRB pathway. When atopic mice were immunized with myelin oligodendrocyte glycoprotein peptide 35-55, experimental autoimmune encephalomyelitis (EAE) developed earlier and was more severe than that in non-atopic mice, while exacerbation of EAE was ameliorated by BQ788 administration.

As allergy has repeatedly been identified as a significant risk factor for developmental neurosensory disorders, such as autism spectrum disorder (ASD), we examined the effects of maternal allergy in mice on the behavior of their offspring. We found that allergy induction in female mice during pregnancy induced ASD-like behaviors in their male offspring. Furthermore, these male offspring showed microglial activation and decreased post-synaptic protein amounts in their hippocampus, suggesting that maternal atopy in mice induces microglial synaptopathy in their offspring.

We screened for autoantibodies that selectively reacted with mouse unmyelinated c-fiber type dorsal root ganglion (DRG) neurons by tissue-based indirect immunofluorescence assay (IFA) using sera from 110 NeP patients with various inflammatory and allergic neurologic diseases, including AM, MS, and neuromyelitits. IgG2 autoantibodies that selectively bound to isolectin B4- and P2X3-positive unmyelinated c-fiber type DRG small neurons and nerve terminals in the dorsal horns were detected by IFA in 11 NeP patients (10%), but no control subjects without NeP. Western blotting of extracted DRG proteins revealed a common immunoreactive band (approximately 220 kDa), which was identified as plexin D1 by liquid chromatography-tandem mass spectrometry of immunoprecipitates. A cell-based IFA using HeLa cells expressing plexin D1 with and without a small interfering RNA (RNAi) for PLXND1 revealed that the IgG signals in NeP patients were significantly decreased after PLXND1 knockdown, confirming plexin D1 as a relevant autoantigen. Plexin D1 existed as plexin D1 isoforms in microglia and astroglia, and was confirmed as plexin D1 by liquid chromatography-tandem mass spectrometry of immunoprecipitates. A cell-based IFA using HeLa cells expressing plexin D1 with and without a small interfering RNA (RNAi) for PLXND1 revealed that the IgG signals in NeP patients were significantly decreased after PLXND1 knockdown, confirming plexin D1 as a relevant autoantigen. Plexin D1 existed as plexin D1 isoforms in microglia and astroglia, and was confirmed as plexin D1 by liquid chromatography-tandem mass spectrometry of immunoprecipitates. A cell-based IFA using HeLa cells expressing plexin D1 with and without a small interfering RNA (RNAi) for PLXND1 revealed that the IgG signals in NeP patients were significantly decreased after PLXND1 knockdown, confirming plexin D1 as a relevant autoantigen. Plexin D1 existed as plexin D1 isoforms in microglia and astroglia, and was confirmed as plexin D1 by liquid chromatography-tandem mass spectrometry of immunoprecipitates. A cell-based IFA using HeLa cells expressing plexin D1 with and without a small interfering RNA (RNAi) for PLXND1 revealed that the IgG signals in NeP patients were significantly decreased after PLXND1 knockdown, confirming plexin D1 as a relevant autoantigen. Plexin D1 existed as plexin D1 isoforms in microglia and astroglia, and was confirmed as plexin D1 by liquid chromatography-tandem mass spectrometry of immunoprecipitates. A cell-based IFA using HeLa cells expressing plexin D1 with and without a small interfering RNA (RNAi) for PLXND1 revealed that the IgG signals in NeP patients were significantly decreased after PLXND1 knockdown, confirming plexin D1 as a relevant autoantigen. Plexin D1 existed as plexin D1 isoforms in microglia and astroglia, and was confirmed as plexin D1 by liquid chromatography-tandem mass spectrometry of immunoprecipitates. A cell-based IFA using HeLa cells expressing plexin D1 with and without a small interfering RNA (RNAi) for PLXND1 revealed that the IgG signals in NeP patients were significantly decreased after PLXND1 knockdown, confirming plexin D1 as a relevant autoantigen. Plexin D1 existed as plexin D1 isoforms in microglia and astroglia, and was confirmed as plexin D1 by liquid chromatography-tandem mass spectrometry of immunoprecipitates. A cell-based IFA using HeLa cells expressing plexin D1 with and without a small interfering
addressed and new knowledge stemming from the analysis of such data.
In summary, it is the firm belief of the presenter that patient registers will be developed greatly in the coming decades and that they will shape the way by which clinical work is both being performed as well as documented. For chronic disorders affecting patients for decades like MS and NMOSD, this will be particularly important and rewarding.

Presidential Symposium: Main Symposium-2

Therapeutics and Health Care Policies for MS and NMOSD in Asia: Present Status and Road Blocks to Change

L-6
Multiple Sclerosis: Challenge on Diagnostic and Management in Vietnam
Nguyen Thi Hung (Vietnam)
Frano-Vietnamese Hospital; Pham Ngoc Thach Medical University, Ho Chi Minh City, Vietnam

Multiple sclerosis (MS) is an uncommon neurological disease in Vietnam compared with Stroke, CNS Infection, Epilepsia and Traumatic Brain Injury. The influence of French medicine for long time made Vietnamese Neurologists in big city quite familiar with the clinical diagnosis of MS but not rarely, this diagnosis was overused regarding other medical conditions such as acute myelitis, granulomatous involvement of CNS, Immunological Encephalomyelitis.

Presently, there is no study yet about prevalence and incidence of MS and NMOSD in Vietnamese community but it probably has the same statistical data as in other South-east Asia Countries with 2-3 / 105 people with high ratio of female to male. The barriers for research and management of MS can be explained by many reasons: Health care budget is limited so rare diseases like MS is not a priority, shortage of specialists to conduct the study on MS and make the right diagnosis and management in daily practice while some other specialty had significant progress in technology (stroke with arterial thrombectomy, deep brain stimulation for Parkinson’s disease). The MS patients have no opportunity to access the new modalities of treatment and were not well educated about this diseases, MRI is not available in rural area to support the clinical diagnosis.

The most common diagnostic criteria used before was from Poser and now is modified Mac Donald Criteria which rely most on MRI, the most common diagnostic criteria used before was from Poser diagnosis.

In conclusion, Health care providers should change the focus to support not only common neurological conditions but also some rare diseases which impact seriously on the quality of life of the patients. The government should provide health care support to MS patients in order to get access to new modalities of treatment.

L-7
Therapeutics and Health Care Policies for MS and NMOSD in Indonesia
Riwanti Estiasari (Indonesia)

Department of Neurology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital Jakarta, Jakarta, Indonesia

MS and NMO in Indonesia are still considered as a rare disease. However, the number of cases continues to increase every year. This is due to the increasing awareness of health workers and the community of MS and NMO diseases.

The national health system in Indonesia (BPJS) is currently sufficient to facilitate the diagnosis process of MS and NMO as it includes both brain and spinal cord MRI examination. Routine analysis of brain fluids and some routine blood tests are also included. However, specific examinations such as oligo clonal band and aquaporin 4 antibodies are still very limited. The referral system and Indonesian geographical situations often made the diagnosis process slower since patient have to wait to get proper para clinical examination.

In treatment, Indonesia only have 2 type of Disease modifying drug but the used is very limited due to the high cost and the Disease Modifying Drug is not covered by National health insurance. NMOSD patient has better situations since several type of immunosuppressant and plasma exchange are covered by the National health Insurance but not all referral hospital has the PE equipment.

Indonesia National Health Insurance is very helpful for MS and NMOSD patients for the diagnosis process but in MS treatment, it need to broaden the coverage including DMD for MS.
treatments as well as an improvement in accessibility to neuroimaging in the various states in Malaysia. A national clinical practice guideline on management of MS launched in 2016 with echo trainings throughout the country in a small way has also improved knowledge and awareness nationally. Nevertheless, numerous challenges still exist in terms of the burden on a single payer system (the government), the need for multi-payer systems and involvement of non-governmental associations including insurance systems. Accessibility and longterm sustainability issues for a chronic disease exists. Furthermore, pharmaceutical companies need to be engaged and realize the challenges of resource limited settings for a rare disease. As such drug development needs to develop low cost DMT’s/immunosuppressants, have realistic costs for patients in countries which are not be able to afford these drugs and encourage generic drug development with bioequivalence studies. Self payers by individual patients in Malaysia is rare though this may be possible through patient advocacy and tax cuts. There is a need too for specialized MS/NMOSD nurses. Patient advocacy through the Multiple Sclerosis society should continue to be encouraged to improve accessibility to treatment and there is a glaring need for a patient advocacy group for NMOSD tied in with international NMOSD societies to improve awareness, knowledge and funding for this disease. This talk focusses on these issues.

Main Symposium-3

Imaging MS and NMO Lesions by Conventional MRI and Novel Methodologies

Part 1. Imaging MS and NMO Lesions by Conventional MRI

L-9

Imaging MS and NMO Lesions by Conventional MRI

Fu-Dong Shi (China)
Department of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin, China

Diagnostic and therapeutic regimen for MS and NMOSD has been challenging for neurologists in China. Demographic data on MS and NMOSD prevalence and incidence are still lacking in that current data are only based on relatively small populations from tertiary hospitals. Like other Asian countries, the incidence of NMOSD seems higher than compared to Caucasian populations. The challenge for diagnosing MS and NMOSD mostly stem from lack of nation-wide standardized laboratory tests for oligoclonal band, IgG index, and/or AQP-4 antibody, etc. This is particularly the case for clinically isolated syndrome when patients do not exhibit clinical manifestations and neuroimaging features that fulfill the diagnostic criteria for MS and NMOSD.

There are currently no FDA-approved disease modifying drugs (DMTs) for preventing relapses of MS in China. Management of NMOSD is even more challenging. Expensiveness of monoclonal antibodies and other disease modifying medications as well as experience of neurologists with these medications become top two barriers for Chinese patients. Many Centers adopt azathiprine, mycophenolate mofetil to prevent relapses. In some cases, patients are left untreated between relapses; In other cases, patients are advised to purchase fingolimod and other medications from Hong Kong or overseas. Long-term follow ups on patients are rarely done in many Centers in part due to challenges of maintaining care under sufficient number of Neurologists. A few centers have used Rituximab for NMOSD and some cases of MS with active MRI lesions, after beneficial report of modified dosages of Rituximab based on Chinese patients. Recently, a promising outcome of a pilot study of targeting plasma cells with a proteasome inhibitor, Bortezumib, in highly relapsing NMOSD patients was reported. Outcomes of two-year follow-up in 10 NMO patients treated with autologous MSC suggest patients may benefit from these therapies at least during the first year after cell infusion. Despite these challenges, Chinese neuroimmunologists have made seminal contributions to basic and clinical science in this area. They recognized several non-motor dysfunctions such as sleep and olfactory dysfunctions. They have proposed an intermediate phenotype between MS and NMOSD based on the presence of autoantibodies against MOG and AQP4. Mechanisms of impaired neurorepair in MS/EAE; and principles of differential expression of complementary inhibiting protein CDS9 govern emergence of autoimmunity to astrocyte have also been elucidated by groups in China.

The outlook of managements of MS/NMO patients in China ultimately depends on government initiatives, i.e. to cover DMD in national medical insurance system, recruitment of more neurologists to the field, and willingness of current neuroimmunologists to collaborate between themselves and with the international community.

L-10

Imaging MS Lesions and Treatment Effects by Conventional MRI

Ernst-Wilhelm Radue (Switzerland)
Biomedical Research and Training (BMRT) GmbH, Affiliated with University Hospital Basel, Basel, Switzerland

In Neuroradiology, highly sophisticated methods such as Magnetic Resonance Imaging (MRI) are implemented to investigate different entities of the central nervous system and to acquire miscellaneous images where tissues display varying degrees of characteristic signal intensity or brightness. MR images represent, in addition to the clinical and the neurophysiology assessment, one of the most important factors in the neurological evaluation and diagnosis. MRI, compared to X-ray, CT and ultrasound, produces clearer images on tissues, body fluids and fat. This lecture will introduce interpretation guidelines and protocols for the imaging of MS lesions for the audience to better understand images and improve diagnosis.

L-11

Imaging NMOSD Lesions and Treatment Effects by Conventional MRI

Su-Hyun Kim (Republic of Korea)
Department of Neurology, Research Institute and Hospital of National Cancer Center, Republic of Korea

Neuromyelitis optica spectrum disorder (NMOSD) is a rare severe central nervous system inflammatory disorder, characterized by attack of optic neuritis, longitudinally extensive transverse myelitis, or area postrema syndrome. While its pathogenesis has not been
fully elucidated, NMOSD is now considered an anti-aquaporin-4 (AQP4) antibody-mediated autoimmune astrocytopathic disease, in which the clinical and therapeutic response is distinct from that in multiple sclerosis (MS). Timely differentiation of NMOSD from MS is imperative for determining both prognosis and treatment strategy. In this regard, magnetic resonance imaging (MRI) is becoming an important tool in the differential diagnosis of NMOSD from MS. Brain lesions are present in about half of patients with NMOSD and can show characteristic patterns, including lesions in the dorsal medulla/area postrema, the peripendymal regions in the brainstem and diencephalic structures, or the cerebral hemispheres, or long diffuse corpus callosum or corticospinal tract lesions. In contrast, inferior temporal lobe, U-fiber, or Dawson’s finger lesions are suggestive of MS. Longitudinal extensive transverse myelitis (LETM) is characteristic of NMOSD, but recent studies have shown that 14%–15% of NMOSD myelitis episodes are associated with lesions < 3 vertebral segments. Other MRI spinal cord features have also been suggested to be involved in NMOSD, including T2-hyperintense bright spotty lesions and ring-enhancing lesions. In contrast to MS where sub-clinical MRI activity is common during inter-relapse, current clinical and imaging evidence suggests that subclinical activity between attacks is absent in NMOSD and thus MRI monitoring during clinical remission does not appear to be as useful as it is in MS. On the other hand, there has been increasing evidence for occult brain injury in normal appearing brains on conventional MRI in NMOSD, though the existence of diffuse injury is disputed and its mechanisms remains unclear. The degree of occult brain injury appears to be less widespread and severe in NMOSD compared to MS; imaging studies in NMOSD are still at an early stage. Further prospective, qualitative, and longitudinal follow-up imaging studies in larger numbers of patients with NMOSD are required to improve the accuracy of diagnosis, particularly in anti-AQP4 antibody negative patients, monitor disease activity, and improve understanding of disease pathogenesis.

Part 2. Imaging Tissue Damage and Repair in MS and NMOSD by Novel Methodologies

L-12 Imaging Tissue Damage and Degeneration in MS and NMOSD
Olga Ciccarelli (UK)
University College London, London, UK

Nonconventional imaging techniques are more specific for pathological changes than conventional MRI and may provide insight into the pathogenic processes in MS and NMOSD. These techniques include proton MR spectroscopy, diffusion tensor imaging, magnetization transfer imaging, quantitative MR volumetry, and ultrahigh-field strength MRI. The number of studies comparing MS to NMOSD is limited, and findings often did not include the information about AQP4-Ab positivity. Overall, the application of these techniques to patient studies has demonstrated that tissue damage in MS occurs within lesions and is widespread outside lesions. In NMOSD, tissue microstructural damage, as detected by nonconventional techniques, may be seen in the normal-appearing tissue outside lesions, but it seems to be secondary to the prevalent damage occurring in the optic nerve and corticospinal tract. Tissue destruction in NMOSD lesions seems to be greater than that occurring in MS lesions. In NMOSD, the tissue degeneration in the white matter is greater than that in the grey matter. NMO patients seem to show predominant spinal cord atrophy, whilst MS patients show greater whole brain atrophy and grey matter atrophy, especially in the progressive phase of the disease. A recent study has suggested that cord atrophy in NMOSD may occur even in the absence of spinal cord lesions. Deep grey matter atrophy and thalamic microstructural changes appear to be more extensive in MS than NMOSD.

A few studies using advanced imaging have suggested that, in both diseases, there are correlations between tissue damage, as detected by imaging measures, including atrophy and diffusion abnormalities, and physical and cognitive disability.

L-13 Imaging Remyelination by q-Space Myelin Map in MS and NMOSD
Jin Nakahara (Japan)
Department of Neurology, Keio University School of Medicine, Tokyo, Japan

MRI has become a vital tool in modern neurology, especially for the diagnosis and the treatment monitoring of inflammatory CNS diseases including MS and NMOSD. For instance, T2 lesions are considered as “demyelinating lesions” in MS according to the McDonald criteria, whereas the similar T2 lesions are considered to be representing “astrocytopathic lesions” in NMOSD according to the IPND diagnostic criteria. In theory, however, T2 signals are neither specific to demyelination nor edema; rather they are mere non-specific signs of proton fluidity. Although “records” of burden can readily be estimated by cumulative T2 lesions, poor correlation exists between such T2 lesion load and the clinical phenotype (often termed “clinico-radiological paradox” in MS in particular), which may in part be attributable to the inability of T2-weighted images to depict myelin-specific signals or remyelination. In order to improve the diagnostic accuracy and to enable precise treatment monitoring afterwards, we have recently developed a novel MRI modality named the q-space Myelin Map (qMM) imaging. qMM detects signals highly specific to myelin and it can be obtained within 10 minutes using conventional MR scanners. We believe that this new modality enables us to more precisely locate true demyelinating lesions for the early diagnosis of MS, to detect signs of remyelination in the course of MS that may influence the long-term prognosis of the patients, and to unveil the pathogenesis of NMOSD lesions. In the presentation, I would like to review the rationale of qMM imaging and present updated findings on the clinical utility of qMM in MS and NMOSD patients.

L-14 Imaging Plasticity in MS and NMOSD
Yao Liu (China)
Department of Neurology and Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin, China; Department of Radiology and Nuclear Medicine, Neuroscience Campus Amsterdam, VU University Medical Center, Amsterdam, The Netherlands

Brain plasticity, also known as neuroplasticity, is a term that refers to the brain’s ability to change and adapt as a result of experience. Imaging plasticity is essential for assessing the brain/spinal cord function and for revealing the extent of disease-specific impact. In multiple sclerosis (MS), the brain is frequently involved, with the majority of patients having more than one brain lesion. However, the number of studies comparing MS to NMOSD is limited, and findings often did not include the information about AQP4-Ab positivity. Overall, the application of these techniques to patient studies has demonstrated that tissue damage in MS occurs within lesions and is widespread outside lesions. In NMOSD, tissue microstructural damage, as detected by nonconventional techniques, may be seen in the normal-appearing tissue outside lesions, but it seems to be secondary to the prevalent damage occurring in the optic nerve and corticospinal tract. Tissue destruction in NMOSD lesions seems to be greater than that occurring in MS lesions. In NMOSD, the tissue degeneration in the white matter is greater than that in the grey matter. NMO patients seem to show predominant spinal cord atrophy, whilst MS patients show greater whole brain atrophy and grey matter atrophy, especially in the progressive phase of the disease. A recent study has suggested that cord atrophy in NMOSD may occur even in the absence of spinal cord lesions. Deep grey matter atrophy and thalamic microstructural changes appear to be more extensive in MS than NMOSD. A few studies using advanced imaging have suggested that, in both diseases, there are correlations between tissue damage, as detected by imaging measures, including atrophy and diffusion abnormalities, and physical and cognitive disability.
The past decade has seen a growing number of patients with autoimmune encephalitis. This lecture will include:

1. The basic concepts and imaging techniques for evaluating brain and spinal cord plasticity.
2. The brain and spinal cord plasticity patterns (both structural and functional plasticity) in MS and NMO and its clinical implications.
3. A summary and future perspective of imaging plasticity in MS/NMO patients.

**PACTRIMS Teaching Session-1: Main Symposium-4**

**Differential Diagnosis for MS/NMOSD/Autoimmune Encephalitis/Other Mimickers: An Interactive Case Discussion**

**L-15 Autoimmune Encephalitis**

Lekha Pandit (India)
Center for Advanced Neurological Research, Nitte University, Mangalore, India

The past decade has seen a growing number of patients with noninfectious causes for encephalitis most of which have an autoimmune etiology. The clinical presentations are varied and diagnostic auto antibodies are seldom available when treatment decisions have to be made. Approach to management has to be based on clinical criteria backed by a high index of suspicion and after exclusion of diseases that mimic these conditions. In this presentation a pragmatic approach will be discussed utilizing real life case scenarios as examples.

**L-16 Neuro-Beihet Disease**

Ha Young Shin (Republic of Korea)
Department of Neurology, Yonsei University College of Medicine, Seoul, Republic of Korea

Behçet’s disease (BD) is a multi-systemic inflammatory disorder, characterized by recurrent oral ulcers and disease manifestations in the mucocutaneous, ocular, joints, vascular, gastrointestinal and nervous systems. The pathomechanism remains unclear, but may be associated with vascular inflammation involving a wide range of vessels. The neurological involvement, neuro-Behçet’s disease (NBD) is one of the most serious causes of long-term mortality and morbidity in BD. NBD usually affects the central nervous system (CNS), predominantly the brainstem and diencephalic regions, but can also involve cerebral cortex and white matter, optic nerve, and/or spinal cord. Current therapeutic approach is the treatment of acute attacks with high-dose corticosteroids followed by a slow taper. Disease modifying therapies such as azathioprine, mycophenolate mofetil, methotrexate, and cyclophosphamide are then considered with relapses or continued symptoms. TNF-alpha-blockers and interferon alpha can also be therapeutic options. NBD has some common clinical features with multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD), for example recurrent course of the disease, visual symptoms (caused by uveitis or optic neuropathy), and spinal cord involvement. Longitudinally extensive transverse myelitis can be the presenting feature of spinal cord involvement in Behçet’s disease. Therefore, NBD sometimes mimic MS or NMOSD. Although NBD is an uncommon disorder, being potentially treatable, NBD should be considered a plausible etiology and differential diagnosis of inflammatory and/or demyelinating CNS diseases including MS and NMOSD.

**L-17 Anti-MOG Antibody Syndrome in Thai Patients**

Sasitorn Sritho (Thailand)
Bumrungrad International Hospital; Siriraj Hospital, Mahidol University, Bangkok, Thailand

The previous 2006 NMO diagnostic criteria requires that a patient exhibits both optic neuritis and transverse myelitis as well as 2 of the 3 supportive criteria: spinal cord involvement equal to or longer than 3 vertebral segments (Vs), a negative brain MRI at onset and the presence of either NMO-IgG or AQP4-antibody. Later the revised 2015 NMOSD diagnostic criteria unites NMO and its spectrum disorders into NMOSD and classifies them, by the presence of anti-AQP4 antibody, into AQP4-positive and AQP4-negative NMOSD. Recently, Anti-MOG antibody was reported in approximately 20 percentages of the AQP4-negative NMOSD. Actually, it has been found and showed its role in inflammatory demyelinating diseases including the seronegative NMO, isolated or recurrent optic neuritis, some cases of MS and some cases of ADEM. It, therefore, seems to be more appropriated to include these clinical presentations under the term “MOG antibody–associated diseases” which is a much broader clinical spectrum. Hereby we present a case example of the MOG – antibody syndrome and how to differentiate this patient from the others.

**PACTRIMS Teaching Session-2: Main Symposium-5**

**Neuroimaging Teaching Course: How to Make Good Use of MRI in Clinical Practice for CNS Demyelinating Disease**

**L-18 How to Use MRI Diagnostic Criteria for MS and NMOSD**

Frederik Barkhof (The Netherlands)
Department of Radiology & Nuclear Medicine, VU University Medical Centre (VUMc), Amsterdam, The Netherlands; UCL Institutes of Biomedical Engineering and Neurology, London, UK

McDonald criteria for MS require dissemination in time and space. Perventricular, infratentorial and juxtacortical lesion can also occur in neuromyelitis optica spectrum disorders (NMOSD). The most recent criteria designate a single term to describe all NMOSD patients. The core clinical characteristics required for patients with NMOSD with AQP4-IgG include clinical syndromes or MRI findings related to optic nerve, spinal cord, area postrema, other brainstem, diencephalic, or cerebral presentations. More stringent clinical criteria, with additional neuroimaging findings, are required for diagnosis of NMOSD without AQP4-IgG or when serologic testing is unavailable. The old doctrine that most NMOSD patients will have normal brain MRIs has now been proven incorrect. Between 43% and 70% of patients have brain lesions at onset, up to 42% of NMO patients may fulfil the Barkhof criteria for MS B4 and 13% may do so at disease onset, although this number appears to be lower in AQP4-Ab positive cohorts. Perventricular lesions, corpus callosum, brainstem and short spinal cord lesions can occur in...
AQP4-Ab disease. Antibody negative NMOSD patients represent a heterogeneous group of disorders, and the overlap of MS and NMOSD clinical and imaging features leads to significant disparity in the diagnosis and management of patients. MRI features that help to distinguish include central vein sign in MS and bright spotty cord lesions in NMO; additional features will be discussed and illustrated.

L-19
How to Use MRI for Differential Diagnosis of MS and NMOSD
Olga Ciccarelli (UK)
University College London, London, UK

MS and NMOSD have many overlapping MRI features, which may lead to misdiagnosis. NMOSD may show periventricular white matter and corpus callosum lesions and short spinal cord lesions, which are indistinguishable from those seen in patients with MS. However, some unique imaging features, in terms of lesion localisation and configuration, may help to differentiate between these two diseases.

Lesion sites that are “typical” of NMOSD are the diencephalic structures surrounding the third ventricles and cerebral aqueduct, which include the thalamus, hypothalamus, and anterior border of the midbrain, the dorsal brainstem adjacent to the forth ventricle, which include the area postrema and the nucleus tracts solitarius, and the periependymal regions surrounding the lateral ventricles, which include the corpus callosum. The callosal lesions in NMOSD are located immediately next to the lateral ventricles, following the ependymal lining, are often edematous and may involve the complete thickness of splenium, forming an ‘arch bridge pattern’. Extensive and tumefactive hemispheric lesions are more frequent in NMOSD than MS. The gadolinium enhancement in NMOSD tends to be poorly marginated and subtle (“cloud-like” enhancement), clearly different from the ovoid and ring enhancement of MS lesions. Cortical lesions are uniquely seen on brain MRI of MS patients and seem to be absent in NMOSD. The proportion of lesions with a central vein sign is higher in MS patients than NMOSD. The most definite manifestation of NMOSD is the longitudinal extensive transverse myelitis, defined as a lesion that involves 3 or more contiguous vertebral segments and predominantly the central grey matter on MRI, although short lesions in the spinal cord may be seen in NMOSD.

Advanced brain and spinal cord imaging may help to distinguish NMOSD from MS. Patients with NMOSD show predominantly spinal cord atrophy with mild brain atrophy, whilst MS patients demonstrate more brain atrophy, especially in the grey matter. Myelin water imaging has shown that a reduction in myelin content occurs in the normal-appearing white matter of the spinal cord in MS, but is restricted to spinal cord lesions in NMO. Spinal cord MR spectroscopy has suggested reduced myo-inositol levels in NMO lesions but not in MS lesions, which may reflect the underlying astrogliotic damage occurring in NMO. Overall, there is a limited number of studies using nonconventional imaging techniques in NMOSD and MS, and, therefore, larger studies are needed to translate these techniques to the clinical setting.

L-20
How to Use MRI For Monitoring Treatment Effects in MS and NMOSD
Ernst-Wilhelm Radue (Switzerland)
University Hospital Basel, Basel, Switzerland

Biomedical Research and Training (BMRT) GmbH, Affiliated with University Hospital Basel, Basel, Switzerland

The topic covers MS and NMO lesions and their MRI appearance, clinical relevance and follow up. MRI Characteristics, MRT, DWI and volume measurements are discussed in detail. The success rates of various treatments of MS and NMO lesions are compared and developmental differences, clinical symptoms and SCF factors are explained. Although many symptoms and signs are similar, differentiation between MS and NMO lesions has to be done due to the adverse effects of various medications.

Main Symposium-6
Understanding Autoantibody-mediated Neuro-inflammation
Part 1. Autoimmunity Against Astrocytes

L-21
A Novel Mechanism of AQP4 Antibody-mediated Demyelination
Alan S. Verkman (USA)
University of California, San Francisco, USA

Activation of the classical complement pathway is thought to play a central role in the pathogenesis of AQP4-IgG seropositive NMOSD, in which activation of complement following AQP4-IgG binding to astrocyte AQP4 initiates inflammatory and cytotoxic events resulting in early and marked demyelination. We recently discovered novel complement-related mechanisms in seropositive NMOSD involving complement bystander cytotoxicity and the complement inhibitor protein CD59. Primary cocultures of astrocytes and oligodendrocytes exposed to AQP4-IgG and complement showed early death of oligodendrocytes in close contact with astrocytes, which was not seen in pure oligodendrocyte cultures, in cocultures exposed to AQP4-IgG and C6-depleted serum, or when astrocytes were damaged by a complement-independent mechanism. The complement membrane attack complex (MAC) was deposited on oligodendrocytes in contact with astrocytes, whereas C1q, the initiating complement protein, was deposited only on astrocytes. Early oligodendrocyte injury with MAC deposition was also found in rat brain following intracerebral injection of AQP4-IgG, complement and a fixable dead-cell stain. These results support a complement bystander mechanism for early oligodendrocyte injury and demyelination in NMO. The strong sensitivity of oligodendrocytes to complement bystander injury is in large part due to their paucity of CD59 expression. In related work, we found that transgenic rats deficient in CD59 are highly sensitive to AQP4-IgG induced injury upon direct injection into the CNS, and that the rats developed profound hyperCKemia and myositis following systemic AQP4-IgG administration. These results indicate a major regulatory role of CD59 in the CNS in NMOSD, and offer an explanation of why peripheral, AQP4-expressing organs are largely spared in NMOSD.

L-22
Mechanism and Spectrum of Autoimmune GFAP Meningoencephalomyelitis
Vanda A. Lennon (USA)
Neuroimmunology Laboratory, Mayo Clinic Rochester, Minnesota, USA

Detection in CSF or serum of IgG specific for glial fibrillary acidic protein (GFAP, a cytoplasmic intermediate filament of astrocytes) aids the diagnosis of a disabling, relapsing, immunotherapy-responsive autoimmune meningoencephalomyelitis. Median symptom onset age for 102 patients (54% female) was 44 yrs (range 8-103). The most frequent presentation was subacute memory loss, confusion (with or without psychiatric symptoms), meningeal symptoms (prominent headache, papillitis without increased intracranial pressure), postural tremor, cerebellar ataxia and generally mild myelopathy. CSF leukocytosis and elevated IgG index are common. Radiological (MRI) hallmarks are striking radial linear periventricular enhancement, resembling angiogram-negative CNS vasculitis, and longitudinally extensive T2 hyperintense spinal lesions. The differential diagnosis commonly includes infectious, granulomatous and inflammatory demyelinating disorders, lymphoma, carcinomatosis and vasculitis. GFAP-IgG seropositivity obviates the need for diagnostic CNS biopsy. One third of cases have serological evidence of endocrinopathy (some clinically evident), 22% have coexisting autoimmunity and about one third have a recent or coexisting cancer of diverse types, but most commonly ovarian teratoma. GFAP-IgG is a reliable biomarker of autoimmune meningoencephalomyelitis when detected by mouse tissue-based immunofluorescence assay, and confirmed by human GFAPα-transfected cell-based immunofluorescence assay. Immunostaining of adult mouse tissues is most intense in an astrocyte-enriched region of the hippocampus, rostral migratory stream, olfactory bulb and central spinal cord. Restriction of IgG binding to neural progenitors suggests a primitive neural-type cell is the driving autoantigen. Interestingly, GFAP expression has been reported in most types of tumor found in paraneoplastic cases. Furthermore, GFAP, aquaporin-4 (AQP4) water channel and NMDA receptor are all tumor found in paraneoplastic cases. Furthermore, GFAP, aquaporin-4 (AQP4) water channel and NMDA receptor are all expressed in ovarian teratoma. When IgGs corresponding to these 3 specificities coexist, teratoma is predicted with 71% certainty, and meningoencephalomyelitis is the dominant neurological phenotype.

GFAP meningoencephalomyelitis is the second autoimmune astrocystopathy identifiable serologically. The first, the aquaporin-4 (AQP4) water channel neurofilament optica spectrum, is caused by pathogenic IgG binding to the astrocytic plasma membrane. CD8+ cytotoxic T cells specific for a peptide derived from GFAP were demonstrated to be pathogenic in a transgenic mouse model of autoimmune GFAP meningoencephalitis triggered by viral challenge. Under the influence of proinflammatory cytokines, intracellular peptides translocated on MHC class I proteins are displayed on glial cell surfaces.

Part 2. Autoimmunity Against Myelinating Cells

L-23
Mechanism and Spectrum of MOG Antibody-mediated Encephalomyelitis
Ichiro Nakashima (Japan)
Tohoku Medical and Pharmaceutical University, Sendai, Japan
Anti-myelin oligodendrocyte glycoprotein (MOG) antibody, which is specifically detected using a cell-based assay (CBA), has been identified in various demyelinating diseases, including neuromyelitis optica (NMO) spectrum disorders, acute idiopathic optic neuritis (ON), and pediatric multiphasic disseminated encephalomyelitis (MDEM). The subclass of the antibody is IgG1 and it can’t be detected in multiple sclerosis (MS) patients. The spectrum of the diseases associated with the antibody seems to be much broader than we had been thinking. Although its pathogenetic role has not been established, antibody seropositive cases appear to share several characteristic features, such as a preferable response to steroid therapy and a good prognosis. Antibody detection at the onset of a demyelinating disease is important to predict the prognosis. The cytokine profile of anti-MOG antibody associated disease was like that of anti-aquaporin-4 (AQP4) antibody positive NMO and was different from that of MS. While glial fibrillary acidic protein (GFAP) level in the CSF of the acute-phase can easily differentiate anti-AQP4 antibody positive patients and anti-MOG antibody positive patients. Further analysis of the clinical features and investigation of the pathogenic roles of the antibody are required to establish the disease spectrum associated with the antibody. Although the associated diseases appear to have a relatively good prognosis, treatment recommendations are offered for patients with severe symptoms or frequent relapses.

L-24
IgG4 Anti-neurofascin 155 Antibody in Peripheral and Central Demyelination
Ryo Yamasaki (Japan)
Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
Neurofascin155 (NF155) is an immunoglobulin superfamily member and contributes to the stabilisation of Ranvier’s node structure in both peripheral and central nervous systems. Our recent clinical study revealed that patients with combined central and peripheral demyelination (CCPD), and chronic inflammatory demyelinating polyneuropathy (CIDP) harbour serum antibodies against NF155. We established a novel strategy to detect anti-NF155 antibody using a cell-based assay and flow-cytometric analysis, and we performed a nationwide survey to characterise serum anti-NF155-positive patients. Antibody was positive in 45.5% (S/11) of CCPD patients and 18% (9/50) of CIDP patients. Antibody-positive CIDP patients shared many clinical characteristics including significantly younger onset, tremor, and distal-type muscle weakness. Cerebrospinal fluid (CSF) protein levels in these patients were markedly increased beyond 100 mg/dl, and neurophysiological analyses showed prolonged distal latency and F-wave latency. On magnetic resonance imaging, patients also showed marked hypertrophy of the cervical and lumbar plexus. Patients with anti-NF155 antibody responded well to corticosteroids and intravenous immunoglobulin therapy, and serum anti-NF155 titres reflected the clinical severity. In conclusion, anti-NF155 antibody defined a new subset of autoantibody-mediated polyneuropathy, which is characterised by a younger onset age, tremor, high CSF protein level, symmetrical spinal root hypertrophy, and marked prolongation of distal latency. Anti-NF155 titres are a useful disease biomarker and surrogate marker.
MedImmune is the global biologics research and development arm of AstraZeneca, a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialization of small molecule and biologic prescription medicines. MedImmune is pioneering innovative research and exploring novel pathways across key therapeutic areas, including respiratory, inflammation and autoimmunity; cardiovascular and metabolic disease; oncology; neuroscience; and infection and vaccines.

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O-1
Contribution of Cortical Lesions to Cognitive Dysfunction in Japanese Patients with Multiple Sclerosis

K Shinoda1, T Matsushita1, Y Nakamura1, S Sakai1, H Nomiyama1, R Yamasaki1, O Togao1, A Hiwatashi1, J-I Kira2
1Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.

Background: We recently reported an association of cortical lesions (CLs) with disability in Japanese multiple sclerosis (MS) patients. However, no previous study examined how CLs contribute to cognitive impairment in Asian MS patients. Objectives: To clarify the effect of CLs on cognitive dysfunction in Japanese MS patients.

Methods: This study enrolled 61 MS patients in remission from February 2016 to July 2017. They were subject to both 3-dimensional double inversion recovery MR imaging and neuropsychological assessment by the Brief Repetitive Battery (BRB-N), Apathy Scale (AS), Fatigue Questionnaire (FQ), and Hospital Anxiety and Depression Scale (HADS) within a week. The cognitive impairment index (CII) scores were calculated as an overall measure of cognitive impairment in each patient.

Results: MS patients with CLs scored significantly lower in all tests of the BRB-N and FQ, but comparably in AS and HADS compared to those without CLs. The number of CLs significantly correlated with scores of all the tests of BRB-N, but not with fatigue, apathy, anxiety or depression measurements. Multiple logistic regression analysis revealed that the potential confounding factors of the highest quartile of CII compared with the lowest quartile were the Expanded Disability Severity Scale (EDSS) score (Odds ratio 1.867, p = 0.0325) and the number of CLs (Odds ratio 2.595, p = 0.0142), but not sex, age at disease onset or disease duration.

Conclusions: The CLs numbers are robustly associated with cognitive dysfunction as well as physical disability defined by EDSS score in Japanese patients with MS.

O-2
Narrowband UVB Phototherapy for Clinically Isolated Syndrome: Delivering the Benefits of All UVB-Induced Molecules

A.G. Kermode1,2, PH. Hart3, M.J. Fabis-Pedrini1, R.M. Lucas4, D.R. Booth5, W.M. Carroll1,2, D. Nolan2,6, J.M. Cole2, A.P. Jones3, S. Trend4
1Centre for Neuromuscular and Neurological Disorders, Pemex Institute for Neurological and Translational Science, University of Western Australia, Sir Charles Gardiner Hospital, Perth, WA, Australia; 2Institute for Inflammation and Infectious Disease, Murdoch University, Perth, WA, Australia; 3Inflammation Research Group, Telethon Kids Institute, University of Western Australia, Perth, WA, Australia; 4National Centre for Epidemiology & Population Health, Research School of Population Health, Australian National University, Canberra, ACT, Australia; 5Centre for Immunology and Allergy Research, Westmead Institute for Medical Research, University of Sydney, Sydney, NSW, Australia; 6Immunology Department, Royal Perth Hospital, Perth, WA 6000, Australia.

Background: Trials of vitamin D supplementation have to date lacked definitive outcomes in MS patients. Narrowband UVB can induce vitamin D production, but also other important immune-regulatory molecules in skin. Objective: The PhoCIS trial (Phototherapy for Clinically Isolated Syndrome) was established in Perth, Australia (32 degrees S), to investigate the clinical, radiological and immunological effects of narrowband UVB phototherapy on MS development in CIS.

Patients and Methods: Nineteen individuals with CIS have been recruited with 53% of them given narrowband UVB phototherapy of 3 sessions per week for 8 weeks. All 19 participants were supplemented when necessary with vitamin D to 25(OH)-vitamin D levels of approximately 80 nmol/L. MRI was performed after 3, 6 and 12 months, and extensive blood cell phenotyping at 1 week, 1, 2, 3, 6 and 12 months after recruitment. No participant was taking any disease modifying drugs at recruitment.

Results: After 6 months, 7 of 9 participants (78%) without phototherapy converted to MS (McDonald criteria). Only 5 of 10 participants (50%) who received phototherapy converted to MS (P = 0.22). UVB therapy prevented the increase in memory B cells in the blood of non-phototherapy CIS participants, and produced a significant increase in immunoprotective IgG4.

Conclusion: These interim results demonstrate UVB effects slowing the progression of individuals with CIS to MS. The PhoCIS trial provides a fresh approach to re-defining the reported associations of 25(OH)-vitamin D levels with MS development and progression. The outcomes suggest that UVB-irradiation of skin is immunomodulatory independent of Vitamin D, and can regulate CIS to MS progression.

O-3
Restoration of Regulatory B Cell Deficiency Following Alemtuzumab Therapy in Patients with Active Multiple Sclerosis

Yeseul Kim1,2, Gayoung Kim1,2, Hyun-June Shin1, Jae-Won Hyun1, Su-Hyun Kim1, Ho Jin Kim1,2
1Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Korea
2Division of Clinical Research, Research Institute, National Cancer Center, Goyang, Korea

Background: Recently defined regulatory B cells (Bregs) exert immune suppression through IL-10 dependent (CD19+CD24+CD388) and IL-10 independent (B cells with high expression of programmed death ligand 1 (PD-L1)h) mechanism. IL-10 secretion by B cells is deficient in multiple sclerosis (MS). Whether PD-L1hi B cells are deficient in MS, and the composition of Bregs in repopulating B cell pool post alemtuzumab is unknown in MS.

Objective: To evaluate the proportion of Bregs in MS and to study the effect of alemtuzumab on Bregs.

Methods: The proportion of Bregs was studied in fresh peripheral blood mononuclear cells (PBMC) of 16 active, 17 inactive MS patients and 11 healthy controls. We evaluated the proportion of...
Bregs longitudinally in frozen PBMC of 10 MS patients treated with alemtuzumab, before and at 6, 9 and 12 months after treatment.

**Results:** The proportion of Bregs was lower in active MS patients than healthy controls (CD19+CD24hiCD38hi: average 1.6% vs 3.5% \( p = 0.033 \) and PD-L1hi B cells: average 5.6% vs 7.8% \( p = 0.015 \)). CD19+CD24hiCD38hi were lower in active MS patients than inactive patients (average 1.6% vs 3.5% \( p=0.049 \)). Post 6 months alemtuzumab treatment, the proportion of Bregs increased (CD19+CD24hiCD38hi: average 3.1% to 8.6% \( p < 0.01 \) and PD-L1hi B cells: average 8.7% to 17.1% \( p < 0.01 \)). Such increase was maintained until 12 month post treatment (CD19+CD24hiCD38hi: average 6.6% and PD-L1hi B cells: average 18.4% \( p < 0.01 \)).

**Conclusion:** Immune suppression by Bregs is deficient in MS, regardless of IL-10 production. Following alemtuzumab, preferential reconstitution of IL-10 dependent and independent Bregs occurs.

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**Oral Presentation-2**

**Neuromyelitis Optica Spectrum Disorder**

**O-4**

**Nationwide Epidemiological Study of Neuromyelitis Optica in Japan**

K. Miyamoto^1, K. Fujihara^2, J. Kira^3, N. Kuriyama^4, M. Matsui^5, A. Tamakoshi^6, S. Kusunoki^1

^1Kindai University Faculty of Medicine, Osaka-Sayama, Japan; ^2Fukushima Medical University, Fukushima, Japan; ^3Kyushu University, Fukuoka, Japan; ^4Kyoto Prefectural University of Medicine, Kyoto, Japan; ^5Kanazawa Medical University, Ishikawa, Japan; ^6Hokkaido University Graduate School of Medicine, Sapporo, Japan.

**Background:** Neuromyelitis optica (NMO) is a neuromyelinnological disorder characterized by transverse myelitis and bilateral optic neuritis, developing over the course of a few weeks. In contrast to multiple sclerosis, only a few epidemiological surveys on NMO have been reported.

**Objective:** Here, we used a cross-sectional survey design to determine the prevalence of NMO and NMO spectrum disorder (NMOSD) in Japan.

**Methods:** We randomly sampled a number of relevant hospital clinic departments through a stratified sampling strategy by sending a questionnaire in January 2012, providing the Wingcherch diagnostic criteria and requesting numbers of NMO and NMOSD patients treated in 2011. This was followed by a second questionnaire to departments that reported such patients requesting specific information. After eliminating duplicate and inappropriate cases and using the 2011 census data of Japan, overall and area-specific prevalence rates were estimated.

**Results:** The number of patients with NMO or NMOSD in Japan in 2011 was estimated to be 4290. Patients were mostly female (M:F = 1:6.4). Mean age of disease onset was 42.2 years. Estimated prevalence rates per 100,000 population were 1.64 (NMO) and 3.42 (NMO plus NMOSD: NMO/NMOSD). Number of NMO/NMOSD patients was significantly higher in southern Japan, showing a pattern opposite to that of multiple sclerosis.

**Conclusion:** We conducted the first nationwide survey on NMO/NMOSD to determine the prevalence rate and characterized the clinical features of NMO/NMOSD in Japan.

**O-5**

**Intestinal Microbiota Distinguish Neuromyelitis Optica Patients from Healthy Individuals in a Chinese Pilot Study**

Gong JL^1,2#, Qiu W^3, Zen Q^3, Sun X^3, Li HJ^3, Lu XY^3,2, Yang Y^3, Wu AM^1, Bao J1, Wang YG^1, Shu YQ^1, Zheng SG^1, Peng LS^1, Ly YJ^3,2, Lu QZ^1

^1School of life sciences, Sun Yat-sen university, Guangzhou, 510275, China; ^2Biomedical Center, Sun Yat-sen university, Guangzhou, 510275, China; ^3Department of Neurology, Third Affiliated Hospital, Sun Yat-sen University, Guangzhou Guangdong, China

**Background:** Neuromyelitis optica (NMO) is a chronic autoimmune disorder mainly affecting the central nervous system (CNS), and leading to severe disability among young people. Recent studies showed that gut microbes are involved in several autoimmune diseases. Therefore, a hypothesis that the gut commensal flora could be an important risk factor for NMO was proposed.

In this study, next-generation sequencing (NGS) is employed to compare the fecal microbial composition between NMO patients (n=64) and healthy controls (HC, n=36). The results are summarized as follows: 1) PCoA analyses showed that the gut microbial composition of NMO and HC were clustered separately, indicating a different bacterial composition between two groups. 2) LEfSe analyses showed that three bacterial genera; Faecalibacteria, Roseburia and Streptococcus, differentially distributed between NMO and HC. Among them, Faecalibacteria and Roseburia are butyric acid producing bacteria, which are depleted in the NMO group; while the Streptococcus in NMO group was significantly higher than that in HC group. A significant positive correlation was found between EDSS and the abundance of Roseburia in NMO group. 3) Additionally, microbial index of NMO (MIN) between NMO and HC was significantly different (P <0.05), and the AUC value from the ROC curve was 0.8086, indicating that those differential genera might be used as sensitive biomarkers for disease diagnosis.

In conclusion, this Chinese study, the gut microbiota of NMO is highly distinctive from healthy individuals in fecal organisinal structures. The deficiency of butyric acid producing bacteria and the increase of Streptococcus are the main gut microbiota features of this disease.

**O-6**

**Bidirectional Degeneration in The Visual Pathway in Neuromyelitis Optica Spectrum Disorder (NMOSD)**

De-Cai Tian, MD^4, Lei Su, MD^4, MoLi Fan, MD^1, Jian Yang, BS^2, Rui Zhang, MD^1, eng Wen, BS^1, Yuluan Han BS^1, Changju Yu, MD^1, Chao Zhang, PhD^1, HongLei Ren, MD^1, Kaibin Shi, MD^1, Zilong Zhu, MD^1, Yinhua Dong, MD^1, Yao Li, MD, PhD^2, Fu-Dong Shi, MD, PhD^3,4

^1Department of Neurology, Tianjin Medical University General Hospital, Tianjin 300082, China; ^2Department of Radiology, Tianjin Third Central Hospital, Tianjin, 300170, China; ^3Department of Neurology, Tianjin Huayin Hospital, Tianjin, 300350, China; ^4Department of Neurology, Tianjin Forth Central Hospital, Tianjin, 300140, China
**O-7**

**Brain Volume Loss Is Present in Japanese Patients with Multiple Sclerosis with No Evidence of Disease Activity**

H. Yokote1, T. Kama1, S. Toru1, N. Sanjo1, T. Yokota1

1Department of Radiology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China; 2Department of Neurology, Barrow Neurological Institute, St. Joseph’s Hospital and Medical Center, Phoenix, AZ 85013, USA; *Dr. Tian and Su contributed equally.

**Objective:** This study aims to investigate whether bidirectional degeneration occurs within the visual pathway and if so, the extent of such changes in neuromyelitis optica spectrum disorder (NMOSD).

**Methods:** 36 NMOSD and 24 healthy controls (HCs) were enrolled. Three-dimensional T1-weighted MRI and diffusion tensor imaging were used to analyze damage to the posterior visual pathway. Damage to the anterior visual pathway was measured by optical coherence tomography.

**Results:** 24 NMOSD with prior optic neuritis (NMOON) patients showed significant reduction of peripapillary retinal nerve fiber layer, inner and outer retinal thickness, lateral geniculate nucleus volume, primary visual cortex volume and decreased integrity of optic radiations, compared with 12 NMOSD without prior optic neuritis (NMONON) patients and 24 HCs. In NMONON, only the inner retinal thickness and the integrity of optic radiations were significantly reduced in comparison with HCs. However, there was no significant association between the damage to anterior and posterior visual pathways.

**Conclusion:** Our study indicated the presence of trans-synaptic degeneration in NMOSD. Damage to the inner retina and optic radiations can be observed even in NMONON. After an episode of optic neuritis, the anterior visual pathway damage is greater than the posterior visual pathway damage.

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**O-8**

**Dynamic Expression of Circulating MicroRNA-155 in Plasma of Patients with Multiple Sclerosis**

Bing Qin, Li Xiao, Zhengqi Lu *

Department of Neurology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong 510630, PR China

**Background:** Multiple sclerosis (MS) is an organ-specific autoimmune disease manifested by chronic inflammatory demyelination of the central nervous system. MicroRNA-155 (MiR-155) is a typical multi-functional miRNA and plays a crucial role in inflammation and autoimmunity.

**Objective:** This study was aimed to investigate the dynamic expression level of miR-155 in the plasma of MS patients.

**Methods:** 22 cases of relapsing-remitting multiple sclerosis (RRMS) in acute relapse phase (within 14d) and 17 healthy volunteers (as a control group) were collected. Expanded Disability Status Scale (EDSS) score and the number of Gd-enhancing lesions were evaluated pre- and post-treatment in the patients group. The plasma level of miR-155 was detected by quantitative PCR, and statistical analysis was performed with IBM SPSS 23.

**Results:** The plasma level of miR-155 in RRMS patients before treatment was higher compared to that of the control group (P<0.05). Four weeks post-treatment, miR-155 level decreased significantly (P<0.05), as compared with that before treatment. The post-treatment EDSS scores declined remarkably compared with baseline EDSS scores in patients group, and the difference was statistical significance (P<0.01). However, the number of Gd-enhancing lesions was not decreased significantly after treatment (P>0.05). The plasma level of miR-155 was positively correlated with the EDSS score and the number of Gd-enhancing lesions in acute relapse phase of RRMS (P<0.05).

**Conclusions:** These findings indicate that miR-155 may play a pro-inflammatory role in the pathophysiological process of RRMS. Manipulation of the circulating miR-155 may offer a novel strategy for treatment of MS.

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**O-9**

**Deviated Repertoire of γδ T Cells is Associated with Disease Severity of Multiple Sclerosis**

G. Maimaitijiang1, K. Shinoda1, Y. Nakamura1, T. Matsushita1, R. Yamassaki1, Y. Yoshiko2, J. Kira1

1Department of Neurology, Neurological Institute, Kyushu University, Fukuoka, Japan; 2Division of Host Defense, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan

**Background:** Deletion type copy number variations in T cell receptor (TCR) α, γ, and δ genes confer susceptibility to multiple sclerosis (MS). Untreated patients with MS (n=24) were compared with controls (n=24) for both copy number and allele count. The TCRα, γ, and δ genes were analyzed with a qPCR assay.

**Objective:** The aim of this study was to elucidate whether copy number variation in TCRα, γ, and δ genes are associated with the disease severity of MS.

**Methods:** This single-centered, retrospective, observational study was designed to investigate patients with MS who had routine neurological examinations every 2 or 3 months from January 2008 to March 2016. Patients who had brain MRI twice with intervals of more than 24 months were included. Brain volume was evaluated using the SIENAX and SIENA tools of the FMRI8 software library.

**Results:** Twenty-two patients with MS were included in the study. Fourteen (63.6%) patients had NEDA-3. From these, however, eight (57.1%) showed significant brain volume loss (BVL), defined as > 0.4% per year, although their cognitive function was not inferior to that of patients without BVL.

**Conclusions:** BVL is evident in patients with NEDA-3, suggesting that NEDA-3 does not suffice as a therapeutic target for MS. Including BVL to NEDA-3 (NEDA-4) would be suitable for evaluating disease activity in patients with MS.
De Novo Trigeminal Neuralgia Induced by Dalfampridine (4-aminopyridine): 3 Cases

Mehmet OZMENOĞLU1, Cavit BOZ2, Demet SEKER1, Hilal HOROZOĞLU2

1KTU Medical School, Farabi Hospital, Neurology Department, Trabzon, Turkey
2Tekirdag State Hospital, Neurology Clinic, Tekirdag, Turkey

Background: Trigeminal neuralgia is well known to neurologists. Dalfampridine (4-aminopyridine, fampridine), a potassium channel blocker, can improve walking in some adult patients with multiple sclerosis (MS). Dalfampridine increases the risk of seizures and may trigger or exacerbate preexisting trigeminal neuralgia in patients with MS. We present 3 cases with clinically definite MS, treated with dalfampridine who developed a new onset of trigeminal neuralgia.

Objective: To report three seconder progressive MS (SPMS) cases, two men and one woman aged 31 to 60 who developed de novo trigeminal neuralgia 3 to 6 months after dalfampridine use. Brain MRI showed hyperintens lesions in the trigeminal nerve distribution in two patients. In two of the cases, pain was relieved when dalfampridine use was discontinued and carbamazepine was administered. Gamma knife therapy was applied to one patient as carbamazepine did not control the pain.

Conclusion: The mechanism by which dalfampridine exerts its therapeutic effect has not been fully elucidated. In animal studies, dalfampridine has been shown to increase conduction of action potentials in demyelinated axons through inhibition of potassium channels. The possible mechanism of trigeminal neuralgia upon exposure to dalfampridine is not known. We suggest that dalfampridine should be used with care in MS patients and the follow-up of all patients must be thorough. If MS plaques are present in the trigeminal nerve distribution brain stem area in the MRI, dalfampridine should not be used. If trigeminal neuralgia does arise in a patient, dalfampridine should be discontinued.
Results: Numbers of patients and spinal cord lesions (SCLs) were SCS (n = 19, 24 SCLs), NMOSD (n = 43, 46 SCLs), and SM (n = 20, 20 SCLs). The predilection for SCL was CS vertebreal segment (11/24, 46%) in SCS, Th6 and Th7 (18/46, 39%) in NMOSD, and CS (16/20, 80%) in SM, respectively. The prevalence of long myelitis (≥ 3 vertebral segments) was SCS (11/19, 58%), NMOSD (36/43, 84%), and SM (6/20, 30%). The characteristic enhancement pattern on MRI was vascular-territorial in SCS, gray-matter predominant in NMOSD, and circumferential in SM. The colocalization of SCL and spondylocotic compression was more frequent in SCS (11/24, 46%) than that in NMOSD (2/46, 4.3%) (P < 0.01). Such colocalization was observed exclusively in elder patients (> 50 years old) with SCS. The SCS patients harboring spondylocotic compression showed recurrent and intractable clinical course compared to those without compression.

Conclusion: SCS manifested as long myelitis at considerably high prevalence. The vascular-territorial enhancement was a discriminative MRI feature of SCS. SCS frequently affected the spinal cord with spondylocotic compression especially in elder patients, leading to intractable clinical course.

O-14 Different Features between Pediatric-Onset and Adult-Onset Patients Who Are Seropositive For MOG-IgG: A Multicenter Study in South China
Lu Chen 1, Chen Chen 1, Xiaoran Zhong 1, Xiaoobo Sun 1, Haixia Zhu 2, Xiaomeng Li 2, Hui Yang 3, Yaqing Shu 4, Yanyu Chang 4, Xueqiang Hu 4, Zhengqi Lu 1, Lisheng Peng 1, Wei Qiu 1
1 Department of Neurology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou
2 Guangzhou Women and Children’s Medical Center, Guangzhou
3 Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou
4 Background: Immunoglobulin against myelin oligodendrocyte glycoprotein (MOG-IgG) is a potential demyelinating disease-associated autoantibody. However, whether clinical features of MOG antibody-associated demyelinating diseases changes with age remains unclear.

Objective: To investigate the different clinical features between pediatric-onset and adult-onset MOG-IgG-seropositive patients in a relatively large cohort.

Methods: A total of 816 patients with the suspicion of demyelinating diseases were prospectively enrolled from three academic centers in South China between January, 2016 and March, 2017. Twenty-one pediatric-onset cases (≤20 years old) and 29 adult-onset cases (>20 years old) with MOG-IgG were identified. Differences in clinical features between the two groups were investigated.

Results: The proportion of pediatric-onset patients with cerebral symptoms was significantly higher than that of adult-onset patients (P=0.009). More adult-onset patients showed isolated involvement of the optic nerve at disease onset (P=0.061) and in the full course of the disease compared with pediatric-onset patients (P=0.04). A higher rate of pediatric-onset patients met the criteria for acute disseminated encephalomyelitis (P<0.001), while patients diagnosed with optic neuritis were mainly adult-onset patients (P=0.004). The titer of MOG-IgG was significantly positively correlated with the white blood cell count (P=0.002) and total protein levels (P=0.054) in cerebrospinal fluid only in

1 Department of Neurology, Institute of Molecular Medicine & Institutes of Regional Health Research, University of Southern Denmark, Odense, Denmark
2 Department of Medicine, Queen Elizabeth Hospital, Kowloon, Hong Kong
3 Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand
4 Nuffield Department of Clinical Neurosciences, West Wing, John Radcliffe Hospital, University of Oxford, Oxford, UK

Objective: To determine if ethnic differences exist in the clinical features of neuromyelitis optica spectrum disorder (NMOSD).

Methods: Clinical and demographic data were retrospectively collected from 660 patients meeting 2015 NMOSD criteria in Denmark, Germany, South Korea, UK, USA and Thailand.

Results: Of 660 patients (340 Asians, 225 Caucasians, and 95 Blacks) with a median disease duration of 8 years, and 91% were seropositive for anti-aquaporin-4 antibody. There was no significant difference in gender ratio or anti-aquaporin-4 antibody positivity among ethnicities. Asians and Blacks had a younger onset age than Caucasians (median 35, 34, and 43 years, respectively; p<0.001). Caucasians (53%) presented with myelitis more commonly than Asians (43%) (p=0.016), whereas Caucasians (15%) had lower frequency of brain/brainstem involvement at onset than Asians (24%) and Blacks (27%) (p=0.014 and p=0.012, respectively). Patients initially manifested with severe attack (visual acuity ≤ 0.1 or Expanded Disability Status Score [EDSS] ≥ 6.0 at nadir) were more frequent in Blacks (60%) than Asians (45%) and Caucasians (38%) (p=0.014 and p<0.001, respectively). At last follow-up, patients with severe disability (converted visual functional system score ≥ 3 or EDSS ≥ 6.0) were more frequent in Blacks (60%) and Caucasians (55%) than Asians (48%) (p<0.001 and p=0.001, respectively).

Conclusion: Our data indicate the ethnic influence on the clinical manifestations of NMOSD. Asian and Black patients had a younger age of onset and higher frequency of brain involvement at onset than Caucasians. Blacks experienced severe attack at onset more frequently than Asians and Caucasians.

O-13 Discrimination of Spinal Cord Sarcoidosis from Neuromyelitis Optica Spectrum Disorder or Spondyloptic Myelopathy
Hiroshi Kuroda 1, Toshiyuki Takahashi 1, Douglas Kazutoshi Sato 1, Ryo Ogawa 1, Kimihiko Kaneko 1, Yoshiki Takai 1, Shuhei Nishiyama 1, Tatsuro Misu 1, Ichiro Nakashima 1, Kazuo Fujihara 1,2, and Masashi Aoki 1
1 Department of Neurology and 2 Department of Multiple Sclerosis Therapeutics, Tohoku University Graduate School of Medicine, Sendai 980-8574, Japan

Background: Spinal cord sarcoidosis (SCS) often manifests as long myelitis or mimics spondyloctic myelopathy (SM). We aimed to reveal clinical and radiological features of SCS to discriminate the disease from neuromyelitis optica spectrum disorder (NMOSD) or SM.

Methods: We retrospectively reviewed clinical data and MRI findings of patients with SCS, compared the features to those with NMOSD or SM.
adult-onset patients. Pediatric-onset patients had a better prognosis compared with adult-onset patients (P=0.009).

Conclusions: Distinctive features are present between pediatric-onset and adult-onset patients with MOG-IgG. Further studies are required to determine the different underlying pathogenesis of MOG antibody according to different ages.

O-15 Cerebrospinal Fluid-Actin Related Protein 2/3 Complex Subunit 4 as an Astrocytic Foot Process Damage Marker of Aquaporin-4-IgG Positive Neuromyelitis Optica Spectrum Disorders
Shuhei Nishiyama1, Tatsuro Misui1, Ichiro Nakashima2, Douglas Kazutoshi Sato3, Kimihiro Kaneko3, Ryo Ogawa3, Hirohiko Ono4, Kazuhiro Kurosawa5, Yoshiaki Takai5, Toshiyuki Takahashi6, Hiroshi Kuroda3, Kazuo Fujihara3, Masashi Aoki3
1Department of Neurology, Tohoku University School of Medicine
2Department of Neurology, Centro Clinico, PUCRS
3Department of Neurology, Osaki Citizen Hospital
4Department of Neurology, Yonezawa National Hospital
5Department of Multiple Sclerosis and Therapeutics, Fukushima Medical University

Background: Aquaporin 4 (AQP4)-IgG-positive neuromyelitis optica spectrum disorders (NMOSD) is an autoimmune neurologic disease characterized by severe optic neuritis and transverse myelitis and caused by AQP4-IgG damaging membranous AQP4 in the foot process of astrocyte. We previously showed an elevated level of collapsin response mediator protein 5 (CRMP5) in the cerebrospinal fluid (CSF) of AQP4-IgG-positive NMOSD, suggesting astrocytic foot process damage in the disease. Actin-related protein 2/3 complex subunit 4 (ARPC4), is another membrane protein localized on the filopodia in the foot process of astrocyte.

Objective: To clarify the pathological and diagnostic implications of CSF-ARPC4 in AQP4-IgG-positive NMOSD.

Methods: We conducted a cross-sectional study enrolling 20 with AQP4-IgG-positive NMOSD, 3 with MOG-IgG-positive NMOSD, 27 with multiple sclerosis (MS), 4 with neurosarcoidosis and 10 with neurosarcoidosis. CSF-ARPC4, CSF-CRMP5, CSF-gliarial fibrillary acidic protein (GFAP), and CSF-myelin basic protein (MBP) and CSF-lactate dehydrogenase (LDH) in those patients during acute exacerbations were measured with ELISA.

Results: CSF-ARPC4 in AQP4-IgG-positive NMOSD was significantly elevated (11.72±2.51 ng/mL, p=0.036) than in MS (4.34±0.57) and other groups. Except AQP4-IgG-positive NMOSD, CSF-ARPC4 was elevated in only one MS patient with severe periventricular lesions. CSF-ARPC4 and/or CSF-CRMP5 is positive in 80% (16/20) patients in NMOSD with AQP4-IgG. CSF-ARPC4 was mildly correlated with CSF-GFAP and CSF-LDH but not correlated with CSF-CRMP5, CSF-MBP, or CSF-AQP4-IgG titer.

Conclusion: Elevated CSF-ARPC4 in AQP4-IgG-positive NMOSD suggests astrocytic foot process damage and may be useful as a CSF pathological and diagnostic biomarker in the autoimmune astrocytopathic disease.

O-16 Choroid Plexitis in Neuromyelitis Optica Spectrum Disorder
Y.J Oh, MD; Y.M Lim, MD; E.J Lee, MD; H.J Kim, MD; K.K Kim MD
1Department of Neurology, Univ of Ulsan, Asan Medical Center, Seoul, Korea

Background & objective: The choroid plexus (CP) is recognized as an important immunological site in modulating adaptive immune responses in the CNS. We aimed to evaluate radiological changes of the CP in neuromyelitis optica spectrum disorders (NMOSD) patients.

Methods: We enrolled 60 AQP4-IgG-seropositive patients who had brain MRI within 3 months after acute attacks. We analyzed size and enhancement of the CP in contrast-enhanced axial and coronal T1-weighted images and compared those with 33 ages- and gender- matched healthy subjects. The size was measured in the thickest part in a minimal axis and the enhancement ratio of the brightest part of CP to adjacent white matter was calculated.

Results: The mean thickness of lateral ventricle CP on both axial and coronal planes were greater in patients than controls (3.97±0.94 vs 2.69±0.78mm, p<0.001 and 3.12±0.64 vs 1.87±0.43mm, p<0.001, respectively). Similarly, the forth ventricle CP on both planes was thicker in patients than controls (1.97±1.10 vs 1.35±0.31mm, p<0.001 and 2.04±0.63 vs 1.41±0.27mm, p<0.001, respectively). In patients group, the enhancement ratios of lateral ventricle CP to parenchyma were higher on both axial and coronal planes (1.84±0.49 vs 1.49±0.26, p=0.001 and 1.85±0.39 vs 1.55±0.27, p=0.003, respectively). The fourth ventricles CP on both planes were more enhanced in patients than controls (1.62±0.32 vs 1.31±0.15, p<0.001 and 1.49±0.30 vs 1.30±0.20, p<0.001, respectively).

Conclusion: NMOSD patients have significant enlargement and enhancement of CP. These findings suggest that the CP may play an important role in autoimmunity of NMOSD.

O-17 Oligodendroglia-Specific Connexin 47 Deletion Induced Relapse-Remitting EAE Model Mice
Ryo Yamasaki, Eikinan Tyou, Hirono Yamaguchi, Jun-ichi Kira
Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University

Background: Multiple Sclerosis (MS) is one of the major neuromyelitis optica spectrum disorder immune responses in the CNS. We aimed to evaluate radiological changes of the CP in neuromyelitis optica spectrum disorders (NMOSD) patients.

Methods: We enrolled 60 AQP4-IgG-seropositive patients who had brain MRI within 3 months after acute attacks. We analyzed size and enhancement of the CP in contrast-enhanced axial and coronal T1-weighted images and compared those with 33 ages- and gender- matched healthy subjects. The size was measured in the thickest part in a minimal axis and the enhancement ratio of the brightest part of CP to adjacent white matter was calculated.

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Ryo Yamasaki, Eikinan Tyou, Hirono Yamaguchi, Jun-ichi Kira
Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University

Background: Multiple Sclerosis (MS) is one of the major neuroinflammatory disease characterized by relapse-remitting neurological symptoms. recent study showed early decrease of connexin (Cx) 47 in the acute MS lesion. Connexins are gap-junction consisting peptides which are organized as a hexagonal cylinder with a central pore. In the CNS, Cx30 and 47 are mainly expressed on astroglia while Cx32 and 47 are expressed on oligodendroglia.

Objective: To elucidate mechanistic contribution of oligodendrogial Cx47 in pathophysiology of EAE.

Method: Tamoxifen was administrated into Plp-CreERT; Cx47 fl/fl mice to allow tamoxifen-inducible oligodendroglia-specific Cx43 deficient mice (Cx43 KO). The induction of EAE was carried out 10 days after tamoxifen treatment. Control mice were also treated by tamoxifen.

Result: EAE was aggravated with more severe peak clinical score in Cx43 KO. In addition, these mice showed increased relapse rate. Histologically, inflammatory cell infiltration was increased, resulted in more severe demyelination in the acute phase. In
Susac’s Syndrome in a Patient Misdiagnosed with Multiple Sclerosis: A Case Report
Jong Sze Chin1; Sibi Sunny2; Raymond Seet Chee Seong2
1Department of Internal Medicine, National University Hospital, Singapore
2Department of Neurology, National University Hospital, Singapore

Susac’s syndrome is a rare neurological condition, presumed to be an autoimmune endotheliopathy, which is often misdiagnosed as Multiple Sclerosis (MS). It is characterized by clinical triad of branch retinal artery occlusions (BRAO), encephalopathy and sensorineural hearing loss. Clinically the diagnosis is difficult to make when patient presents only part of the triad. We present a 46-year-old gentleman with left-sided inferior quadrant vision loss secondary to left BRAO. He is otherwise well and healthy, without any neurological deficit. His mother has MS. Physical examination and routine laboratory studies were normal. Fluorescein angiography revealed a BRAO of the left eye. He was treated presumptively of MS with high dose steroid and referred to us. MRI brain was performed, showing multifocal infarct. Audiometry showed left sided sensorineural hearing loss. Based on the triad, the diagnosis of Susac’s syndrome was made. He was treated with methylprednisolone 1000 mg/day, followed by oral prednisolone 1 mg/kg/day and aspirin. His disease progress further where he developed right BRAO with new lesions on MRI Brain and required the initiation of cyclophosphamide. His disease better care of patient with this rare but potentially debilitating disorder.

Case Presentation from The Ordinary Submissions-2

O-19
Fingolimod-Associated PML with Mild Immune Reconstitution Inflammatory Syndrome in Multiple Sclerosis
Shuhei Nishiyama1, MD, PhD; Tatsuro Misu1,2, MD, PhD; Yukiko Shishido-Hara1, MD, PhD; Kazuo Nakamichi1, PhD; Masayuki Saijo3, MD, PhD; Yoshiki Takai1, MD, PhD; Kentarou Takei1, MD; Naoki Yamamoto1, Hiroshi Kuroda1, MD, PhD; Ryuta Saito1, MD, PhD; Mika Watanabe5, MD, PhD; Teiji Tominaga4, MD, PhD; Ichiro Nakashima1, MD, PhD; Kazuo Fujihara1, MD, PhD; Masashi Aoki1 MD, PhD
1Department of Neurology, Tohoku University Graduate School of Medicine
2Department of Neurology, National University Hospital, Singapore
3Department of Internal Medicine, National University Hospital, Singapore
4Laboratory of Neurovirology, Department of Virology 1, National Institute of Infectious Diseases
5Department of Neurosurgery, Tohoku University Graduate School of Medicine

Background: Today, the disease-modifying therapy for multiple sclerosis (MS) including fingolimod has been confronted with issues concerning the risk of progressive multifocal leukoencephalopathy (PML) due to JC virus reactivation. However, there has been no case of fingolimod-associated PML with immune reconstitution inflammatory syndrome (IRIS).

Case: A 34-year-old MS patient using fingolimod for 4 years had gradual progression of right hemiparesis and aphasia with a new subcortical white matter lesion in the precentral gyrus by initial MRI. One month after the cessation of fingolimod, brain MRI depicted a diffusely exacerbated hyperintensity on fluid-attenuated inversion recovery and diffusion-weighted imaging in the white matter with punctate gadolinium enhancement, suggesting PML-IRIS. A very low level of JCV-DNA (15 copies/mL) was detected in CSF as judged by quantitative PCR. Brain tissues were biopsied from the left frontal lesion, which showed several small demyelinated foci with predominant loss of myelin-associated glycoprotein with infiltrations of lymphocytes and macrophages. Clear viral inclusion was not observed with Hematoxylin-Eosin staining, but JCV genomic DNA was detectable in mildly-enlarged nuclei of 7 oligodendroglia-like cells by in situ hybridization. DNA extracted from brain sample was positive for JCV DNA (151 copies/cell). The patient was treated with one gram of IV methylprednisolone for 3 days and a weekly oral dose (375mg) of mefloquine, and her symptoms gradually improved.

Discussion: The rarity of fingolimod-associated PML-IRIS with low CSF JCV-DNA and unfound viral inclusions initially made her diagnosis difficult. The clinical course of fingolimod-associated PML-IRIS may be milder than that of natalizumab-associated PML.

Poster Session 1
MS Epidemiology

P-1
The Absence of Epidemiology Data of Multiple Sclerosis in the Pacific, South Asia, South East Asia, and East Asian Regions
W.L. Cheong1, D.D. Reidpath7
1School of Pharmacy, Monash University, Malaysia
2Jeffrey Cheah School of Medicine and Health Sciences, Monash University, Malaysia
Background: Comprehensive and up-to-date epidemiology data are required for policy makers to allocate sufficient resources towards the care of patients with multiple sclerosis (MS).

Objective: The objective was to review the availability of published MS epidemiology data for the countries and territories within the Pacific, South Asia, South East Asia, and East Asian regions.

Methods: Eligible studies on the epidemiology of MS that were conducted within the selected countries and territories were identified by searching the MEDLINE, SCOPUS, PubMed, EMBASE, Cochrane, and CINAHL databases from 1st January 1985 till present. This review adopted the PRISMA guidelines for systematic reviews.

Results: The review identified 65 eligible studies. Only 11 out of the 32 countries and territories (34.4%) had any published literature on the epidemiology of MS: China, Hong Kong, India, Japan, South Korea, Malaysia, Mongolia, Pakistan, Sri Lanka, Taiwan, and Thailand. Epidemiology data was only available for a small number of countries: prevalence (8 countries; 25%), incidence (5 countries; 15.6%), mortality (9 countries; 28.1%), time to EDSS (6 countries; 18.8%). Nationwide data for prevalence and incidence was only available for 4 (12.5%) and 3 (9.4%) countries respectively. Countries with nationwide data appear to indicate an increasing trend in MS prevalence over time.

Conclusion: The majority of countries and territories in the reviewed regions do not have any MS epidemiology data published in the scientific literature. The lack of data prevents policy makers from allocating sufficient resources towards treating MS, leading to its potential neglect.

P-2
The Steady Rise of Multiple Sclerosis in Sri Lanka: The Largest Series of Patients to Date
De Alwis SR, Gunasekera SN, Senanyake B
Institute of Neurology, National Hospital of Sri Lanka

Background: Multiple Sclerosis (MS) is characterized by inflammatory demyelination of the central nervous system. Data on MS has been limited in South Asia which includes Sri Lanka. Although MS is considered uncommon in this region, a steady rise in its prevalence has been observed.

Objectives: The study aims to identify epidemiological, clinical & radiological characteristics of MS patients in Sri Lanka while evaluating the treatment options available. Further, this study aims to describe the level of function and the quality of life of its population.

Methods: This was a retrospective cross-sectional study in patients diagnosed with MS, registered at the MS Clinic at the Institute of Neurology, National Hospital of Sri Lanka from September 2016 to present. Diagnosis of MS was according to the 2010 revised McDonald criteria. All patients were tested for AQP4 and MOG-IgG with a cell based assay to exclude NMOSD. Diagnosis of MS was according to the 2010 revised McDonald criteria. A total of 160 patients showing a clear onset or relapse time over 2011-2017 period were included. A year is divided into four consecutive seasons: spring (March to May), summer (June to August), fall (September to November) and winter (December to February). Seasonal trend for the occurrence of CNSDDs was analyzed by multinominal Cochran-Armitage trend test using R-software (v.3.4.1).

Results: A total 177 events including 17 relapses were identified. Of them, 79 events were related with myelitis, followed by optic neuritis (44), neuromyelitis optica (40) and multiple sclerosis (14). We did not find any statistically significant seasonal trend for the occurrence of CNSDDs, although fall showed the least events of these disorders.

Conclusions: Season could not be a major environmental factor implicated in CNSDDs development.

P-3
Seasonality for the Occurrence of Central Nervous System Demyelinating Diseases
Cui Y, Joo IS
Department of Neurology, Ajou University School of Medicine, Suwon, Korea

Background: Seasonal change has been known as one of the environmental factors affecting the development of first demyelinating events or relapses in central nervous system demyelinating diseases (CNSDDs) such as multiple sclerosis and optic neuritis.

Objective: To explore how the onset of first clinical event or relapse is different according to seasons across idiopathic myelitis, neuromyelitis optica, optic neuritis and multiple sclerosis.

Methods: In total, 160 patients showing a clear onset or relapse time over 2011-2017 period were included. A year is divided into four consecutive seasons: spring (March to May), summer (June to August), fall (September to November) and winter (December to February). Seasonal trend for the occurrence of CNSDDs was analyzed by multinominal Cochran-Armitage trend test using R-software (v.3.4.1).

Results: A total 177 events including 17 relapses were identified. Of them, 79 events were related with myelitis, followed by optic neuritis (44), neuromyelitis optica (40) and multiple sclerosis (14). We did not find any statistically significant seasonal trend for the occurrence of CNSDDs, although fall showed the least events of these disorders.

Conclusions: Season could not be a major environmental factor implicated in CNSDDs development.

P-4
The Association between Sodium Intake and Multiple Sclerosis in Isfahan Population
S Ghorbani, MJ Eslami, S Raeisi, AH Mahmoodzade, M Etemadifar
Isfahan University of Medical Sciences, Hezar Jarib Avenue, Isfahan, Iran

Background: The number of patients with Multiple Sclerosis (MS) is increasing in Iran, which has encouraged researchers to search about factors affecting MS. Studies have shown that high-salt intake is associated to development of MS and is considered as an environmental trigger. In presence of additional salt, developed T helper 17 (Th17) cells are more pathogenic and are involved in attacking the body’s own cells, which can lead to autoimmune diseases such as MS.

Objective: Because of the role of salt in Th17 development, we hypothesized that sodium chloride would be higher in MS patients than healthy controls. Therefore, we investigated the association between salt intake and MS in Isfahan population.

Method: A case-control study containing 23 patients and 23 healthy controls was performed in Isfahan, Iran. Na level was measured in 24-hour urine since it is the best representative of sodium intake. Laboratory values of the patients were compared with healthy controls, using the Chi-square test. The level of significance was set at p<0.050 in all analysis. All calculations were done using SPSS.
Results: In this study, the OR obtained was 0.988 (95% CI: 0.215–1.618) with a p-value of 0.027. These results show a significant relationship between urine-Na and MS. In other words, 1 (mEq/day) increase in urine-Na can increase the chance of MS development 0.988 times.

Conclusion: Based on this study, salt consumption can be considered as a MS trigger factor in genetically susceptible people.

P-5
The Effect of Exclusive Breastfeeding on Postpartum Multiple Sclerosis Relapses
N. Sahebi Vaigan1, A. Abadi2, R. Ghozat1, H. Delavar Kasmaei3, K. Gharagozlil
1 Shahid Beheshti University of Medical Sciences, 2Department of Community Medicine, Shahid Beheshti University of Medical Sciences, 3Department of Neurology, Shohadaye Tajrish Hospital, Shahid Beheshti University of Medical Sciences, 4Loghman Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran

Importance: The rate of multiple sclerosis relapses increases after delivery.

Objective: To assess if exclusive breastfeeding could reduce the risk of postpartum relapse.

Design: 66 women with relapsing remitting multiple sclerosis became pregnant during the years 2010-2013 were enrolled in our prospective study. 27 patients were excluded because of spontaneous abortion. 39 pregnant patients with the mean age of 30.6±5.1 were closely followed up in each trimester and 36, 12, 24 and 36 months after delivery. Disease-modifying drugs were terminated in all patients. The effect of exclusive breastfeeding (no supplemental feeding for at least 3 months) was compared on the first postpartum MS relapse with non-exclusive breast feeding (partial or no breast feeding at all), using Cox proportional hazards regression model.

Results: 69.2% of patients with full term delivery were intended to exclusively breastfeed for at least 3 months. 25.8% did not breastfeed at all and 5.1% included supplemental feeding. Relapse did not occur during pregnancy for those who did not exclusively breastfeed, the chance of experiencing at least one relapse during the first 6 months postpartum was 21.66 times (hazard ratio: 21.66, CI: 2.65-177.01, p=0.004). During the 36 months follow up, those who did not exclusively breastfeed were as almost as 2.45 times as likely to have at least one relapse in comparison to those patients who had exclusively breastfeed (hazard ratio: 2.541, CI: 1.19-5.40, p=0.015).

Conclusion: Patients with multiple sclerosis could benefit from exclusive breastfeeding breastfeeding as significantly reduce the rate of postpartum relapses. Encouraging patients to exclusively breastfeed could be regarded as one of the modalities of treatment.

P-6
Mortality in Multiple Sclerosis
M. Terzi1, S. Şen2, G. Koziates1, M. Onar3
1 Ondokuz Mayıs University Medical Faculty Neurology Department, Samsun, Turkey
2 Vezipkøpru State Hospital Neurology Clinic, Samsun, Turkey

Introduction: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system. In this study we investigated patients who were treated with MS diagnosis in our clinic and died.

Materials and Methods: From 1485 patients who were treated in our clinic center, 16 patients who died were included in the study. Data were obtained from iMed database. For statistical analysis SPSS 21.0 program has been used.

Findings: 12 of these 16 patients were female and 4 were male. Final EDSS values ranged between 1.5 and 8.0 and the mean value was 5.37. Patients’ age ranged between 28 and 64 year and the mean age was 47.2. Disease duration ranged between 1 months to 26 years at the time of death. Analyses made separately for female and male patients are shown in the table 1. EDSS and number of attacks of patients who died and patients who survived were compared. While high level of EDSS was found to be associated with mortality (P<0.001), diagnosis time and total number of attacks were not associated with mortality.

9 patients died as a result of infections and 3 patients died of heart attack. Detailed reasons for their death are shown in the table 2.

Conclusion: Infections seem to be the most important cause of mortality in MS. The reason for this could be the disease nature and/or the therapeutic agents used. Disability levels of patients are associated more with mortality than number of attacks and disease duration.

Poster Session 2
MS Clinical Aspects

P-7
Initial and Final Diagnosis: Multiple Sclerosis Versus Mimics
F. Belgin Balı, Aytul Mutlu, Birgül Bastan, Ayse Özlem Cokar
Haseki Training and Research Hospital, Neurology Department, Istanbul, Turkey

Objectives: To explore the frequency and type of multiple sclerosis (MS) mimics in patients referred with an initial diagnosis of MS.

Methods: This retrospective study includes all patients with an initial diagnosis of MS referred to our multiple sclerosis outpatient clinics in Istanbul between March 2013 and March 2017. The final diagnosis was recorded and demographic, clinical, laboratory, electrophysiological and radiological variables were collected.

Results: Two-hundreds and thirty-five patients were referred for diagnostic confirmation of MS. The final diagnosis of MS was confirmed in 166 (70.6%) patients, while 69 (29.4%) turned out to have an alternative diagnosis. Half of the patients referred with clinical suspicion had a final diagnosis of MS, however only 8,1% of patients referred based on radiological findings had a final diagnosis of MS. The most frequent alternative diseases were as follows: non-specific white matter lesions in MRI (17,9%), migraine (11,5%), psychogenic (8,9%), systemic autoimmune diseases (6,4%), NMO spectrum disease (4,7%), and hereditary diseases (CADASIL, CARASIL) (1,7%).

Abnormality in neurological examination was the only statistically significant parameter confirming the final diagnosis of MS (p<0.003). Other clinical and laboratory features suggestive for a final diagnosis MS were; abnormal evoked potentials, MRI findings fulfilling 2010 McDonald criteria, presence of oligoclonal bands in the cerebrospinal fluid, non-cognitive presenting symptoms, negative family history.
Conclusions: The final diagnosis was not MS; but a mimic in 29.4% of patients referred to our outpatient clinics with an initial diagnosis of MS. The most common mimics in our patients were similar with the literature.

P-8
Establishment of a Multidisciplinary Neuroimmunology Clinic Improves Care of Multiple Sclerosis Patients
Peng XJ1, Tye SN1, Yeo T1, Wong SK2, Tan K1
1Department of Neurology, National Neuroscience Institute, Singapore
2Department of Research, National Neuroscience Institute, Singapore

Background: Multiple Sclerosis (MS) is a chronic disease requiring a multifaceted approach for disease management. The National Neuroscience Institute (NNI) established a Multidisciplinary Neuroimmunology Clinic (MDNIC) with 2 neurologists and 2 nurses in December 2015 with an aim to improve MS care.

Objective: To compare the level of MS care, using (with modifications) the American Academy of Neurology (AAN) MS quality measures, before and after MDNIC establishment.

Methods: Seven (out of 11) items from the AAN recommendation were selected as our quality measures. The percentages of patients (blinded consecutive recruitment) who achieved each measure before (n=40) and 1 year after (n=40) MDNIC establishment were calculated. New immununology case waiting time and total number of patients seen before and after MDNIC establishment were also compared. X2 test (Fisher’s Exact) was used to compare group proportions (p<0.05 taken as statistical significance).

Results: There was improvement across most measures: new MS diagnosis using 2010 McDonald criteria (0% to 80%, p=0.143), MS disability documentation (86.1% to 97.4%, p=0.099), fall screening (7.5% to 47.5%, p<0.001), fatigue screening (0.0% to 60.5%, p<0.001), depression screening (0.0% to 60.5%, p<0.001), performing comparison MRI within 24 months of diagnosis (92.3% to 100.0%, p=1.000), cognitive impairment testing (84.3% to 96.8%, p=0.196). The average new case waiting time reduced from 86.0 to 54.8 days and total patients seen per session increased from 12.0 to 14.2.

Conclusions: The MDNIC improved MS care across a majority of quality measures, without compromising new case waiting time and number of patients seen.

P-9
Clinical Characteristics of The First Manifestation in Multiple Sclerosis
Yuge Wang1*, Yanqiang Wang2*, Bingjun Zhang1, Yu Yang1, Wei Qiu1, Xueqiang Hu1, Zhengqi Lu1**
1Department of Neurology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China
2Department of Neurology, The Affiliated Hospital of Weifang Medical University, Weifang, China

Background: Multiple sclerosis (MS) is a chronic, immune-mediated and degenerative CNS disease. The clinical manifestations of MS complex and changeable, and can easily be clinical leakage, misdiagnosed. To improve clinician understanding of MS, and improve the cure rate and early diagnosis. The objective of this study was to describe the clinical characteristics of the initial manifestation in MS.

Methods: The study was retrospective. 287 MS patients were included. Data regarding the demographics, initial symptoms, the degree of recovery from the initial relapse, neuroimaging, cerebrospinal fluid analysis, long-term disability, and progression were collected from the medical registry.

Results: The mean age was 35.4, and there was a female predominance (80.1%). Age of onset mean duration was 4-160.8 months, the time from onset of symptoms to other symptoms occurred was 0.5-27.2 months, the mean time between the first symptom and diagnosis was 4.18 years. The initial symptoms were headache (3.3%), nystagmus (3.1%), vision disorder including diplopia (20.1%), bowel or bladder dysfunction (3.3%), movement disorders (22.4%), sensory disturbances (18.3%), neuropathic pain (2.1%), Paroxysmal nausea and vomiting, hiccup (3.6%), choking cough or dysphagia (2.1%), vertigo and dizziness (3.2%), Paroxysmal itching and pruritus (4.5%), Ataxia (3.3%), Cognitive dysfunction (1.4%), Lhermitte sign (1.4%), Painful spasm (3.2%), Trigeminal neuralgia (2.1%), Seizures (2.6%).

Conclusions: The MS initial clinical manifestation is very variable, movement disorders, sensory disturbances and vision disorder were the first most frequent brainstem symptoms. All of these would be helpful to the early diagnose and treatment of the MS.

P-10
Differences Between Patients with Multiple Sclerosis and Healthy Individuals in Terms of Falls, Balance, Mobility and Hand Functions
A Göz1, B Balçı2, E Göz3, A Kıskdereoglu4, M Gedizlioglu5
1SBU İzmir Boyazka Teaching Hospital, Physical Therapy and Rehabilitation Department
2Dokuz Eylül University, School of Physical Therapy and Rehabilitation
3SBU İzmir Boyazka Teaching Hospital, Neurology Department

Objective: Patients with multiple sclerosis (PwMS) frequently experience difficulties in balance, mobility and hand functions. Falling is a common problem in PwMS. The objective of this study is to examine comparatively the number of falls, balance, mobility and hand functions in MS patients and healthy controls.

Methods: Thirty-two PwMS and 32 healthy age and gender matched controls were recruited. Patients with musculoskeletal or cognitive problems, significant tremor in upper extremities, relapse in the last month, severe visual impairment, neurological disorders other than MS, EDSS score 6 and over were excluded. Balance was evaluated with Activities-specific Balance Confidence Scale and Biodex Balance System (Postural Stability Test and modified Clinical Test of Sensory Interaction on Balance); mobility with Timed Up and Go Test; and hand functions with 9-Hole Peg Test.

Results: Mean ages of PwMS and controls were 37.3±7.06 and 35.3±10.02 years respectively. PwMS had a much higher incidence of falling than controls (up to 25 vs up to 3 in one year). Modified sensory interaction test and Biodex Balance system were very efficient to reveal postural instability on static or unstable surfaces, either eyes open or closed. The performance scores of balance, mobility and hand functions were all markedly worse in PwMS than the controls (p<0.0001, for all tests applied).

Conclusions: MS patients, even the ones with mild disability had worse outcomes in terms of falls, balance, mobility and hand functions. So that, balance, mobility and hand function training should be included into MS physiotherapy programs in general.
P-11
**Olfactory Dysfunction in Multiple Sclerosis**
A. Çimen ATALAR1, Ufuk Emre1, Yuksel Erdal1, Muhammed Yildiz2, Betul Tekin Güveli3
1 İstanbul Education and Research Hospital Neurology Clinic, İstanbul, Turkey
2 İstanbul Education and Research Hospital Otorhinolaryngology Clinic, İstanbul, Turkey
3 Private Rumeli Hospital Department of Neurology, İstanbul, Turkey

**Background:** Multiple sclerosis (MS) is one of the most common chronic neurological diseases that can cause disability. MS can have various clinical manifestations (sensory, motor, etc.), one of which is olfactory dysfunction. In clinical practice, olfactory disturbances are usually underdiagnosed.

**Objective:** To analyze the clinical and electroneurophysiological characteristics of peripheral neuropathy in patients with MS.

**Methods:** We assessed 31 MS patients and a control group of 24 healthy people matched in sex and age in our MS outpatient clinic. Each subject is interiewed for detailed demographic data (age, sex, duration of disease, number of clinical attacks, EDSS (Expanded Disability Status scale) score). Connecticut Chemosensory Clinical Research Center (CSCRC) olfactory test and Montreal Cognitive assessment (MOCA) is applied to each participant.

**Results:** The CCCR test scores (smell identification, smell threshold and mean scores) of the MS patients were lower than the control group significantly (p<0.05). As the disease duration elongates and number of attacks increase, the CCCR scores decreased and this was significant (p<0.05). EDSS scores had no effect on the CCCR Test scores. The MOCA score was positively correlated with the olfactory test and the CCCR Test scores were higher at the higher MOCA scored patient group.

**Conclusions:** As a result, our study suggests that cranial nerve involvement in MS is not only specific to the optic nerve and there is an olfactory dysfunction at MS patients which is usually underdiagnosed. The assessment of the olfactory nerve can be important at the follow-up visits of the MS patients.

P-12
**Peripheral Neuropathy in Multiple Sclerosis: A Clinical and Electroneurophysiological Study**
Bing Qin, Li Xiao, Zhengqi Lu *
Department of Neurology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong 510630, PR China

**Background:** Peripheral neuropathy (PN) in combination with multiple sclerosis (MS) is very unusual, and it remains unclear if they are parts of the same entity or coincidental findings.

**Objective:** To analyze the clinical and electroneurophysiological characteristics of peripheral neuropathy in patients with MS.

**Methods:** Thirty-six MS patients were enrolled in this study and their clinical manifestation were documented. Through using the technique of nerve conduction velocity (NCV), motor conduction velocity (MCV), sensory conduction velocity (SCV) and latency and amplitude of peripheral nerves were examined. F-wave and H-reflex of median and tibial nerves were also observed.

**Results:** Thirty-six cases were all definitely diagnosed with MS combined with PN. The clinical symptoms included extremity numbness in 17 cases (47.2%), and limb weakness in 13 cases (36.1%), radicular pain in 6 cases (16.7%). Signs included peripheral sensory disturbances in 15 cases (41.7%), attenuation or absence of tendon reflex in 21 cases (58.3%), muscle strength decreases in 10 cases (27.8%), and myatropy in 4 cases (11.1%). The electroneuropathological abnormalities included prolonged latent phase of F-wave and H-reflex, low F-wave response frequency, decreased MCV and SCV and prolonged distal latencies.

**Conclusions:** In some MS patients peripheral nerves are involved in the process of demyelination. It is sound to evaluate the function on peripheral nerves of MS by using techniques of clinical electroneurophysiology.

P-13
**The Investigation of Relationship between Core Stability and Trunk Position Sense with Disability Level in Multiple Sclerosis Patients**
C. Irkec2, A. Guclu-Gunduz3, T. Ozkan1, Y. Aydin1, K. Cekim1, G. Yazici1, F. Soke1
1 Gazi University, Faculty of Health Sciences, Ankara, Turkey,
2 Gazi University, Faculty of Medicine, Ankara, Turkey,
3 Ankara Yildirim Beyazit University, Faculty of Health Sciences, Ankara, Turkey

**Background:** Depending on the influence in the CNS, functional systems and walking are affected, the level of disability is increased, various sensory and motor problems are observed in Multiple Sclerosis (MS) patients.

**Objective:** To investigate the relationship between balance, core stability and trunk position sense with disability level in MS patients.

**Methods:** 45 MS patients were included in the study. Disability level of MS patients was assessed with Expanded Disability Status Scale (EDSS). Core stability was examined with assessing core endurance and core power. Core endurance was assessed with trunk flexion, modified Biering-Sorensen, bridge, right and left lateral bridge tests; core power was assessed with sit-ups and modified push-ups tests. Trunk position sense was assessed using digital inclinometer with trunk reposition tests. Measurements were made at 2 levels; Lumbosacral (LS) and Thoracolumbar (TS) regions.

**Results:** The results of the study showed that the EDSS was associated with core endurance tests (except for modified Biering-Sorensen test), core power tests and LS reposition tests on eyes closed-firm surface and eyes open-foam surface (r= -0.298/-0.544, p<0.05). EDSS wasn’t related with LS position sense (p>0.05).

**Conclusions:** It was observed that as the level of disability increased, core stability decreased. However, there wasn’t clear relationship between disability level and trunk position sense in our MS patients. Although core stability seems to be affected at mild level of disability, the results suggest this there isn’t an affection of trunk position sense so as to cause disability. However, we think that there are more controlled studies involving more individual is needed.

P-14
**The Effects of Core Endurance and Trunk Position Sense on Balance in Patients with Multiple Sclerosis**
T. Ozkan4, A. Guclu-Gunduz2, C. Ozkul1, C. Irkec1, K. Cekim1, Y. Aydin1
1 Gazi University, Faculty of Health Sciences, Ankara, Turkey,
2 Gazi University, Faculty of Medicine, Ankara, Turkey,
Background: Balance disorders are seen at various grades in Multiple Sclerosis (MS) patients. Trunk stability is an important factor providing the balance. Core stability and trunk position sense are also important motor and sensory factors that provide body stability.

Objective: To investigate the effects of core endurance and trunk position sense on balance in patients with MS.

Methods: 45 MS patients with EDSS score of 0.5-4 were included in the study. Core endurance was assessed with trunk flexion, modified Biering-Sorensen, prone bridge, and right and left lateral bridge tests. Trunk position sense was assessed using digital inclinometer with trunk reposition tests. Measurements were made at 2 levels; Lumbosacral (LS) and Thoracosacral (TS) regions. Balance was assessed using the Biodex-BioSway Balance device with the postural stability (PS) test, limits of stability (LOS) test and the modified sensory organization test (MSOT). The PS test was performed on both feet and on the left and right foot.

Results: As a result of the study, while there wasn’t relationship between the prone bridge test with one leg PS test and modified Biering-Sorensen and prone bridge test with LOS, all other balance parameters were associated with the core endurance tests (r=-0.323/0.602, p<0.05). While some LS and TS region reposition test results weren’t related to LOS test, all other parameters were related to each other (r=0.258/0.518, p<0.05).

Conclusions: These results indicate that many aspects of core endurance and trunk position sense is correlated with balance. Thus, it is thought that approaches to develop core endurance and trunk position sense will be useful for improving balance in patients with MS.

P-16
Description of Quality of Sleep and Sleep Disorder Among Indonesian Multiple Sclerosis Foundation Members

Gilang Nispu Saputra1, Yustiani Dikot1, Ahmad Rizal2
1Resident, 2 Consultant of Neurology, Department of Neurology Hasan Sadikin Hospital, University of Padjajaran, Bandung, Indonesia.

Introduction: Multiple Sclerosis (MS) and Neuromyelitis Optica (NMO) is an inflammation demyelinating condition of Central Nervous System (CNS) due to an autoimmune process. In Indonesia MS prevalence is 1 – 5 /100,000. Fatigue is the most common symptom seen in patients with MS and patients with NMO, and it affects their quality of life. A study in Germany showed a significant correlation between fatigue and sleep disorders in MS patients. There has been no study yet about sleep disorders among the MS bearers in Indonesia.

Methods: This was a descriptive study. The respondents were members of Indonesian Multiple Sclerosis Foundation. Data was collected via self-administered questionnaires that assessed the quality of sleep and sleep disorders. Sleep disorder were measured using Pittsburgh Sleep Quality Index (PSQI). This study was done from June – August 2016.

Results: Twenty-seven respondents filled the questionnaires; 85% were MS, and 15% were NMO patients. Most of the respondents were women (81%), and 89% were university graduates. The PSQI was poor for 81% of the subjects. This study also showed that 52% of the patients experienced mild sleep disorder and 26% medium sleep disorder.

Conclusion: Most of the respondents were in category of poor sleep quality (81%) and mild sleep disorder (52%). Quality of sleep and sleep disorder need to be managed among MS bearers.

P-17
Always Alone with my MS

S Demirci, MD Unlu
Suleyman Demirel University School of Medicine Neurology Department, Isparta, Turkey

Aim: Multiple sclerosis patients have to cope with not only general physical health problems but also psychosocial problems. Enacted or internalized stigma is one of the important aspects of psychosocial function.

Objective: To evaluate the internalized and enacted stigma in MS patients.
Method: Thirty patients from the outpatient clinic agreeing to participate in the study were asked to fill in the Stigma Scale for Chronic Disease (SSCD), UCLA-Loneliness Scale, Liverpool Self-Efficacy Scale (LSES), Beck Depression Inventory and Rosenberg Self-Esteem Scale after being fully informed about the goal and content.

Results: Patients (24 female) aged 34±9.5 years, with disease duration of 6.8±5.2 years. Mean EDSS was 2.2±1.9. They had mild depressive symptoms (BDI:18.0±10.3). BDI scores showed a positive correlation with SSCI scores (r=0.607, p<0.01). With advanced age and disease duration both enacted (r=0.652, p<0.001; r=0.399, p=0.043 respectively) and internalized stigma (r=0.634, p=0.001; r=0.692, p<0.001; respectively) increased positively. Either enacted or internalized, stigma caused increased feeling of loneliness (r=0.799, p<0.001; r=0.744, p<0.001; respectively), low self-esteem (r=0.573, p=0.002; r=0.601, p=0.001; respectively) and decreased self-efficacy (r=0.519, p=0.007; r=0.641, p<0.001; respectively). High negative correlation between the personal agency subscale of LSES and enacted (r=0.763, p=0.000) and internalized stigma (r=0.730, p<0.001) suggests partial adaptation to the impact of the disease with experienced stigma.

Conclusion: The proven stigma affects mood, self-esteem, efficacy and adaptation to disease even in mild-moderately affected MS patients.

P-18 Variables That Affect Life Satisfaction Of Multiple Sclerosis Patients A Comparative Study

M.Terzi1, S. Şen2, H. Kumcağız1, Y.Terzi4
1 Ondokuz Mayıs University Medical Faculty Neurology Department, Samsun, Turkey
2 Vezirköprü State Hospital Neurology Clinic, Samsun, Turkey
3 Ondokuz Mayıs University Education Faculty Educational Sciences, Samsun, Turkey
4 Ondokuz Mayıs University Science Faculty Department Of Statistics, Samsun, Turkey

Introduction: The main objective of this study is to investigate life satisfaction of a group of patients with multiple sclerosis (MS).

Materials and Methods: This study included 60 ms, 63 healthy control. For data collection, ‘Personal Information Form’, ‘Beck Depression Scale’, ‘SP 36 Life Quality Scale’, ‘Satisfaction of Life Scale’, ‘Multidimensional Scale of Perceived Social Support’, ‘Beck Hopelessness Scale’, ‘The Ways of Stress Coping Scale’, ‘STA State-Trait Anxiety Inventory’ and ‘Fatigue Assessment Scale’ were used. Demographics data.

Findings: According to the analysis results, a negative significant relationship was found between the dependent variable, life satisfaction and the independent variable, depression variable in MS patients at a significance level of 1%. A negative significant relationship was found between life satisfaction of MS patients and the variable, hopelessness at a significance level of 1.

The variables, state anxiety and hopelessness of the sub-dimension mental health of the SF-36 Quality of Life Scale in MS patients have a significant effect on the quality of life scores (R=0.667, R²=0.445, p<0.01). The three abovementioned variables account for approximately 41.5% of the change in life satisfaction. In the control group, the variables hopelessness and trait anxiety have a significant effect on the life satisfaction scores (R=0.595, R²=0.354, p<0.01).

Conclusion: MS clearly and negatively affects life satisfaction and life quality of patients. Fatigue, hopelessness and depression are the most significant factors that negatively affect life satisfaction.

P-19 The Role of Coping Styles in the Relationship between Personality Traits and Quality of Life of Multiple Sclerosis Patients

Seyed Amir Hejazi Taghanaki,1 Hamid Reza Hatami2, Fatemeh Najafi Ghodsi3, Ehsan Sharifipour4
1 Associated professor of Neurology, Qom University of Medical Sciences, Qom, Iran
2 Imam Hossein University, Tehran, Iran
3 Islamic Azad University, Arak, Iran
4 Assistant professor of Neurology, Qom University of Medical Sciences, Qom, Iran

Background and Objectives: Individuals with multiple sclerosis (MS) show different reactions to the disease according to their personality traits, which can affect their quality of life. In this research, the mediator role of coping styles was investigated in the relationship between personality traits and quality of life in individuals with multiple sclerosis (MS).

Methods: Of all individuals with MS, who were member of MS Society of Qom province, 170 persons were selected using probability convenient sampling. All the patients were investigated using a general questionnaire in addition to 3 international approved standard tools (including Stress Coping Styles, Quality of life, and Personality Traits) questionnaires. Data analysis was performed by descriptive-analytical statistics, Pearson’s correlation coefficient. The significance level was considered as p<0.05.

Results: The mean age of the patients was in the range of 18-59 years, 32.34±8.71, of whom 138 subjects (83.2%) were female. In this research, there was a significant correlation between coping styles and quality of life and its dimensions in MS patients. The correlation between coping styles and personality traits was significant. There was a significant correlation between personality traits and quality of life and its dimensions in MS patients. In this study, path analysis results proved the mediator role of coping styles in the relationship between variables of quality of life and personality traits.

Conclusion: According to the results of this study, there is a significant correlation between personality traits of the individuals with MS and type of the used coping styles, which can affect the quality of life in these patients.

Poster Session 3 MS Imaging and Electrophysiology

P-20 The Role of Diffusion Weighted Imaging in Demonstrating Acute Demyelinating Lesions

H. Sariahmetoglu1, I. E. Kurtpinar1, H.C. Serindag2, B. Kara, H.H. Selçuk1, A. Soysal2
1 Assoc. Professor of Neurology, Qom University of Medical Sciences, Qom, Iran
2 Assistant professor of Neurology, Qom University of Medical Sciences, Qom, Iran

Programme & Abstracts | 33
Background: Diffusion weighted images (DWI) evaluates water mobility and usually used for diagnosing acute ischemic infarction. Objective: The objective of this study is to investigate whether diffusion MRI has a role in detecting acute demyelinating lesions compared to contrast enhanced T1-weighted images (CET1WI).

Methods: Using the data recorded in MSBase, we detected MS patients in acute attack between January 2014–July 2017 followed in our clinic. Retrospectively, we examined total 165 new lesions of 71 patients having 74 attacks in this period of time.

Results: 50 women 21 men were included in this study ages ranging from 18 to 64. 165 new lesions were detected compared to previous MRI before acute attack. 153 out of 165 new lesions were contrast enhanced in CET1WI. 12 lesions are not contrast enhanced. 114 lesion was hyperintense in both DWI and ADC, 21 new lesions were hyperintense in DWI, isointense in ADC (HDWADC). We found that HDWADC lesions was significantly higher in number than DWIADC lesions during acute attack in MS patients (p<0.01).

Conclusion: Our results demonstrated that diffusion MRI may help diagnosing acute attack in MS patients. During acute attack, if we find out a new lesion hyperintense in both DWI and ADC, and if it is compatible with the patient’s symptom, contrast enhanced T1 weighted MRI is not crucial especially for patients who are pregnant or has kidney disease.

P-21 Differential Associations of Spinal Cord Atrophy with Clinical Disability between Japanese Patients with Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder
Y Nakamura1, Z Liu2, K Shinoda1, T Matsushita1, A Hiwatashi3, J-I Kira1
1Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
2Medical School of Kyushu University, Fukuoka, Japan
3Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Background: Spinal cord atrophy in multiple sclerosis (MS) correlates with disability in Caucasian patients, while such a correlation remains to be established in Asian patients with MS and neuromyelitis optica spectrum disorder (NMOSD).

Objective: To investigate the relationship between spina cord atrophy and disability in Japanese patients with MS and NMOSD.

Methods: Cross-sectional spinal cord areas at the C2/C3, C3/C4, T8/9, and T9/10 disc levels were measured in 117 relapsing-remitting MS (RRMS), 27 progressive MS (PMS), and 47 NMOSD patients with AQP4-IgG. Expanded Disability Status Scale (EDSS) scores were used to assess disability.

Results: NMOSD patients had significantly smaller thoracic cord areas than MS patients (p=0.03 at T8/T9, p=0.047 at T9/T10), while there were no significant differences in cervical cord areas between the two conditions. PMS patients showed smaller cervical cord areas than RRMS patients (p=0.03 at C2/C3, p=0.006 at C3/C4). In MS, both cervical and thoracic cord areas were significantly associated with EDSS scores (p<0.001 at C2/C3, p=0.001 at C3/C4, p=0.001 at T8/T9, p=0.002 at T9/T10). In NMOSD, only thoracic cord areas were associated with EDSS scores (p=0.002 at T8/T9, p=0.012 at T9/T10). Multivariate analyses revealed that age, PMS, number of relapse, and smaller C2/C3 areas were associated with higher EDSS scores in MS, while age and smaller T9/T10 areas were associated with higher EDSS scores in NMOSD.

Conclusions: Spinal cord atrophy is a potentially useful marker of disability in Japanese patients with MS and NMOSD when a relevant spinal cord level is measured according to the disease.

P-22 Differentiation of Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder Using Deep Learning on Brain MRI
Min JH, MD, PhD1,2, Kim Y1, Seok JM, MD2, Kim DS, MD2, Kim BJ, MD, PhD2, Seong JK, PhD2
1Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
2Neuroscience Center, Samsung Medical Center, Seoul, South Korea

Background: Although neuromyelitis optica (NMO) is characterized by brain lesions specific to this disorder, patients with NMOSD sometimes fulfill the diagnostic MRI criteria for multiple sclerosis (MS). Therefore, the differentiation of MS and NMOSD on brain MRI is still challenging.

Objectives: In this study, we tried to elucidate the new method using deep learning for differentiation of NMO from MS on brain MRI.

Methods: From the prospective registry of CNS demyelinating disorders in Samsung Medical Center (Seoul, South Korea), we collected MRI scans of patients with MS and NMO spectrum disorder (NMOSD). We investigated MRI scans, including high resolution T1-weighted Turbo field echo (TFE) and T2-weighted Fluid Attenuated Inversion Recovery (FLAIR). To extract white matter hyperintensities (WMH), we used Freesurfer, brain MRI image analyzing tool, and FusionNet, Convolutional Neural Network for biomedical image segmentation.

Results: We analyzed 128 MS and 70 NMOSD MRI scans. MRI slices that are likely to have WMH were selected as training set. We then trained VGGNet for image classification with the training set and finally predicted whether the MRI scan is NMO or MS.

Conclusions: Our study suggests that this new method using deep learning can be helpful to differentiate between NMOSD and MS on brain MRI.

P-23 Contribution of Cortical Lesions to Cognitive Dysfunction in Japanese Patients with Multiple Sclerosis
K Shinoda1, T Matsushita1, Y Nakamura1, S Sakai1, H Nomiyama1, R Yamasaki1, O Togao2, A Hiwatashi2, J-I Kira1
1Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
2Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Background: Magnetic resonance imaging (MRI) is a useful method for evaluating MS lesions. In this study, we tried to elucidate the new method using deep learning for differentiation of NMO from MS on brain MRI.

Methods: From the prospective registry of CNS demyelinating disorders in Samsung Medical Center (Seoul, South Korea), we collected MRI scans of patients with MS and NMO spectrum disorder (NMOSD). We investigated MRI scans, including high resolution T1-weighted Turbo field echo (TFE) and T2-weighted Fluid Attenuated Inversion Recovery (FLAIR). To extract white matter hyperintensities (WMH), we used Freesurfer, brain MRI image analyzing tool, and FusionNet, Convolutional Neural Network for biomedical image segmentation.

Results: We analyzed 128 MS and 70 NMOSD MRI scans. MRI slices that are likely to have WMH were selected as training set. We then trained VGGNet for image classification with the training set and finally predicted whether the MRI scan is NMO or MS.

Conclusions: Our study suggests that this new method using deep learning can be helpful to differentiate between NMOSD and MS on brain MRI.

P-24 Brain Volume Loss Is Present in Japanese Patients with Multiple Sclerosis with No Evidence of Disease Activity
H Yokote1,2, T Kamata3, S Toru3, N Sanjo3, T Yokota3
1Department of Neurology, Nihote Memorial Nakano General Hospital, Tokyo, Japan
2Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Background: Despite the introduction of disease-modifying drugs (DMDs), several studies have demonstrated that multiple sclerosis (MS) is associated with brain volume loss. The purpose of this study was to investigate brain volume loss in Japanese patients with MS with no evidence of disease activity (NEDA).

Methods: From the prospective registry of CNS demyelinating disorders in Samsung Medical Center (Seoul, South Korea), we collected MRI scans of patients with MS and NMO spectrum disorder (NMOSD). We investigated MRI scans, including high resolution T1-weighted Turbo field echo (TFE) and T2-weighted Fluid Attenuated Inversion Recovery (FLAIR). To extract white matter hyperintensities (WMH), we used Freesurfer, brain MRI image analyzing tool, and FusionNet, Convolutional Neural Network for biomedical image segmentation.

Results: We analyzed 128 MS and 70 NMOSD MRI scans. MRI slices that are likely to have WMH were selected as training set. We then trained VGGNet for image classification with the training set and finally predicted whether the MRI scan is NMO or MS.

Conclusions: Our study suggests that this new method using deep learning can be helpful to differentiate between NMOSD and MS on brain MRI.
P-25
Correlation Between Brain Volume Loss and Long-term Disability Worsening in Patients With MS: SIENA Analysis of TEMSO MRI Data

T Sprenger,1,2 L Gaetano,1,3 N Mueller-Lenke,1 K Thangavelu,4 S Cavalier,4 EW Radue,2 JS Wolinsky,6 MP Sormani,5 L Kappos2

1DKD HELIOS Klinik, Wiesbaden, Germany; 2University Hospital Basel, Basel, Switzerland; 3Medical Image Analysis Center (MIAC) AG, Basel, Switzerland; 4Sanofi, Cambridge, MA, USA; 5McGovern Medical School, UTHealth, Houston, TX, USA; 6University of Genoa, Genoa, Italy

Background: In TEMSO (NCT00134563), Structural Image Evaluation using Normalization of Atrophy (SIENA) analysis showed that teriflunomide significantly reduced brain volume loss (BVL) vs placebo.

Objective: To explore the relationship between BVL and long-term confirmed disability worsening (CDW) in TEMSO and its extension (NCT00803049).

Methods: Blinded SIENA analysis of patient scans from TEMSO (N=969) determined BVL in Years 1 and 2. A 13-trial meta-analysis evaluating correlation between treatment effects on BVL and CDW in patients with relapsing-remitting MS was updated to include SIENA analysis of BVL in TEMSO. To evaluate the predictive value of BVL during the first 2 years related to 12–24-week CDW over 5 years, the total population (n=709) was categorized into quartiles (Q1–Q4) defined by percentage brain volume changes from baseline to Year 2. Probability of CDW was derived from Kaplan–Meier estimates. Quartiles were compared using the Cox proportional hazards model.

Results: After SIENA analysis of BVL in TEMSO, coefficient of determination for relationship between BVL and CDW strengthened from 0.48 in the original meta-analysis to 0.61. In quartile analyses, Q4 had a significantly greater probability of 12- and 24-week CDW after 5 years vs Q1 (lowest BVL): Q1 vs Q4 hazard ratios, 0.611 (95% CI 0.432, 0.865; P=0.0055) and 0.566 (95% CI 0.386, 0.830; P=0.0036) for 12- and 24-week CDW after 5 years, respectively.

Conclusions: Analyses support a correlation between BVL and teriflunomide’s effects on these outcomes, and highlight the predictive value of BVL earlier in the disease course.

P-26
EEG Changes in Patients with Multiple Sclerosis Who were Used Fampridine

G Kutlu, Y Unal, M Korkmaz, Mugla SK University, School of Medicine, Department of Neurology, Mugla-TURKEY

Objective: Fampridine is potassium channel blocker; increase central nervous system and neuromuscular junction acetylcholine release; possibly restores conduction in central demyelinated axons. However, it is contraindicated in patients with epilepsy. The aim of this study was to investigate electroencephalography (EEG) in patients with multiple sclerosis who were used fampridine.

Methods and Patients: This study was included four patients with multiple sclerosis. Demographic data, treatment and EDSS score for each patient were recorded. EEG was performed to the patients at the beginning, 3rd and 6th month of treatment.

Results: The mean age of patients was 45 years old. All of them were female. Three of them was used fingolimod, the remaining of one was used interferon beta 1b. The mean EDSS score was 4.75. No history of epileptic seizure is present in these patients. EEG was normal before treatment in all patients. Repeated EEG’s was also normal in three patients, however one patient had abnormal findings in EEG’s at 3rd and 6th month of treatment. Sharp and slow waves were detected in bilateral temporal region in her EEG. There were no differences between EEG’s at 3rd and 6th month of fampridine treatment. Despite these EEG findings, the fampridine treatment was continued. This patient had no history of epilepsy seizure before and during treatment of fampridine.

Conclusion: Although some EEG changes was determined during treatment, fampridine should continue in the absence of epileptic seizure.

P-27
Visual Evoked Potential Abnormalities in Indonesian Multiple Sclerosis and Neuromyelitis Optic Spectrum Disorder Patients

A Diwyacitta, Al Rusmana, David, A Yanuar, R Estiasari

Department of Neurology Faculty of Medicine Universitas Indonesia – RSUPN Dr. Cipto Mangunkusumo, Jakarta, Indonesia

Background: In Multiple Sclerosis (MS) and Neuromyelitis Optic Spectrum Disorder Patients (NMOSD), Visual Evoked Potential (VEP) typically indicates an elongation of P100 latency and a decreased amplitude.

Objective: To determine VEP abnormalities in Indonesian MS and NMOSD patients and its association with optic disc appearance, disease duration and number of relapse.

Method: A retrospective cross-sectional study was conducted by reviewing medical record of MS and NMOSD patients (age 19-63 years) in RSUPN Dr-Cipto Mangunkusumo Jakarta. Latency, amplitude and interocular amplitude ratio (IAR) of pattern reversal VEP were analyzed and compared with healthy control.

Results: Delayed P100 latency was found in 17 eyes of MS (from 12 patient) and 14 eyes of NMOSD (from 10 patients) patients. The P100 latencies in MS and NMOSD was significantly more delayed compared to healthy control (p<0.001). MS and NMOSD without optic disc abnormality also showed significant prolonged latency (p<0.001). The amplitude was significantly higher in MS compare to control, but it was not evidence in NMOSD. We found no different in IAR between MS/NMOSD and healthy control. Strong correlation was found between P100 amplitude and number of relapse in MS (r=0.694), and moderate correlation between IAR and disease duration in MS and NMOSD (r=0.470).

Conclusion: VEP is remain important tools in MS/NMOSD cases evaluation. It can show optic nerve abnormality even in MS/NMOSD with normal optic disc. It also correlate with number of relapse and disease duration.
Poster Session 4
MS Immunology and Laboratory Tests

P-28
Deviated Repertoire of γδ T Cells is Associated with Disease Severity of Multiple Sclerosis
G. Maimaitijiang1, K. Shinoda3, Y. Nakamura1, T. Matsushita2, R. Yamazaki1, Y Yoshikai1, J. Kira3
1Department of Neurology, Neurological Institute, Kyushu University, Fukuoka, Japan
2Division of Host Defense, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan
3Refer to O-9 in the Oral Presentation

P-29
Serum CCL20 and Its Association with SIRT1 Activity in Multiple Sclerosis Patients
Rui Li7, Xiaoabo Sun1, Yaqing Shu1, Yuge Wang1, Li Xiao1, Zhanhang Wang1, Xueqiang Hu1, Allan G Kermode1,2, Wei Qiu1
1Multiple Sclerosis Center, Department of Neurology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, Guangdong Province, China
2Department of Neurology, Guangdong 999 Brain Hospital
3Centre for Neuromuscular and Neurological Disorders, University of Western Australia, Department of Neurology, Sir Charles Gairdner Hospital, Queen Elizabeth II Medical Centre, Perth, Australia
4Institute of Immunology and Infectious Diseases, Murdoch University, Perth, Australia

Background: CCL20, an inflammatory chemokine, is a potentially important component in the pathogenesis of MS. SIRT1 exhibits a negative regulatory effect on a variety of inflammatory cytokines and can relieve EAE. The association between the level of CCL20 and SIRT1 expression in MS patients has not been investigated.

Methods: Blood samples were collected from 38 RRMS patients and 40 healthy controls. Serum and peripheral blood mononuclear cells (PBMCs) were purified. The serum levels of CCL20 in MS patients were measured by ELISA. SIRT1 activity was evaluated from mononuclear cells of multiple sclerosis (MS) patients.

Results: Serum levels of CCL20 were significantly higher in MS patients compared with controls. A statistically significant decrease in SIRT1 activity was seen in MS patients with relapse compared to controls. Pearson’s correlation test showed that serum CCL20 levels were negatively correlated with SIRT1 concentrations ($R = -0.335$, $p = 0.040$). SIRT1 activity was negatively correlated with H3K9 acetylation ($R = -0.335$, $p = 0.040$).

Conclusion: Elevated serum CCL20 concentrations were observed in MS, and there was an association between CCL20 and SIRT1 activity in MS patients.

P-30
Gut Microflora: Association between Appendectomy and Multiple Sclerosis and Neuromyelitis Optica

Authors: HS Ooi1, S Viswanathan2, NP Botross1, YT Chin3, GB Eow4, R Kanesalingam5, MAR Isman6, S Sood7, MAR Isman6, S Sood7,
1Monash University, 2Selangor, Malaysia; Hospital Kuala Lumpur, Kuala Lumpur, Malaysia; Hospital Sultanah Aminah, Johor Bahru, Malaysia; Hospital Pulau Pinang, Pulau Pinang, Malaysia.

Background: Appendicitis has a well-established relationship with ulcerative colitis (UC). Altered gut microflora is a plausible cause for inflammatory gut diseases. Gut microflora plays a role in immunity too. Appendicitis could be associated with other immune-mediated disorders such as multiple sclerosis (MS) or neuromyelitis optica (NMO).

Objective: To explore the association between appendectomy for appendicitis and two diseases: MS and NMO.

Methods: Patients older than 40 were identified from neurology records from three tertiary referral hospitals in Malaysia. MS and NMO diagnosis were based on the Revised McDonalds Criteria (2010) and Wingerchuk Criteria (2015) respectively. Controls were sampled from Malaysia’s normal population. Individuals were interviewed telephonically or face-to-face. The age inclusion criterion was used to differentiate high or low lifetime risk of appendicitis as appendicitis incidence is rare after 40 years old. Subjects were assessed for appendectomy for inflamed appendix (we excluded patients who gave a history of normal appendix at surgery). Ethics approval for each site was obtained. Fischer’s exact test was used for comparison.

Results: 49 MS, 71 NMO, and 880 controls met the inclusion criteria. 72 individuals (59 control, 9 MS, 4 NMO) had appendectomy for an inflamed appendix. Appendectomy rates in MS, NMO, and controls were 18.37% (95% CI 7.5-29.2%), 5.6%(0.3-11%) and 6.7%(5.1-8.4%) respectively (MS vs NMO $p=0.036$, MS vs controls $p=0.007$).

Conclusions: MS is positively associated with appendectomy for appendicitis. Our study suggests commonality in the pathogenesis of MS and appendicitis. Altered microflora should be evaluated for a possible link.

P-31
Elevated Serum Levels of Sirtuin 1 in Multiple Sclerosis During Remission
C. Irkec, F. Yekeler, T. Altparmak, R. Tural, N. Altan
Gazi University Faculty of Medicine, Neurology and Biochemistry Departments

Sirtuin 1 (SIRT1) is a member of the histone deacetylase class III family proteins and contains 747 amino acids. SIRT1 plays an important role as a key regulator of DNA damage, cell survival, energy metabolism, aging and neurodegeneration. SIRT1 expression was found to be decreased in the peripheral blood mononuclear cells of multiple sclerosis (MS) patients during relapses. Experimental studies have demonstrated, a protective role of SIRT1 in autoimmune demyelination and neurodegenerative diseases. However, little is known about the alteration of SIRT1 levels in MS patients.

In the present study, we investigated the serum levels of SIRT1 in MS patients and compared them with healthy controls. Serum SIRT1 levels were measured by enzyme linked immunosorbent assay (ELISA) method. We found a statistically significant difference between relapses, remission phases of MS patients than control group for serum SIRT1 level.
These results suggest us that SIRT1 increase in MS remission phase to compensate the probable neurodegeneration process and may contribute to prevent the demyelinating lesions to become permanent. These findings shows that there is an anti-inflammatory, antioxidant and compensatory mechanism against neuroinflammation and neurodegeneration. According to our findings and previous datas, SIRT1 may represent a biomarker and a potential new target for therapeutic intervention in MS.

P-32
Effects of Therapy on The Serum Levels of Apelin and Sirtuin 1 In Responder and Non- Responder Multiple Sclerosis Patients
C. Irikec, F. Yekeler, T. Altıparmak, R. Tural, N. Altan
Gazi University Faculty of Medicine, Neurology and Biochemistry Departments
Multiple Sclerosis (MS) is a neuroinflammatory and neurodegenerative disease of the central nervous system (CNS). In MS treatment interferon beta (IFN-β) and glatiramer acetate (GA) are fundamental medicines. IFN-β phosphorylate the signal transducer and activator of transcription (STAT) that regulate inflammatory genes. GA as an altered peptide ligand to inhibit myelin basic protein-specific T helper cells. GA increase anti-inflammatory cytokines so called “bystander suppression” at CNS. Some of patients fail to achieve adequate response at therapeutic doses of IFN-β and GA. This variability in response to treatment has prompted the search for prognostic markers in order to personalize MS therapy.

Our goal was to investigate apelin and SIRT1 serum levels as a possible predictor of response to IFN-β and GA in MS. IFN-β and GA treated responder and non- responder patients blood samples were collected. Serum levels of apelin and SIRT1 were assessed by enzyme linked immunosorbent assay (ELISA) before and after treatment.

GA responder group had significantly higher SIRT1 levels than all other groups. There wasn’t any significant difference for apelin levels in all groups. In literature there have some studies about drug response in MS. One is suggested that IFN-β responder patients has higher levels of NLR family, pyrin domain containing 3 (NLRP3) levels and other showed that SIRT1 levels were higher in GA responder patients as the result of our study. Consequently our data suggest that SIRT1 could a possible biomarker to evaluate patients’ responsiveness to GA therapy.

P-33
Adiponectin in Multiple Sclerosis and Neuro-Beḥçet’s Disease
C. Irikec, T. Kuz, T. Altıparmak, I. Fidan
Gazi University Faculty of Medicine, Neurology and Microbiology Departments
The adiponectin molecule is a protein composed of 247 aminoacids and four segments synthesized by adipocytes. The signal transduction pathways and physiological functions of adiponectin receptors have not been fully elucidated yet. Recently it has been discovered that adiponectin inhibits the activation of nuclear factor kappa beta (NF-κB) by tumor necrosis factor alpha (TNF-α) modulation and suppressing the inflammatory effect on the endothelium. Pharmacological modulation of adiponectin activity may have important implications in the treatment of various autoimmune or inflammatory conditions.

Multiple Sclerosis (MS) and Neuro-Beḥçet’s Disease (NBD) are important immune mediated diseases of the central nervous system (CNS). The pathogenesis of these diseases remains unclear, with particularly little known about the role of adipocytokines. To clarify the role of adiponectin in MS and NBD; we studied adiponectin levels in the sera of patients with MS and NBD by enzyme linked immunosorbent assay (ELISA) method.

As a result, serum levels of adiponectin was statistically significant low in MS than NBD and controls. In the present study we demonstrated that adiponectin may play a role in the immunopathogenesis of MS. Our findings suggested that, NBD is a nonspecific inflammatory condition compared to autoimmune mediated disorders such as MS.
P-36  
Serum Homocysteine Levels and Cognitive Dysfunction in Multiple Sclerosis Patients
M.K. Omar 1, T. Yazici2
Ondokuz Mayis University Samsun, Turkey1, Ordu University, Turkey2

Background: Cognitive dysfunction is seen in 45-60% of multiple sclerosis (MS) patients. Recent reports have shown that high serum homocysteine levels are related with cognitive dysfunction in MS patients.

Objective: To examine serum homocysteine levels, vitamin B12, folic acid in relapsing remitting MS patients and healthy controls and perform neuropsychological tests to evaluate higher brain functions in order to show if there is a relation between high homocysteine levels and these tests.

Methods: Serum homocysteine levels vitamin B12 and folic acid were determined in 60 relapsing remitting MS patients and 30 healthy age and sex matched controls. Paced Auditory Serial Addition Test (PASAT), Stroop test and Line Orientation Tests are used to assess various cognitive functions.

Results: Serum homocysteine levels were found higher in MS patients than controls. There was no difference between B12 and folic acid levels. There were no correlations between patients age, disease duration and Expanded disability scores (EDDS), level of education and serum homocysteine levels. Neuropsychiatric test results were impaired in MS patients with high serum homocysteine levels and also in healthy controls with high serum homocysteine.

Conclusions: Homocysteine levels are increased and may contribute to cognitive dysfunction in relapsing remitting MS patients.

P-37  
Evaluation of Thyroid Functions in Multiple Sclerosis: Preliminary Study
Ufuk Emre*, Çağla Şişman*, A. Çimen Atalar*, A. Batuhan Çiplak*, Sibel Kran**
Health Sciences University, Istanbul Education and Research Hospital Neurology Clinic*, Istanbul, Turkey
Hacettepe University, Faculty of Medicine, Department of Public Health*, Ankara, Turkey

Background: Multiple Sclerosis (MS) is a chronic, inflammatory demyelinating disease of the central nervous system. Both the systemic and organ-specific autoimmune diseases are frequently reported in MS patients. One of these autoimmune diseases are thyroid functional disorders or anti-thyroid antibody positivity. These disorders can both be related with the disease itself or to the medications used for treatment of MS. Autoimmune thyroid diseases are commonly reported in MS patients under Interferon treatment but there is no long-term studies with other medications used in treatment of MS.

Objective: In this retrospective study we aimed to assess the thyroid function tests of the MS patients that we follow-up in our multiple sclerosis clinic in Istanbul Education and Research Hospital.

Methods: We included 35 patients to our study. The age, gender, beginning age and duration of the disease, MS subtype, MS relapse type and frequency, traetments, cerebrospinal fluid (CSF) analysis results were recorded. We also recorded the thyroid function test results (free T3, free T4, TSH) before and after MS-specific treatment is administered at the follow-up.

Results: The mean age of 35 patients (21 female/ 14 male) was 33.8±8.4. The mean EDSS was 4.5±1.3. The majority of the medications used were Interferon group. The thyroid function tests of all the subjects were normal. The interesting point was fT4 and TSH test results were lower at the Glutamime Asetat (GA) using group.

Conclusions: The thyroid function test results were generally normal except the GA using patients in which free T4 and TSH levels were lower than the other groups.

P-38  
Effect of Apolipoprotein E Genotypes in Prognosis of Patients with Multiple Sclerosis
Y Tamam, B Tamam
Dicle University, Faculty of Medicine Department of Neurology

Background: Although the association between apolipoprotein E (APOE) genetic polymorphisms and multiple sclerosis (MS), has been debated, the presence of the e4 allele has been associated with an aggressive disease progression.

Objective: The aim of this study is to investigate whether or not the APOE allele has an impact on disease progression in patients with MS. The study investigated the presence and clinical correlations of certain APOE genotypes in patients with MS.

Methods: Ninety six patients were enrolled in the study. APOE genotype was determined by polymerase chain reaction (PCR), the total apoE level was established using the nephelometric method. Expanded Disability Status Scale (EDSS) scores were also established. The progression index (PI) was calculated as the EDSS score/disease duration.

Results: The most common APOE genotype in MS patients was ε3/ε3 (79.1%). Male patients with MS were significantly more likely to have ε4, and at baseline, the disease duration was shorter, the EDSS scores were higher, the serum total ApoE levels were lower, and the PI was significantly higher. The MS onset age, clinical types, EDSS scores, and PI were not significantly correlated with ε4 allele-positive. Visual onset and sensory onset are good prognostic factors. There were no patients with visual onset and few patients with sensory onset in the ε4-positive group.

Conclusions: The present study established male patients with MS had a higher APOE ε4 frequency and disease severity, but were likely to have lower serum ApoE levels. An additional study is needed with a larger sample to include all genotypes.

Poster Session 5

MS Treatment

P-39  
Improvements and Success in the Management of Multiple Sclerosis: Fifteen years of Experience from a Single-centre Public Hospital
Vijayasingham, L.1, Viswanathan S.2, Md Zain, N. R.1, Chee, K. Y.1, Arip, M.3
1Multiple Sclerosis Society Malaysia; Monash University, Bandar Sunway, Malaysia
2Department of Neurology, Kuala Lumpur, Malaysia
3Department of Radiology, Kuala Lumpur, Malaysia
Background: Clinical management of patients with Multiple Sclerosis (MS) has developed as an important neurology focus, with significant improvements in accessibility to neurologists, investigations and multidisciplinary care over the last 15 years in Malaysia.

Objective: To recognize achievements in the delivery of MS care within the Malaysian Health System


Results: Improvements in diagnostic and treatment capabilities within the centre are due to concerted governmental efforts and positive investment. These include increases to multi-disciplinary teams and resources, comprising of neurologists both general and MS trained, neuroradiologists (n=2), neuropsychiatrists (n=2), nurses with MS-exposure, establishment of a speciality demyelinating disease clinic, MRI machines (n=2), laboratory tests for CSF, oligoclonal bands and anti-aquaporin-4 antibody, rehabilitation facilities and expertise; and access to disease modifying treatments. Other examples of successes are the inclusion of MS-training in a local post-basic neurology-nursing syllabus and the establishment of a medication adherence clinic run by neuro-pharmacists. Local clinical practice guidelines within the multi-actor and multi-level perspective. Through this analysis, we find that more cohesive efforts at a systemic level is required to optimize access and use of DMTs. These can include more active procurement of generic therapeutic options, engagement of pharmaceutical industry, regulation and leverage of private financiers and increased patient advocacy and education programs.

Conclusion: Through this analysis, we find that more cohesive efforts at a systemic level is required to optimize access and use of DMTs. These can include more active procurement of generic therapeutic options, engagement of pharmaceutical industry, regulation and leverage of private financiers and increased patient advocacy and education programs.

P-40
Access to Disease-modifying Treatment in Malaysia: A Multi-level and Multi-Actor Perspective
Vijayasingham, L. 1, Viswanathan, S. 2
1Jeffrey Cheah School of Medicine, Monash University Malaysia, Bandar Sunway; Multiple Sclerosis Society Malaysia, Kuala Lumpur
2Department of Neurology, Kuala Lumpur

Background: Effective local access to current therapeutic innovations is influenced by numerous dynamics of supply and demand for disease modifying treatments (DMTs) within the broad Malaysian public-private system of healthcare.

Objective: To explore and identify dynamics and mechanism that influence access within a multi-level and multi-actor context

Methods: Using WHO’s Systems Framework for Access to Medicines, and data on 202 patient-events from 2002 to 2017 in a single-centre public hospital, we describe multi-level and multi-actor mechanisms and dynamics of supply and demand that support and challenge access to DMTs from a system’s perspective.

Results: Health financing remains the largest influencer of DMT access. Over the years, the public sector has increased investments in DMT access, and remains the largest financing contributor through public institutions such as the hospital neurology medicine fund, Ministry of Health Patient Assistance Fund and the hospital social welfare department. Only few patients have successfully continued treatment through private out-of-pocket payment, non-governmental organization support or private health insurance. Additionally, individual perceptions and factors, resources, voice of the local MS society, policies and practices within the national and regional health sector such as the pharmaceutical, employment and private health insurance sectors influence access dynamics.

Conclusions: Through this analysis, we find that more cohesive efforts at a systemic level is required to optimize access and use of DMTs. These can include more active procurement of generic therapeutic options, engagement of pharmaceutical industry, regulation and leverage of private financiers and increased patient advocacy and education programs.

P-41
Comparative Effectiveness Among the First-line Disease Modifying Therapies Multiple Sclerosis Relapse – A Nationwide Observational Study in Taiwan
Chih-Ho Chou 1, 2, Tzu-Chieh Lin 1, 3, Ching-lan Cheng 1, 3 and Yee-Huei Kao Yang 1, 3
1Institute of Clinical Pharmacy and Pharmaceutical Sciences, National Cheng Kung University, Taiwan; 2Division of Neurology, Department of Internal Medicine, Chi Mei Medical Center, Taiwan, and 3Health Outcome Research Center, National Cheng Kung University, Taiwan

Background: Interferons (INF) and glatiramer acetate(GA) are major first-line disease-modifying therapy (DMT) for MS. Their benefits in clinical settings are not elucidated yet.

Objective: To evaluate the comparative effectiveness of first-line DMT for preventing MS relapse in Taiwan

Methods: We retrieved patients with MS and receiving INF beta1A, INF beta 1B, or GA to conduct a retrospective cohort study by using National Health Insurance Research Database between 2001 and 2009. The patients were classified according to their initial DMT. We use proportional hazard regression and Kaplan-Meier estimation to estimate the first relapse after receiving treatments.

Results: We recruited 631 patients (427 in INF beta 1A, 161 in INF beta 1B, and 43 in GA group). Median following time was 1677 days. In comparison to INF beta 1A, The OR of INF beta-1B and GA were 1.1855, and 1.5105 respectively. Female, and who had two events (or more) prior to initiation of DMT was associated with early relapse.

Conclusion: Females, and those who had more pre-treatment events were associated with higher risk of relapse, but not different DMTs.

P-42
Is the New Brand-Generic of Glatiramer Acetate (Copamer®) 40 Mg Safe and Effective in Iranian Patients with RRMS?
R. Abolfazli 1, S. Pournourmohammadi 2, S. Samadzadeh 1, A.R. Shamshini 1
1Tehran university of medical sciences-Amiralam hospital, Tehran, Islamic Republic of Iran
2Zahravi Pharmaceutical Company, Tehran, Islamic Republic of Iran
3Tehran University of Medical Sciences-School of Public Health, Tehran, Islamic Republic of Iran

Objective: The aim of this study is to evaluate the safety, tolerability and efficacy of a brand-generic Glatiramer acetate (GA)
and Immunomodulatory Therapy in Patients with Multiple Sclerosis (RRMS) over a 12-month period.

Methods: A non-interventional cohort study was conducted on 185 patients who had a confirmed and documented RRMS diagnosis as defined by the Revised McDonald criteria (2010), besides who were ambulatory with a Kurtzke Expanded Disability Status Scale (EDSS) score of 0-5.5, and whose treatment by Copamer® 40 mg/ml was just started. Adverse drug reactions (ADR), relapse rate, MRI parameters and EDSS were evaluated over one year.

Results: of 185 enrolled patients, 170 patients completed the study. The mean value of EDSS at the time of screening was 1.97±0.75 and 100% of subjects had experienced one relapse during one year before screening. The most common ADRs were local pain (45.4%) and erythema (38.9%). The immediate post injections reaction were dyspnea (10.3%), anxiety (9.7%), palpitation (8.1%), urticaria (5.4%), flushing (3.24%), chest pain (2.16%), throat constriction (0.54%). The percentage of relapse-free patients at month 12 was 87% compared to 77% and the annual relapse rate was 0.134 compared to 0.301 reported on free patients at month 12 was 87% compared to 77% and the annual relapse rate was 0.134 compared to 0.301 reported on Copaxon®. Increased in EDSS was found in 20% of subjects and new T2 and GAD enhancing lesions were found in 34.7% and 9.4%, respectively. Treatment failure were 1.6% and 4.3% according to Modified Rio- and Rio-scores, respectively.

Conclusion: Copamer® 40 mg is safe, well tolerated and effective in Iranian patients with RRMS and it is fully substitutable for Copaxone®.

P-44
Longitudinal Variations of Neuro Metabolites and MS Fatigue in Patients Treated with Dimethyl Fumarate
Jameen Arm1, Karen Ribbons2,3, Rod Lea4, Saadallah Ramadan1,4, Jeannette Lechner-Scott2,3,4, Kathrin Ringwald1, Daniela Piani Meier3, Rajesh Bakshi3, Krzysztof Selmi5
1School of Health Sciences, Faculty of Health and Medicine, University of Newcastle, Callaghan, NSW, Australia, 2Department of Neurology, John Hunter Hospital, Newcastle, Australia, 3Hunter Medical Research Institute, Newcastle, Australia, 4School of Medicine and Public Health, Faculty of Health and Medicine, University of Newcastle, Callaghan, NSW, Australia.

Background: Fatigue is common in MS, and although metabolic and morphological alterations in the brain have been implicated, the pathophysiology of fatigue is still unclear. Two dimensional localised correlation spectroscopy (2D L-COSY) is a non-invasive technique that enables the metabolic profiling in the brain.

Objective: The objective of this study was to evaluate the impact of Dimethyl Fumarate (DMF) treatment on fatigue and brain neurometabolite levels.

Methods: Fatigue was evaluated using the Modified Fatigue Impact Scale (MFIS). Total N-acetylaspartate (tNAA), Gamma-aminobutyric acid (GABA) and Glx (Glutamine/Glutamate) were measured in the posterior cingulate cortex using 2D L-COSY in Fifteen RRMS patients at baseline (BL) and 12 months (12mFU) following the inception of DMF treatment. Fifteen age and sex matched healthy controls (HC) were included at BL. Mann Whitney U and Spearman’s rho were used for statistical analysis.

Results: There were significant changes between RRMS and HC in all parts assessed by MFIS, which did not change at 12mFU. There were also significant differences in tNAA, GABA and Glx. While GABA and Glx did not change over time, tNAA reduced significantly at 12mFU. tNAA and GABA were not correlated with MFIS scores but Glx was negatively correlated with cognitive fatigue ($r=−0.566$, $p<0.028$) both at BL and 12mFU.

Conclusion: Although tNAA, GABA and Glx are highly correlated with each other and have been previously associated with disease severity in MS, only Glx was associated in our cohort with fatigue scores.

P-45
Early Fingolimod Treatment Improves Disease Outcomes at 2 and 4 Years in Patients with Relapsing-Remitting Multiple Sclerosis
Reinhard Hohlfeld1, Ludwig Kappos2, Davorka Tomic3, Diego Silva4, Kathrin Ringwald5, Daniela Piani Meier1, Rajesh Bakshi4, Krzysztof Selmi4.
1Ludwig-Maximilians University of Munich and Munich Cluster for Systems Neurology (SyNergy), Munich, Germany; 2Neurologic Clinic and Policlinic, Departments of Medicine, Clinical Research, Biomedicine and Biomedical Engineering, University Hospital, Basel,
Background: Early treatment optimisation with high-efficacy therapies may improve short- and long-term disease outcomes in patients with multiple sclerosis (MS).

Objective: To compare the effect of fingolimod 0.5 mg on four measures of disease activity at 2 and 4 years between treatment-naive patients and those who switched to fingolimod after receiving one or more disease-modifying therapies (DMTs).

Methods: Data were pooled from FREEDOMS/FREEDOMS-II core and their respective extension studies. Patients were grouped into treatment-naive (N=683), 1 DMT (N=515) and ≥2 DMTs (N=358). Study outcomes included relapses, 6-month confirmed disability progression (6mCDP), T2 lesions and percent brain volume loss (BVV) at 2 (end of core phase) and 4 (extension phase) years.

Results: The odds of being free from relapses, 6mCDP, T2 lesions or BVV were higher for fingolimod-treated patients vs placebo, favouring the treatment-naive group (odds ratios [OR]: 3.75, 2.11, 4.48 and 1.57; p<0.007 for all 4 outcomes) vs 1 DMT (OR: 2.11, 1.74, 4.15 and 2.51; p<0.05) and ≥2 DMTs (OR: 2.03, 1.35 [p=ns], 4.06, and 1.75, remaining outcomes ps0.03) groups at 2 years. Similarly, when fingolimod-treated patients were compared with ≥2 DMTs, treatment-naive were more frequently free from relapses (76.0% vs 53.5% at 2 years; 60.2% vs 33.3% at 4 years) and T2 lesions (48.7% vs 44.4% and 31.8% vs 22.0%); p≤0.05 for all comparisons.

Conclusion: These data suggest that treatment with fingolimod results in better clinical and MRI disease outcomes at 2 and 4 years in treatment-naive vs patients who switched to fingolimod after one or more DMTs.

P-47 Efficacy and Safety of Fingolimod for Multiple Sclerosis in Singapore

A.M.L. Quek,1,2 D. Soon,1,2 B.K.C. Ong,1,2 X.J. Pang,1 J.S.N. Tye,1 K. Tan1,4 1National University Hospital, National University Health System, Singapore 2Department of Neurology, National Neuroscience Institute, Singapore 3Duke-NUS Medical School, Singapore

Background: Scarce data are available on the safety and efficacy of fingolimod in the treatment of relapsing-remitting multiple sclerosis (MS) in Singapore.

Objective: To investigate the indications, safety and efficacy of fingolimod in a multiethnic real-world setting in Singapore.

Methods: Between 2012 and 2017, clinical features, disease course and adverse effects of fingolimod in the treatment of relapsing remitting MS were collected from the National University Hospital and National Neuroscience Institute in Singapore.

Results: Thirty-three MS patients (median age, 36 years; 82% women) were identified. Fingolimod was used as first-line treatment in a third of patients while the remaining had prior disease-modifying treatments. Fingolimod was initiated at a median of 59 months (interquartile range, 16-120) into the disease course, for median treatment duration of 29 months (interquartile range, 9-42). Indications for initiating fingolimod were failure of prior treatments to achieve disease control (33%), needle-phobia (33%), poor tolerability of prior treatments (27%) and JCV-positivity on natalizumab (9%). For 17 patients who received fingolimod for at least 2 years duration, median annualized relapse rate was reduced from 0.56 to 0.13 (Wilcoxon signed-rank test, p<0.05). Lymphopaenia (≤0.2 x 10⁹) was reported in 29% patients. Two patients developed shingles; both had prior acquired varicella immunity, confirmed by pre-treatment varicella seropositivity. None developed cardiac arrhythmias or macular oedema.

Conclusion: Fingolimod was efficacious in reducing MS relapses in Singapore. Vigilance for lymphopaenia and shingles should be sought in these patients.
A Pilot Time and Motion Study for Treatments of Relapsing Remitting Multiple Sclerosis (RRMS) in Australia

Professor J Lechner-Scott1, R Davey2, P Davey2, Dr G Bogeski3, Dr E Cheah2

1University of Newcastle, Newcastle, Australia; 2Illuminate Health Consulting, Sydney, Australia; 3Merck, Sydney, Australia

Background: The time burden of managing RRMS for patients and healthcare staff is not well quantified despite its importance in treatment choice. Of interest were three higher efficacy RRMS therapies, cladribine tablets, alemtuzumab, and fingolimod because of their different modes of administration. Time and motion (T&M) surveys have previously been used to quantify time burden by asking respondents about duration of treatment administration.

Objective: To determine the time taken by patients, nurses, neurologist and other specialists to treat RRMS with cladribine tablets, alemtuzumab and fingolimod using purposely developed T&M surveys.

Methods: We created two T&M surveys, one for neurologists and nurses, and another for patients. Surveys were informed by product information documents, validated by an MS nurse, and completed by telephone with patients (n=3), neurologists (n=3), and nurses (n=8) from eight MS clinics.

Results: The overall mean time spent on treatment with cladribine tablets, fingolimod, and alemtuzumab extrapolated over 4 years was 25±3, 62±6, and 189±18 hours (p<0.0001, 1-way ANOVA, repeated measures). Neurologists’ overall time spent also favoured cladribine tablets (2.3±0.7 hours) over alemtuzumab (9.5±1.8 hours) and fingolimod (2.9±0.7 hours), (overall p=0.001). Similar results were found for nurses and patients, with the largest difference between therapies (favouring cladribine tablets) recorded for patients.

Conclusions: Cladribine tablets were associated with a significantly lower overall time taken to treat RRMS compared to fingolimod and alemtuzumab. This warrants further research to determine if cladribine tablets could (a) increase productivity for doctors and nurses, and (b) improve patient quality of life by reducing the burden of managing their disease.
Conclusions: In CLARITY, patients identified using HDA criteria showed clinical and MRI responses to CT3.5 that were generally better than, or at least comparable with, the overall patient population.

P-52 Cladribine Tablets for Treatment of Patients with Multiple Sclerosis (MS): Integrated Analysis of Safety from the MS Clinical Development Programme

S. Cook1, T. Leist1, G. Comi1, X. Montalban4, E. Sylvester1, C. Hicking1, F. Dangond2 J. King7
1Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, USA; 2Division of Clinical Neuroimmunology, Thomas Jefferson University, Jefferson Medical College, Philadelphia, USA; 3Department of Neurology and Institute of Experimental Neurology, Università Vita-Salute San Raffaele, Ospedale San Raffaele, Milan, Italy; 4Department of Neurology-Neuroimmunology, Hospital for Nervous Diseases, Medical Park Loipl and University Ospedale San Raffaele, Milan, Italy; 5Merck KGaA, Darmstadt, Germany; 6EMD Serono, Inc., Billerica, MA, USA; 7Department of Neurology, Royal Melbourne Hospital, Parkville, Victoria, Australia.

Background: The efficacy of cladribine tablets (CT) for early MS and relapsing MS (RMS) has been shown in ORACLE-MS, CLARITY, and CLARITY Extension with adverse events (AEs) reported separately.

Objective: Report the AE profile from integrated safety data for CT3.5 mg/kg (CT3.5) monotherapy.

Methods: The CT3.5 cohort comprised 923 patients (3432.65 patient years [PY] exposure) derived from CLARITY, CLARITY Extension, ORACLE-MS and the PREMIERE registry; the placebo cohort comprised 641 patients (2025.97 PY).

Results: The mean study period for patients receiving CT3.5 was 194 weeks; 165 weeks for placebo recipients. Adjusted-AE (Adj-AE) per 100PY rates for CT3.5 and placebo, respectively, were: treatment-emergent AE (TEAE), 103.3 and 94.3; TEAEs leading to discontinuation, 2.1 and 1.1; serious AEs, 4.0 and 3.6; serious AEs leading to death, 0.26 and 0.25. Regarding known events expected with CT treatment, Adj-AE per 100PY for lymphopenia were 7.94 (CT3.5) and 1.06 (placebo), and for systemic organ class of infection and infestations, 24.93 (CT3.5) and 27.05 (placebo); herpes zoster, 0.83 (CT3.5) and 0.20 (placebo). Adj-AE per 100PY for the system organ class of neoplasms, benign, malignant and unspecified were 1.14 and 1.01, for CT3.5 and placebo, respectively.

Conclusion: The AE profile for CT3.5 as monotherapy has been well-characterised in a pooled population of patients with early MS and active RMS. Lymphopenia was expected from CTs' mode of action. Herpes zoster was reported more frequently in patients experiencing Grade 3 or 4 lymphopenia, and no malignancies commonly associated with immunosuppression were observed.

P-53 Long-Term Lymphocyte Counts in Patients with RRMS Treated with Cladribine Tablets (CT)

P. Soelberg-Sorensen1, F. Dangond2, C. Hicking1, G. Giovannoni4
1Danish MS Center, Department of Neurology, University of Copenhagen, Rigshospitalet, Copenhagen, Denmark; 2EMD Serono, Inc., Billerica, MA, USA; 3Merck KGaA, Darmstadt, Germany; 4Queen Mary University of London, Blizard Institute, Barts and The

Conclusions: For patients who received PBO in CLARITY, switching to CT3.5 in CLARITY-EXT significantly reduced ARR and increased the proportion of relapse-free patients. CT also produced durable clinical benefits: patients who received CT in CLARITY and PBO in CLARITY-EXT maintained low relapse rates throughout. Patients who received CT in CLARITY and CT in CLARITY-EXT showed no additional benefit vs treatment with CT in CLARITY only.

P-51 Efficacy of Cladribine Tablets 3.5 mg/kg in High Disease Activity (HDA) Subgroups of Patients with Relapsing Multiple Sclerosis (RMS) in the CLARITY Study

Gavin Giovannoni1, Kottit Ramrathan4, Stuart Cook3, Giancarlo Comi1, Peter Rieckmann4, Per Soelberg-Sorensen6, Patrick Vernmacht1, Fernando Dangond8, Christine Hicking9, John King10
1Queen Mary University of London, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK; 2Department of Neurology, MS Research Center University of Miami School of Medicine, Miami, FL United States; 3Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, NJ, United States; 4Department of Neurology and Institute of Experimental Neurology, Università Vita-Salute San Raffaele, Ospedale San Raffaele, Milan, Italy; 5Hospital for Nervous Diseases, Medical Park Loipl and University of Erlangen, Germany; 6Danish MS Center, Department of Neurology, Copenhagen University Hospital, Copenhagen, Denmark; 7Université de Lille, CHU Lille, LIRIC-INSERM U995, FHU Imminent, Lille, France; 8EMD Serono, Inc., Billerica, MA, USA; 9Merck KGaA, Darmstadt, Germany; 10Department of Neurology, Royal Melbourne Hospital, Parkville, Victoria, Australia.

Background: In the CLARITY study, treatment with cladribine tablets (CT) showed strong efficacy vs placebo in a large cohort of patients with RMS over 2 years. Patients with HDA are at higher risk of relapses and disability progression.

Methods: For patients who received PBO in CLARITY, patients randomised to CT3.5 (N=433) or placebo (N=437) were retrospectively analysed using two different HDA definitions based upon 1) evidence of high relapse rate [HRA] ≥2 relapses in previous year) regardless of prior treatment, or 2) HRA plus treatment nonresponse ([HRA+TNR] ≥2 relapses in previous year, or ≥1 relapse in previous year while on DMD therapy and ≥1 T1 Gd+ or ≥9 T2 lesions).

Results: In the overall population, CT3.5 reduced the risk of 6-month-confirmed EDSS progression vs placebo (HR=0.53,95%CI:0.36;0.79). A larger risk reduction for CT3.5 vs placebo occurred (HR=0.18 each,95%CI:0.08;0.44 and 0.07;0.43) in the HRA (p=0.0036 vs non-HRA) and the HRA+TNR subgroups (p=0.0037 vs non-HRA+TNR), indicating greater responsiveness to CT3.5 in patients identified by these criteria. Risk of 3-month EDSS progression was also reduced. ARR was lower with CT3.5 than placebo in the overall population (RR=0.42,95%CI:0.33;0.52), and even lower with HRA (RR=0.32,95%CI:0.22;0.47) and HRA+TNR (RR=0.33,95%CI:0.23;0.48), each p<0.0001 vs placebo. Strong treatment effects on radiological markers were observed in each HDA subgroup.
Mary University of London, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK.

**Background:** The CLARITY study demonstrated CT’s efficacy. Lymphopenia was the most common AE, consistent with CT’s mechanism of action.

**Objective:** Investigate absolute lymphocyte counts (ALC) to 312 weeks, and B/T-cell subsets to 240 weeks, after the first CT dose, in patients with RMS receiving 2 annual courses of CT (3.5mg/kg cumulative dose).

**Methods:** Data from patients receiving CT in CLARITY/CLARITY Extension and the PREMERIE registry (N=685) were pooled. Median cell counts are reported.

**Results:** Baseline ALC=1.86×10^9/L. During Year (Y)1, ALC reached nadir at Week (Wk) 9 (1.00×10^9/L) and then gradually increased; Y2 nadir was at Wk55 (0.81×10^9/L), recovering to normal (≥1.00×10^9/L) by Wk96; continuing to increase thereafter. ALC was normal in 75% patients by Wk144. Baseline CD4+=851 cells/μL. After Y1 treatment, CD4+ reached nadir at Wk16 (385 cells/μL) and then gradually increased; Y2 nadir was reached at Wk60 (292 cells/μL). Values reached threshold (350 cells/μL) by ~Wk120, continuing to improve thereafter. Baseline CD8+=378 cells/μL; Y1 nadir was reached at Wk16 (239 cells/μL) and Y2 at Wk72 (232 cells/μL). CD8+ recovered after treatment and never dropped below threshold (200 cells/μL). Baseline CD19+=205 cells/μL; Y1 nadir occurred at Wk9 (18 cells/μL) and Y2 at Wk52 (31 cells/μL). CD19+ gradually recovered, reaching threshold (100 cells/μL) by Wk96 and continued to improve.

**Conclusion:** Lymphocyte recovery begins soon after CT treatment, with ALC, B cells and CD4+ T cells reaching threshold values between 7.5, 12 and 18 months, respectively, after the last dose in Y2. CD8+ cells never dropped below the threshold.

**P-54**

**Selective and Discontinuous Reduction of B and T Lymphocytes and NK Cells by Cladribine Tablets in Patients with Early and Relapsing MS**

O. Stuve1, P. Soelberg-Sorensen2, G. Giovannoni3, T. Leist4, Y. Hyvert4, D. Damiani5, U. Boschert4

1Department of Neurology, Jefferson University, Philadelphia, USA; 2Danish MS Center, Department of Neurology, University of Copenhagen, Rigshospitalet, Copenhagen, Denmark; 3Queen Mary University of London, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK; 4Division of Clinical Neuroimmunology, Thomas Jefferson University, Philadelphia, USA; 5EMD Serono, Inc, Billerica, USA.

**Background:** Efficacy of cladribine tablets (CT) in patients with early multiple sclerosis (MS). Due to the durable effects of CT, the influence on regulatory immune cells is of interest.

**Objective:** To examine effects on central and effector memory CD4+ T cells and naturally occurring regulatory CD4+ T cells (nTregs) after the first CT administration in the ORACLE-MS study.

**Methods:** Peripheral blood T lymphocytes were immunophenotyped in patients treated with CT in ORACLE-MS (3.5 mg/kg group; n=41) using T lymphocyte surface markers. Absolute numbers and proportions of central memory, effector memory, Th1-type and nTregs were measured.

**Results:** Greatest median reductions from baseline in absolute cell numbers occurred at week 13 for effector memory cells (~54%) and week 24 for central memory (~63%) and Th1-type cells (~51%) with similar/slightly increased levels of these CD4+ cell subtypes at week 48. Over time, there was a reduction (~5%) in the proportion of the central memory cells in total CD4+ cells, but no change in proportion for effector memory and Th1-type cells. Absolute numbers of nTregs (~48%), naive-like nTregs (~67%) and memory-like nTregs (~42%) were decreased at week 48. The proportions of nTregs and naive-like nTregs in total CD4+ cells were not changed. Memory-like nTregs slightly increased up to 48 weeks after treatment with CT (median increase from baseline in the proportion of memory-like nTregs= 11% at week 48).

**Conclusion:** The first administration of CT has a comparable magnitude of effect on CD4+ T cell subpopulations, with no dramatic shifts in their proportions.
P-56
Efficacy and Safety of Alemtuzumab in Korean Patients with Multiple Sclerosis: 1-Year Preliminary Results

Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Republic of Korea

Background & Objective: Alemtuzumab, a humanized anti-CD52 monoclonal antibody, is a potent treatment option licensed for active relapsing type of multiple sclerosis. This observational cohort study aimed to assess the clinical outcome of active relapsing-remitting multiple sclerosis (RRMS) undergoing alemtuzumab treatment.

Methods: Clinical, MRI and laboratory data from 17 patients treated with alemtuzumab at National Cancer Center were reviewed. Efficacy of alemtuzumab was assessed in terms of relapse rate, Expanded Disability Status Scale (EDSS) score and MRI disease activity defined by the presence of new or enlarging T2 lesions or T1 gadolinium-enhancing lesions. The safety profiles including infusion-associated reactions (IARs), secondary autoimmunity and other adverse events were also investigated.

Results: Of 17 patients, 12 reached 1-year follow-up. During 1 year, there were 3 relapses in 2 patients. Annualized relapse rate was markedly reduced from 1.47 for the preceding 1 year before alemtuzumab infusion to 0.25. EDSS score was stable or improved in 11 patients (92%). MRI disease activity was observed in 7 patients, of which 5 had only radiologic disease activity. Five patients (42%) showed no evidence of disease activity. Fourteen (82%) of 17 patients experienced IARs. All IARs were transient or controlled well by symptomatic medications. Three patients had urinary tract infection, influenza, and sinusitis, respectively. No patients exhibited secondary autoimmunity.

Conclusions: Alemtuzumab infusion in active RRMS reduced the relapse rate and MRI disease activity following 1 year. No significant safety concerns arose. Further study to assess longer-term outcome of alemtuzumab is ongoing.

P-57
Tolerability of Alemtuzumab in SPMS: Experience from One Center

Lee J, Hua HH, Dorfman LJ
Department of Neurology and Neurological Sciences, Stanford Neuroscience Health Center, Stanford, California 94304, USA

Background: Alemtuzumab (Lemtrada) is a monoclonal antibody targeted at CD52 proteins found on T and B lymphocytes, and is approved by the United States Food and Drug Administration (FDA) for treatment of relapsing forms of multiple sclerosis (MS). The pivotal studies, Care MS I and Care MS II, included patients with relapsing MS as well as patients with secondary progressive multiple sclerosis (SPMS). In clinical practice, Lemtrada has been used as an option for patients who have exhausted all other MS therapies.

Objective: We describe tolerability aspects of Lemtrada in SPMS patients from our center.

Method: We performed retrospective chart review of 24 patients, looking at baseline characteristics, infusion experiences, drug side-effects, and self-reported symptomatology.

Results: Our findings concurred with those from the pivotal studies: patients with SPMS tolerated Lemtrada well, with no excess incidence of side-effects or infusion reactions. Some patients with SPMS self-reported improvement in quality-of-life measures.

Conclusions: A larger well-controlled study in patients with SPMS treated with Lemtrada would be helpful in providing additional support for its use.

P-58
Long-term Improvement in Clinical Outcomes in Alemtuzumab-Treated RRMS Patients Who Relapsed Between Courses 1 and 2 (CARE-MS I)

S. Broadway1, H. Wiendl2, O. Fernández3, M. S. Freedman4, G. Izquierdo5, J. Lycke6, C. Pozzilli7, B. Sharrack8, B. A. Singer9, B. Steingo10, P. Vermersch11, S. Wray12, B. V. Wijmeersch13, T. Ziemssen14, D. H. Margolin15, J. Thangavelu16, A. Boster17; on behalf of the CARE-MS I and CAMMS03409 investigators.

1Griffith University School of Medicine, Gold Coast Campus, Southport, QLD, Australia; 2University of Münster, Münster, Germany; 3Fundación IMAMIS, Hospital Universitario Carlos Haya, Malaga, Spain; 4University of Ottawa and the Ottawa Hospital Research Institute, Ottawa, Ontario, Canada; 5Virgen Macarena University Hospital, Seville, Spain; 6University of Gothenburg, Gothenburg, Sweden; 7University of Rome, Rome, Italy; 8Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; 9MS Center for Innovations in Care, Missouri Baptist Medical Center, St Louis, MO, USA; 10Fort Lauderdale Multiple Sclerosis Center, Fort Lauderdale, FL, USA; 11University of Lille, Lille, France; 12Hope Neurology, Knoxville, TN, USA; 13Rehabilitation and MS Centre Overpelt BIOMED, University Hasselt, Hasselt, Belgium; 14Center of Clinical Neuroscience, Carl Gustav Carus University Hospital, Dresden, Germany; 15Sanofi, Cambridge, MA, USA; 16OhioHealth Neurological Physicians, Columbus, OH, USA

Background: In CARE-MS I (NCT00530348), 2 courses of alemtuzumab (baseline: 5 days; 12 months later: 3 days) improved outcomes vs SC IFNB-1a over 2 years in treatment-naive RRMS patients. Durable 6-year efficacy was demonstrated in an extension (NCT00930553) in absence of continuous treatment.

Objective: Evaluate alemtuzumab efficacy over 6 years in CARE-MS I patients who relapsed between Courses 1 and 2.

Methods: Assessments: annualised relapse rate (ARR); 6-month confirmed disability worsening (CDW); 6-month confirmed disability improvement (CDI); MRI disease activity (Gd+ and new/enlarging T2 lesions); new T1 hypointense lesions; brain volume loss (BVL).

Results: 15% of alemtuzumab-treated patients relapsed between Courses 1 and 2. Of these, 93% enrolled in extension; 87% remained through Year 6. ARR in Year 1 (1.3) declined in the year after Course 2 (0.3) and remained low over Years 3–6 (0.3–0.5). At Year 6, 60% were CDW-free, 24% achieved CDI, and most were free of Gd+ (84%) and new/enlarging T2 (71%) lesions, MRI disease activity (69%), and new T1 hypointense lesions (90%). Median percent yearly BVL declined (Years 1–6: –0.67%, –0.17%, –0.20%, 0.11%, –0.21%, –0.24%). After Course 2, 48% of patients received no additional treatment (alemtuzumab or other disease-modifying therapy).

Conclusions: Among 15% of patients who relapsed between alemtuzumab Courses 1 and 2, long-term outcomes were favourable, with nearly one-quarter achieving CDI. These data indicate that relapse after Course 1 is not indicative of subsequent limited treatment response and support administering alemtuzumab according to the approved 2 courses to achieve optimal clinical benefit.
Efficacy of a Third Course of Alemtuzumab in Patients with Active Relapsing-Remitting Multiple Sclerosis Who Experienced Disease Activity After the Initial Two Courses: Pooled Analysis of CARE-MS I and II

H. J. Kim1, A. Traboulsee2, A. Boster3, A. D. Bass4, R. Berkovich5, G. Comi6, Ó. Fernández7, V. Llimroth8, J. Lycke9, R. AL. Macdonell10, B. Sharrack11, P. Vermersch12, H. Wiendi13, T. Ziemssen14, M. Melanson15, N. Daizadeh15, B. A. Singer16; on behalf of the CARE-MS I, CARE-MS II, and CAMMS03409 Investigators

1Research Institute and Hospital of National Cancer Center, Goyang, South Korea; 2University of British Columbia, Vancouver, BC, Canada; 3OhioHealth Neurological Physicians, Columbus, OH, USA; 4Neurology Center of San Antonio, San Antonio, TX, USA; 5University of Southern California, Keck School of Medicine, Los Angeles, CA, USA; 6University Vita-Salute San Raffaele, Milan, Italy; 7Fundacion IMABIS, Hospital Universitario Carlos Haya, Málaga, Spain; 8Klinik für Neurologie und Palliativmedizin, Cologne, Germany; 9University of Gothenburg, Gothenburg, Sweden; 10Austin Health and Florey Institute of Neuroscience and Mental Health, Melbourne, Victoria, Australia; 11Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; 12University of Lille, Lille, France; 13University of Münster, Münster, Germany; 14Center of Clinical Neurosciences, Carl Gustav Carus University Hospital, Dresden, Germany; 15Sanofi, Cambridge, MA, USA; 16MS Center for Innovations in Care, Missouri Baptist Medical Center, St Louis, MO, USA

Background: Alemtuzumab improved clinical and MRI outcomes in 2-year (y) phase 3 trials vs SC IFNB-1a in RRMS patients (CARE-MS I: treatment-naïve [NCT00530348]; CARE-MS II: inadequate response to prior therapy [NCT00548405]). Efficacy was durable over a 4-y extension study (NCT00930553); 24% (CARE-MS I) and 30% (CARE-MS II) of patients received a third course (C3) through Y6.

Objective: Evaluate alemtuzumab retreatment efficacy in pooled CARE-MS I/II patients receiving C3.

Methods: Patients received 2 alemtuzumab courses (baseline: 5 days; 12 months later: 3 days) in CARE-MS I/II. In the extension, patients could receive as-needed alemtuzumab retreatment (for relapse/MRI activity) or other DMT (investigator discretion). Assessments: Annual MRI scored for disease activity; 90%, 67%, and 88% were free of Gd-enhancing lesions, new/enlarging T2 lesions, and new T1 hypointense lesions, respectively. Alemtuzumab consistently slowed median yearly BPF change vs SC IFNB-1a over 2 y, remaining low in Y7.

Results: Through Y6, 90% of patients remained on study; 27% received C3 (of which Y2: 2%, Y3: 31%, Y4: 27%, Y5: 23%, Y6: 17%) without further retreatment or other DMT. Mean time from C2 to C3 was 2.6 y. ARR decreased from 12 months before C3 (0.74) to 12 months after (0.06; P<0.0001), remaining low (0.08) 3 y after C3. Mean EDSS change 12 months post-C3 was −0.12. Percentage with stable/improved EDSS increased from 62% at C3 to 71% 12 months later; percentage with CDI increased from 5.0% to 17.5% (P=0.0117).

Conclusions: A third alemtuzumab course reduced relapses and improved disability without subsequent treatment. These data support administering C3 in patients with disease activity following C2 to achieve durable outcomes.

Durable Suppression of MRI Disease Activity and Reduction in Brain Volume Loss with Alemtuzumab in Patients with Active RRMS: 7-Year Follow-up of CARE-MS II Patients (TOPAZ Study)

M. Barnett1, D. Pelletier1, A. Traboulsee1, G. Comi1, J. De Séze1, A. Rovira5, S. Schippling7, D. H. Margolin3, N. Daizadeh2, K. Nakamura2, D. L. Arnold10,11; on behalf of the CARE-MS II, CAMMS03409, and TOPAZ Investigators

1University of Sydney, Sydney, NSW, Australia; 2Keck School of Medicine of University of Southern California, Los Angeles, CA, USA; 3The University of British Columbia, Vancouver, BC, Canada; 4University Vita-Salute San Raffaele, Milan, Italy; 5University of Southern California, Keck School of Medicine, Los Angeles, CA, USA; 6University Vita-Salute San Raffaele, Milan, Italy; 7Fundacion IMABIS, Hospital Universitario Carlos Haya, Málaga, Spain; 8Klinik für Neurologie und Palliativmedizin, Cologne, Germany; 9University of Gothenburg, Gothenburg, Sweden; 10Austin Health and Florey Institute of Neuroscience and Mental Health, Melbourne, Victoria, Australia; 11Montréal Neurological Institute, McGill University, Montréal, Québec, Canada

Background: In CARE-MS II (NCT00548405), alemtuzumab (12 mg/day, baseline: 5 days; 12 months later: 3 days) significantly improved clinical/MRI outcomes, including brain volume loss (BVL), vs SC IFNB-1a over 2 years (y) in RRMS patients with inadequate response to prior therapy. Alemtuzumab efficacy was durable over 6 y in an extension (NCT00930553; 93% enrolled; 86% completed Y6), in which patients could receive alemtuzumab retreatment as-needed for relapse/MRI activity or receive other DMTs per investigator’s discretion. Further long-term evaluation is ongoing (TOPAZ; NCT02255656).

Objective: To evaluate MRI lesion/BVL outcomes over 7 y in alemtuzumab-treated CARE-MS II patients.

Methods: In TOPAZ, patients can receive alemtuzumab retreatment (≥12 months apart) or other DMTs (both per investigator’s discretion). Assessments: Annual MRI scored for disease activity (Gd-enhancing lesions; new/enlarging T2 lesions); new T1 hypointense lesions; and BVL (derived by relative change in brain parenchymal fraction [BPF]).

Results: 317/336 patients (94%) who entered TOPAZ remained through Y7. At Y7, 67% remained free of MRI disease activity; 90%, 67%, and 88% were free of Gd-enhancing lesions, new/enlarging T2 lesions, and new T1 hypointense lesions, respectively. Alemtuzumab consistently slowed median yearly BPF change vs SC IFNB-1a over 2 y, remaining low in Y7 (−0.14%). 47% of patients received no alemtuzumab retreatment or another DMT.

Conclusion: Alemtuzumab durably suppressed MRI disease activity and reduced BVL over 7 y in patients with inadequate response to prior therapy. Alemtuzumab may provide a unique treatment approach for RRMS patients, offering durable efficacy without continuous treatment.

P-61

Durable Clinical Outcomes with Alemtuzumab in Patients with Active RRMS in the Absence of Continuous Treatment: 7-Year Follow-up of CARE-MS II Patients (TOPAZ Study)

H. J. Kim1, B. A. Singer2, R. Alroughani3, S. Broadley4, H.-P. Hartung5, E. Havrdova6, C. Oreja-Guevara7, C. Pozzilli8, P. Vermersch9, S. Wray10,
Background: In CARE-MS II (NCT00548405), alemtuzumab (12 mg/day, baseline: 5 days; 12 months later: 2 days) significantly improved clinical outcomes vs SC IFNB-1a over 2 years (y) in RRMS patients with inadequate response to prior therapy. Efficacy of alemtuzumab was durable over 6 y in an extension study (NCT00930553; 93% enrolled; 86% completed Y6), in which alemtuzumab was durable over 6 y in an extension study (TOPAZ; NCT00225565). In CARE-MS II patients.

Methods: In TOPAZ, patients can receive alemtuzumab retreatment as-needed for relapse/MRI activity or receive other DMTs per investigator’s discretion; MRI scans were performed annually. Assessments: annualised relapse rate (ARR); 6-month confirmed disability worsening (CDW); 6-month confirmed disability improvement (CDI); no evidence of disease activity (NEDA); AEs. Results: 317/336 patients (94%) who entered TOPAZ remained through Y7. ARR remained low (Y7: 0.14); percentage of patients with stable/improved EDSS remained high (Y7: 73%). At Y7, 69% were 6-month CDW-free, 44% achieved 6-month CDI, and the majority achieved NEDA each year. 47% received no additional treatment (alemtuzumab or other DMT) after initial 2 courses. Overall AE incidence decreased over time. Thyroid AE incidence peaked at Y3 and then declined.

Conclusion: Alemtuzumab efficacy was maintained for 7 y in patients who had inadequate response to prior therapy. 44% also showed improvement in disability. Alemtuzumab may provide a unique treatment approach for RRMS patients, offering durable efficacy without continuous treatment.

Patient-Reported Satisfaction with Teriflunomide Treatment in Patients with RRMS in Australian Clinical Practice: AubPRO Study Design

S Vucic,1 MH Barnett,1 S Blum,2 N Shuey,3 R Worrall,4 R Macdonell5
1University of Sydney, Sydney, NSW, Australia; 2Princess Alexandria Hospital, Woolloongabba, QLD, Australia; 3St Vincent’s Hospital, Melbourne, VIC, Australia; 4Sanofi, Cambridge, MA, USA; 5Medical University of Lodz, Lodz, Poland

Objective: To describe the design of AubPRO, a prospective observational study to evaluate treatment satisfaction with teriflunomide using patient-reported outcomes (PROs) in patients with RRMS in routine clinical practice in Australia.

Methods: The AubPRO study will include ~150 adult patients with RRMS initiating treatment with teriflunomide 14 mg according to local clinical practice. Study duration for each patient will be ~13 months. The primary endpoint is treatment satisfaction with teriflunomide, measured using the Treatment Satisfaction Questionnaire for Medication (TSQM, v1.4), comprising 4 domains: Effectiveness, Side Effects, Convenience, and Global Satisfaction. Secondary endpoints include changes in other PROs: the Multiple Sclerosis Performance Scale (MSPS), the 12-item Multiple Sclerosis Walking Scale (MSWS-12), the Multiple Sclerosis Impact Scale (MSIS-29, v2), and the Health-Related Productivity Questionnaire (HRPQ, v2). Relapses, treatment adherence, and safety will also be recorded. Patients will be assessed at 3 clinic visits: baseline, Week 24, and Week 48. All PROs and adherence questionnaires will be administered by MOD-MS (Medical Safety Systems, Sydney, Australia), a novel digital tool that enables automated platform-independent data collection with smartphones, tablets, or computers.

Results: TSQM v1.4, MSPS, MSWS-12, MSIS-29 v2, and HRPQ v2, assessments used in AubPRO will be discussed. Results from AubPRO will be reported after study completion.

Conclusions: AubPRO will evaluate patient-reported satisfaction with teriflunomide treatment in a real-world setting and will extend clinical knowledge of the benefits of teriflunomide as a therapy for RRMS.

P-64

The Retrospective Evaluation of Effectiveness of Teriflunomide Treatments in Multiple Sclerosis Patients

Ömer Faruk Turan, Ahmet Candost Ertaç, Aylin Bican Demir, Ali Özhan Sıvacı

Uludag University Department of Neurology, Bursa, TURKEY

Teriflunomide is one drugs that can be used orally in relapsing and remitting MS. Teriflunomide is also approved by FDA in 2012 for adults who has RRMS. Our purpose in this study is to search the effects of Teriflunomide treatments on annual attack rate (AAR) and Expanded Disability Status Scale (EDSS) and also present the side effect profiles of these drugs in real world.

We include to our study 82 with fingolimod using patients who diagnosed with MS according to McDonald’s Criteria. Of the 82 patients who used teriflunomide, 23 were male and 59 were female. The mean age of the patients was 40.89% (SD 11.67), the mean age of diagnosis was 35.79 (SD 11.21), the mean age of first attack was 32.85 (SD 10.50), the mean follow up time was 4.52 (SD 2.80)
3,76) and the previous treatment duration was 5.45 (SD 3.84). Patients using teriflunomide have a median duration of treatment of 1 year. Teriflunomide were statistically significant (p <0.01). The same statistical analysis was performed for the EDSS change and Median, minimum and maximum were calculated the change was statistically significant (p <0.01).

These results showed that Teriflunomide had a positive effect on Annual Attack Rate and EDSS compared to previous treatments. The potential for adverse effects in teratunomide is low and patient comfort is effective in drug selection. With these drugs, far fewer side effects were observed compared to preclinical studies and patient tolerance was shown to be good.

**P-65**

A Subgroup Analysis of the Phase 3 TOWER Study Assessing Efficacy and Safety of Teriflunomide in Asian Patients with Relapsing Forms of MS

R. Macdonell,1 M. S. Freedman,; X. Xu,; S. Vucic,; P. Truffinet,; M. Benamor,; K. Thangavelu,; A. E. Miller,; R. Macdonell,; M. S. Freedman, 2 X. Xu, 3 S. Vucic, 4 P. Truffinet, 5 M. Relapsing Forms of MS

**Objective:** To report efficacy and safety outcomes in a subgroup of Asian patients in TOWER.

**Methods:** In the core study, patients were randomized 1:1:1 to placebo or teriflunomide 7 mg or 14 mg and treated for ≥12 weeks. ARR, 12-w CDW, and adverse events (AEs) were assessed.

**Results:** Of 1165 treated patients, 168 (14.4%) were of Asian descent. Demographic and baseline disease characteristics were comparable to the overall TOWER population, although Asian patients had a shorter mean (SD) time since first MS symptoms (5.01 [5.20] years vs 8.00 [6.73] years overall), and a smaller proportion had received another disease-modifying therapy within the last 2 years (3.6% vs 33.0% overall). Within the Asian subgroup, teriflunomide 14 mg significantly reduced annualized relapse rate (ARR) by 36.3% (P=0.0001) and risk of ≥12-week confirmed disability worsening (12-w CDW) by 31.5% (P=0.0442).

**Conclusions:** Efficacy outcomes in Asian patients enrolled in TOWER were consistent with the overall study population. Safety was also similar to that seen in the overall study population, with no new or unexpected findings.

**P-66**

Narrowband UVB Phototherapy for Clinically Isolated Syndrome: Delivering the Benefits of All UVB-Induced Molecules

A.G. Kermode,1 P.H. Hart,1 M.J. Fabis-Pedrini,2 R.M. Lucas,3 D.R. Booth,1 W.M. Carroll2,3 D. Nolan2,3 J.M. Cole2, A.P. Jones1, S. Trend1

1Centre for Neuromuscular and Neurological Disorders, Perton Institute for Neurological and Translational Science, University of Western Australia, Sir Charles Gardiner Hospital, Perth, WA, Australia; 2Institute for Immunology and Infectious Disease, Murdoch University, Perth, WA, Australia; 3Inflammation Research Group, Telethon Kids Institute, University of Western Australia, Perth, WA, Australia; 4National Centre for Epidemiology & Population Health, Research School of Population Health, Australian National University, Canberra, ACT, Australia; 5Centre for Immunology and Allergy Research, Westmead Institute for Medical Research, University of Sydney, Sydney, NSW, Australia; 6Immunology Department, Royal Perth Hospital, Perth, WA 6000, Australia; 7St John of God Dermatology, St John of God Hospital Suite 306, Subiaco, WA, Australia

**Objectives:** To report a preliminary observational study to evaluate integrative medicine in managing fatigue and cognitive deficits associated with multiple sclerosis.

**Methods:** We recruited subjects with MS to an 8-week, open-label, prospective study with acupuncture (twice weekly) and Chinese herbal medicine (daily) based on semi-individualized regimen by a multidisciplinary team (neurologists, CMPs, nurses, neuropsychologists, immunologists, clinical toxicologists, and health informaticians) for neurocognitive disorders (EDSS), fatigue (modified fatigue impact scale, MFIS), cognition (a 45-minute neuropsychological battery) and quality of life (SF-36) at baseline and week-8, together with blood monitoring and joint-consultations.

**Results:** Of 34/37(92%) subjects (35 females, 27 relapsing and 10 progressive MS, mean age 39.8+/11.9 years, and EDSS 3.7+/2.8) completed the program. Of the 35, 95% of patients had cognitive impairment(s) and 27/35 reported fatigue. Of 34(89%) subjects completed week-8 evaluations; there was improvement in fatigue and cognition as measured by MFIS (mean difference -12.1+/20.3, p=0.001) and HK-MOCA (1.3+/2.2, p=0.002). Improvements were observed among patients with varying disability (EDSS), disease duration (years), and disease subtypes (relapsing vs. progressive). In particular, we observed improvement in memory domains (auditory) (week-1 vs. week-8,
Poster Session 6
NMOSD Clinical Aspects

P-68 Neuromyelitis Optica: An 18-case Experience at Ho Chi Minh City University Medical Center in Vietnam

Thuy Thi Vu1, Tais Nguyen Tran1, Khang Chung Ngoc Vo1, Thang Ba Nguyen2, Minh Le1
1University Medical Center, Ho Chi Minh City, Vietnam
2University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam
Refer to O-11 in the Oral Presentation

P-69 Clinical Characteristics Analysis of Neuromyelitis Optica Spectrum Disorders Manifesting Brainstem Involvement as Initial Symptoms

Yuge Wang1, Yanqiang Wang1, Bingjun Zhang1, Yu Yang1, Wei Qiu1, Xueqiang Hu1, Zhengqi Lu2
1Department of Neurology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China
2Department of Neurology, The Affiliated Hospital of Weifang Medical University, Weifang, China

Background: Neuromyelitis optica spectrum disorders (NMOSD) is a group of the demyelinating and inflammatory disease that preferentially involve the optic nerve and spinal cord. Mounting evidence indicates that brain abnormalities are being recognized more frequently in NMOSD, especially, have accompanied pre-existing NMOSD. However, Clinical studies related to NMOSD manifesting brainstem involvement as initial symptoms are still scarce.

Methods: We retrospectively analyzed 78 NMOSD patients manifesting brainstem involvement as initial symptoms. Data were collected regarding clinical characteristics, laboratory tests, and magnetic resonance imaging findings.

Results: 85.9% of patients were female. Median age at onset was 25 years (21.3-34 years), mean duration was 13.2 months. The frequently initial symptoms were headache (36.9%), diplopia (39.7%), paresthesia (31.2%), bowel or bladder dysfunction (44.9%), movement disorders (44.9%), sensory disturbances (71.8%), neuropsychic pain (41%), nausea and vomiting (80.8%) • hiccups (39.7%) • choking cough or dysphagia (21.8%), vertigo and dizziness (41%), in dorsal part (92.3%), in medulla lesions extending to upper cervical (34.6%), hypothalamus (30.8%), periaqueductal regions (28.2%). Anti-AQP4 antibody was positive in 34.7%.

Conclusions: The NMOSD could initially present with different brainstem symptoms, nausea and vomiting, hiccups were the first most frequent brainstem symptoms, the medulla lesions, including the medulla lesions extending to upper cervical, especially in dorsal part, and periaqueductal regions were unique to NMOSD. All of these would be helpful to the early diagnose and treatment of the NMOSD.

P-70 Ethnic Differences in Clinical Manifestation of Neuromyelitis Optica Spectrum Disorder

Kim SH1, Maureen MA2, Levy M3, Schmidt F4, Paul F5, Ringelstein M6, Aktas O4, Hartung HP4, Asgari N7, Li JT8, Siritso S7, Prayoonwiwat, N7, Shin HJ1, Hyun JW1, Palace J9, Kim HJ1
1Department of Neurology, Research Institute and Hospital of National Cancer Center, South Korea
2Department of Neurology, Johns Hopkins University, USA
3NeuroCure Clinical Research Center, Charité University Medicine, Berlin, Germany
4Department of Neurology, Medical Faculty, Heinrich Heine University, Düsseldorf, Germany
5Department of Neurology, Institute of Molecular Medicine & Institutes of Regional Health Research, University of Southern Denmark, Odense, Denmark
6Department of Medicine, Queen Elizabeth Hospital, Kowloon, Hong Kong
7Department of Medicine, Siraj Hospital, Mahdol University, Bangkok, Thailand
8Nuffield Department of Clinical Neurosciences, West Wing, John Radcliffe Hospital, University of Oxford, Oxford, UK
Refer to O-12 in the Oral Presentation

P-71 Nationwide Epidemiological Study of Neuromyelitis Optica in Japan

K. Miyamoto1, K. Fujihara2, J. Kira3, N. Kuriyama4, M. Matsui5, A. Tamakoshi6, S. Kusunoki1
1Kindai University Faculty of Medicine, Osaka-Sayama, Japan; 2Fukushima Medical University, Fukushima, Japan; 3Kyusyu University, Fukuoka, Japan; 4Kyoto Prefectural University of Medicine, Kyoto, Japan; 5Kanazawa Medical University, Ishikawa, Japan; 6Hokkaido University Graduate School of Medicine, Sapporo, Japan
Refer to O-4 in the Oral Presentation

P-72 Antibody Serology Can Influence Clinical Presentations in Neuromyelitis Optica Spectrum Disorder

Byeol-A Yoon, Geum-Bong Lee, Jong Kuk Kim
Department of Neurology, Dong-A University College of Medicine

Background: The discovery of anti-aquaporin-4 (AQP4) antibody has led to increased understanding of neuromyelitis optica spectrum disorder (NMOSD). The anti-AQP4 antibody is now widely used in clinical practice as an important marker for diagnosis. However, this antibody is negative in many patients, which makes it difficult to establish adequate diagnosis and treatment plans.

Objectives: We tried to show the effect of AQP4 antibody positivity on clinical outcome in NMOSD.

Methods: We retrospectively studied NMOSD patients who visited Dong-A University Hospital from 1990 to 2017.

Results: Of the 36 patients, 16 (44.4%) were seropositive. More elderly patients were included in seropositive group, but there was no difference in sexual distribution (p>0.03). The relapse rate of optic neuritis was higher in seropositive group (p<0.002) and
Characteristics of Patients Double-Seropositive of P-73 optic neuritis and worse clinical prognosis. Associated with older age of initial attack, higher frequency of clinical features. Especially, positivity of this antibody is strongly associated with older age of initial attack, higher frequency of optic neuritis and worse clinical prognosis.

P-73 Characteristics of Patients Double-Seropositive of Antiphospholipid Antibody and Aquaporin4-Antibody

Min JH, MD, Ph.D1, Seok JM, MD2, Kim DS, MD2, Kim BJ, MD, Ph.D3, Lee KH, MO, Ph.D2,3

1Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
2Neuroscience Center, Samsung Medical Center, Seoul, South Korea

Background: Coexistence of autoimmune disorders including systemic lupus erythematosus, Sjogren syndrome and antiphospholipid syndrome (APS) are common in patients with neuromyelitis optica (NMO). NMO is an inflammatory demyelinating disease with the positivity of anti-aquaporin4-antibody (AQP4-ab) and APS is defined by the occurrence of venous and arterial thromboses, recurrent fetal losses, in the presence of antiphospholipid antibodies (aPL).

Objectives: Herein, we investigated clinical and radiological characteristics in patients with AQP4-ab and aPL.

Methods: We collected 83 patients having AQP4-ab from the prospective registry of CNS demyelinating disorders in Samsung Medical Center and evaluated clinical, radiological and serological data including anti-cardiolipin antibody (ACLA), lupus anticoagulant (LA), and anti-beta-2 glycoprotein I antibody (aB2A). Results: Among 83 AQP4-ab-positive patients, 45 were tested for aPL, which was positive in only 7 patients (15.5%) (all females; median age of onset, 32 years). They showed clinical features of APS, vascular thrombosis (N=4), pregnancy morbidity (N=3), and increased D-dimer or fibronectin. (N=6). Most frequent aPL was ACLA (N=5) and LA (N=5), followed by aB2A (N=3). Five patients with cord involvement showed all longitudinal extensive myelitis and four patients showed compromised retinal vascular changes with poor recovery following optic neuritis. In addition, three patients with brain involvement showed vasogenic edema with or without microinfarct.

Conclusions: The presence of aPL in AQP4-ab-positive patients can suggest of the APS and thrombotic tendency, which may be associated with the severe disability with characteristic MRI features, warranting the more aggressive immunotherapy in patients with NMO.

P-74 Low Prevalence of Anti Aquaporin 4 Antibody in Neuromyelitis Optica Spectrum Disorder and Multiple Sclerosis in Western Australia

MJ Fabis-Pedrini1, C Bundell2,3, CK Wee1, W Qiu2, M Lucas2,5, WM Carroll1, AG Kermode1,6

1Centre for Neuromuscular and Neurological Disorders, Perron Institute for Neurological and Translational Science, UWA, Sir Charles Gairdner Hospital, Queen Elizabeth II Medical Centre, Perth, Western Australia, Australia
2PathWest Laboratory Medicine, Queen Elizabeth II Medical Centre, Perth, Western Australia, Australia
3School of Pathology and Laboratory Medicine, University of Western Australia, Nedlands, Western Australia
4Department of Neurology, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China
5School of Medicine and Pharmacology, School of Pathology and Laboratory Medicine, UWA, Perth, Australia
6Institute of Immunology and Infectious Diseases, Murdoch University, Perth, Western Australia, Australia

Background: NMOSD is an inflammatory disease of the CNS distinct from MS, and relatively rare in Western countries. Many patients with NMOSD have detectable serum antibodies that target the water channel aquaporin-4 (AQP4-immunoglobulin G IgG).

Objective: To evaluate the prevalence of anti-AQP4 antibody in neuromyelitis optica spectrum disorder (NMOSD) and multiple sclerosis (MS) patients from the Western Australian cohort using highly sensitive test.

Methods: 420 sera of patients with NMOSD, MS and suspicious demyelinating diseases were assessed for the presence of AQP4 antibody using a cell-based assay in cells transfected with 2 isoforms of AQP4 (M1 and M23) and in primate cerebellum tissue (Euroimmun, Luebeck, Germany). The anti-AQP4 antibody test was performed at PathWest Laboratory Medicine, QEII Medical Centre.

Results: Only 6 out of 420 patient sera were AQP4 antibody-positive. Our study showed a low frequency of anti-AQP4 antibody in this predominantly Anglo-Celtic Western Australian population. All of the 6 AQP4 antibody-positive patients had a final diagnosis of NMOSD; four out of six AQP-4 positive patients had longitudinally extensive myelitis (LEM). Prevalence of AQP4 antibody positivity in Western Australia was as low as 0.25 (0.05-0.43) per 100,000. We did not find any statistical difference in age between AQP4 antibody-positive and negative patients. All AQP4 antibody-positive patients were females.

Conclusions: Testing AQP4 antibody positivity on cerebellar tissue is less sensitive than the cell-based assay. Our study confirmed the low anti-AQP4 antibody prevalence in the Western Australian idiopathic inflammatory CNS disease population. Our results are comparable with data from other Western populations.

P-75 Discrimination of Spinal Cord Sarcoidosis from Neuromyelitis Optica Spectrum Disorder or Spondylotic Myelopathy

Hiroshi Kuroda1, Toshiyuki Takahashi1, Douglas Kazutoshi Sato1,3, Ryo Ogawa1, Kimihiko Kaneko1, Yoshiki Takai1, Shuhei Nishiyama1, Tatsuro Misu1,2, Ichiro Nakashima1, Kazuo Fujihara1,2, and Masashi Aoki1

1Department of Neurology and 2Department of Multiple Sclerosis Therapeutics, Tohoku University Graduate School of Medicine, Sendai 980-8574, Japan, 3Brazil Institute and Hospital Sao Lucas Pontifical Catholic University of Rio Grande do Sul, Neurology, Porto Alegre, Brazil
P-76
Differences in The Clinical and Laboratory Features According to The Lesion Length in Non-infectious Myelitis
Sa-Yoon Kang
Department of Neurology, Jeju National University School of Medicine, Jeju, Republic of Korea

Background & Objective: Non-infectious myelitis consists of post-infectious myelopathy, multiple sclerosis, neuromyelitis optica, myelopathy related with connective tissue and paraneoplastic syndrome. We investigated to determine if any difference in the clinical characteristics of the patients of the non-infectious myelitis as compared with the lesion length.

Methods: We included patients who had more than 18 years old and diagnosed of non-infectious myelitis. Each patient was divided into long and short segments group according to the lesion length by MRI findings. Long segments group was defined as having lesion length more than three vertebral segments. We compared the clinical and laboratory features between both groups.

Results: Among 38 non-infectious myelitis patients, long and short segments group were 23 and 15 patients, respectively. Demographic features had no significant differences between two groups. The CSF oligoclonal band (OCB) was positive in 7 patients (30%) among long segments group, but none of patients in short segments group showed OCB. The CSF OCB positive rate had significant difference statistically between two groups. CSF protein is much higher in long segments group than short segment group. Anti-aquaporin-4 antibodies were detected in 5 patients and 3 patients belonged to long segments group. The etiology of myelitis between two groups had no significant differences.

Conclusions: As both CSF oligoclonal band and protein reflect the inflammatory condition, we assumed that more severe inflammatory responses were developed in non-infectious myelitis patients with long segments lesion. However the difference in lesion length did not give help to predict the etiology of non-infectious myelitis.

P-77
Different Features between Pediatric-Onset and Adult-Onset Patients Who Are Seropositive For MOG-IgG: A Multicenter Study in South China
Lu Chen1,2, Chen Chen1,2, Xiaonian Zhong1,2, Xiaobo Sun1, Haixia Zhu3, Xiaojing Li3, Hui Yang3, Yaqing Shu4, Yanyu Chang1, Xueqiang Hu1, Zhengqi Lu1, Lisheng Peng1, Wei Qiu1
1 Department of Neurology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou
2 Guangzhou Women and Children’s Medical Center, Guangzhou
3 Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou

Refer to O-14 in the Oral Presentation

P-78
Overlapping MOG Antibody Disease or NMOSD and Anti-NMDA Receptor Encephalitis: A Clinical Series and Systematic Review of the Literature

S. Fany, M.D., H. Remy, B.S., H. Guan1, M.D., G. Shah2, Ph.D., T. Guan4, Ph.D., Y. Zhang1, M.D., Y. Dai1, M.D., M. Yao1, M.D., F. Feng1, M.D., Y. Zhong1, M.D., B. Peng1, M.D., Y. Zhu1, M.D., L. Cui1, M.D., Y. Xu1, M.D.
1 Department of Neurology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
2 Department of Epidemiology and Statistics, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Beijing, China.
3 School of Basic Medicine, Peking Union Medical College, Beijing, China.
4 School of Public Health, Peking Union Medical College, Beijing, China.
5 Department of Radiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
6 Department of Ophthalmology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.
7 Neurosciences Center, Chinese Academy of Medical Sciences, Beijing, China.

Background: Patients with myelin oligodendrocyte glycoprotein (MOG)-antibody (ab) disease or neuromyelitis optica spectrum disorders (NMOSD) co-existing with anti-NMDA receptor encephalitis (NMDARe) are rarely reported. No study has compared the characteristics of these two disorders.

Methods: We report a clinical series of overlapping MOG-ab disease or NMOSD and NMDARe. The published cases of these overlapping syndromes were systematically reviewed and analyzed together with our patients.

Results: 3 of 40 patients with MOG-ab disease and 3 of 491 patients with NMOSD co-existed with NMDARe (7.5% vs 0.6%, P < 0.01) in our cohorts. Another 11 patients with overlapping MOG-ab disease and NMOSD and NMOSD ab disease and NMOSD were identified from published cases. Analyzed together, they were mainly from East Asian (64% vs 59%, P = 0.756), frequently presenting with infratentorial or spinal cord lesions (64% vs 65%, P = 0.704) and infrequently accompanying with tumors (0 vs 6%, P = 1.000). Compared with overlapping NMOSD and NMOSDRe, overlapping MOG-ab disease and NMOSDRe had lower female/male ratio (43% vs 94%, P < 0.01), younger onset age (19.8 vs 32.4, P = 0.025), and better prognosis (mRS 0-2 scores, 86% vs 41%, P < 0.01).

Conclusions: Patients with MOG-ab disease or NMOSD presenting with psychiatric behavior or cognitive dysfunction, should be tested for anti-NMDAR-ab. Compared with overlapping NMOSD and NMOSDRe, overlapping MOG-ab disease and NMOSDRe is more prevalent and has lower female/male ratio, a younger onset age and a better prognosis.

P-79
Neuromyelitis optica spectrum disorders with Aquaporin-4 and Myelin-Oligodendrocyte Glycoprotein antibodies in Turkish Population: A Comparative Study
Egemen Idıman1, F. Idıman1, M. Kaya1, O. Hasankoyoglu1, D. Kaya1, H. Limoncu1, O. Bulut1, Z. Altun1
1 Department of Neurology, Dokuz Eylül University Faculty of Medicine, Izmir, Turkey
2 Department of Ophthalmology, Dokuz Eylül University Faculty of Medicine, Izmir, Turkey
3 Geniatrics Medicine, Dokuz Eylül University Faculty of Medicine, Izmir, Turkey

Refer to O-13 in the Oral Presentation
NMOSD Imaging and Electrophysiology

P-80
Differential Patterns of Demyelination and Remyelination Revealed by q-Space Myelin Map Imaging in NMOSD and MS
K. Kufukihara1, J. Nakahara, M. Tanikawa1, J. Hata1, S. Suzuki1, K. Fujiiyoshi1, H. Fujiwara, M. Jinzaki2, M. Nakamura1, S. Okado3, S. Takahashi1, N. Suzuki1

From Departments of Neurology, Physiology, Orthopedic Surgery, Radiology, Keio University School of Medicine, Tokyo, Japan; Laboratory for Marmoset Neural Architecture, RIKEN Brain Science Institute, Saitama, Japan; National Hospital Organization Muroyama Medical Center, Tokyo, Japan.

Background: Distinct pathologies exist in NMOSD and MS, however the correct diagnosis is often jeopardized by the nonspecific nature of T2 signals. We have recently developed a novel myelin-specific qMR technique named qMM which is capable of visualizing demyelination and remyelination in vivo.

Objective: To explore possible differential patterns in qMM appearance between NMOSD and MS.

Methods: A 54-year-old female patient with newly diagnosed NMOSD with anti-aquaporin 4 antibody and a 30-year-old female patient with 7-month history of relapsing-remitting MS were evaluated. Both patients experienced acute exacerbation with Gdolinium (Gd)-enhancing T2 lesion and they were treated with intravenous methylprednisolone therapy (IVMP).

Results: qMM studies including qMM were repeated before and after IVMP.

P-81
Choroid Plexitis in Neuromyelitis Optica Spectrum Disorder
Y.J Oh, MD1, Y.M Lim, MD1, E.J Lee, MD1, H.J Kim, MD1, K.K Kim MD1
1Department of Neurology, Univ of Ulsan, Asan Medical Center, Seoul, Korea;
Refer to O-16 in the Oral Presentation

P-82
Optical Coherence Tomography Versus Visual Evoked Potentials in Optic Neuritis of Neuromyelitis Optica Spectrum Disorders
Joong-Yang Cho1, Nam-Hee Kim2, Ho Jin Kim3, Cheol-Yong Park4
1Department of Neurology, Ilsan Paik Hospital, Inje University College of Medicine, South Korea
2Department of Neurology, Dongguk University Ilsan Hospital, South Korea
3Department of Neurology, Research Institute and Hospital of National Cancer Center, South Korea
4Department of Ophthalmology, Dongguk University Ilsan Hospital

Objective: To assess the sensitivity of optical coherence tomography (OCT) and visual evoked potentials (VEPs) for detecting visual involvements in neuromyelitis optica spectrum disorders (NMOSD).

Methods: Cross-sectional study was performed in 73 aquaporin-4 antibody seropositive NMOSD patients with 101 eyes of optic neuritis (ON). Measures included clinical characteristics, visual acuity (VA) in logMAR, expanded disability status scale (EDSS), OCT retinal nerve fiber layer (RNFL) thickness, and VEPs.

Results: OCT and VEPs were abnormal in 68% and 73% respectively in eyes with ON (p=0.42), and 2% versus 9% in eyes without a history of ON (p=0.38). Abnormal OCT and VEPs increased with the number of ON; after first episode of ON, OCT and VEPs were abnormal in 50% and 67% (p=0.041) and combination of either tests was abnormal in 75% (p=0.01 vs OCT, p=0.06 vs VEPs), while after second or more episodes, the sensitivity of OCT and VEPs increased by 95% and 83% respectively (p=0.06) with 95% abnormal in combined tests.
thickness correlated with VEP latency (r=-0.8, p<0.01) and amplitude (r=-0.69, p<0.01). These measures were correlated with EDSS (RNFLT: r=-0.42, p<0.01, VEP latency: r=0.47, p<0.01, VEP amplitude: r=-0.44, p<0.01) and VA (RNFLT: r=-0.75, p<0.01, VEP latency: r=0.84, p<0.01, VEP amplitude: r=-0.61, p<0.01).

Conclusions: VEPs seem to be superior for detecting subclinical or first ON, whereas OCT appears to be better for multiple episodes of ON in NMOSD. The correlation between clinical disability and measures of OCT and VEPs suggests their potential as markers of disease burden in NMOSD.

P-83
Bidirectional Degeneration in The Visual Pathway in Neuromyelitis Optica Spectrum Disorder (NMOSD)
De-Cai Tian, MD, Lei Su, MD, MoLi Fan, MD, Jian Yang, BS, Rui Zhang, MD, eng Wen, BS, YuluAn Han BS, Changlu Yu, MD, Chao Zhang, PhD, HongLei Ren, MD, KaBin Shi, MD, ZlXing Zhu, MD, YinHu a Dong, MD, Yaou Liu, MD, PhD, Fu-Dong Shi, MD, PhD
1Department of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin 300052, China; 2Department of Radiology, Tianjin Third Central Hospital, Tianjin, 300170, China; 3Department of Radiology, Tianjin HuanHu Hospital, Tianjin, 300350, China; 4Department of Neurology, Tianjin Forth Central Hospital, Tianjin, 300140, China; 5Department of Radiology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China; 6Department of Neurology, Barrow Neurological Institute, St. Joseph’s Hospital and Medical Center, Phoenix, AZ 85013, USA.

* Dr. Tian and Su contributed equally.

Refer to O-6 in the Oral Presentation

Poster Session 8
NMOSD Immunology and Laboratory Tests

P-84
Clinical Characteristics and Outcomes of Connective Tissue Disease Accompanied Neuromyelitis Optica Spectrum Disorder in Chinese Patients
Y Zhang1, JL Zhao2, MT Li3, XF Zeng2, Y Xu
1Multiple Sclerosis Center, Department of Neurology, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Sciences, No. 1 Shuaifuyuan, Beijing 100030, China; 2Department of Rheumatology, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Sciences, No. 1 Shuaifuyuan, Beijing 100030, China; 3Department of Radiology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China.

Background: Optic neuritis (ON) or longitudinally extensive transverse myelitis (LETM) may be present in patients with connective tissue disease (CTD), especially systemic lupus erythematosus (SLE) and primary Sjogren’s syndrome (pSS). A subset of these patients can be diagnosis of NMOSD (termed CTD-NMOSD) while others cannot (termed CTD-non-NMOSD).

Objective: To compare the clinical characteristics and outcomes of CTD-NMOSD patients to CTD-non-NMOSD patients.

Methods: We retrospectively collected data from 40 CTD (SLE: 24, 60%; pSS: 16, 40%) patients with ON or LETM or both who were admitted to the rheumatology department of our hospital from Jan 2006 to Dec 2016. They are divided to CTD-NMOSD and CTD-non-NMOSD two groups. Demographic characteristics, clinical and laboratory features of the two groups were retrieved from the database. Relapse rates were studied by Kaplan-Meier method, and Cox proportional hazard model was adopted to perform the analysis of predicting factors for mortality.

Results: Among 40 patients with CTD, 28 (70%) could be diagnosed NMOSD while 12 (30%) could not. The frequencies of anti-SSA antibodies to aquaporin-4 (anti-AQP4) were significantly higher in patients with NMOSD, compared with those patients with non-NMOSD (p<0.05). There were no significant differences in age, gender, clinical features, disease duration, anti-dsDNA, anti-rRNP, APLs, EDSS, scores, and MRI features between two groups. Kaplan-Meier curve show CTD-NMOSD patients had significantly higher disease relapse rate, compared with CTD-non-NMOSD (75% vs 25%, P<0.01).

Conclusion: The significant association of anti-SSA and anti-AQP4 with NMOSD and higher relapse rates suggests that NMOSD and CTD-non-NMOSD representing two distinct entities with different pathogenesis.

P-85
Frequent Positivity of ANA and SSA during NMOSD Attacks in Patients without Co-existing SLE and Sjogren Syndrome: A Preliminary Observation
Jyh Yung Hor1, Yee Ming Ching2, Kooi Heng Ng3, Masita Arip1
1Department of Neurology, Penang General Hospital, Penang, Malaysia; 2Autoimmune Unit, Allergy & Immunology Research Centre, Institute for Medical Research, Kuala Lumpur, Malaysia; 3Division of Rheumatology, Penang General Hospital, Penang, Malaysia.

Background: It is observed that there is frequent positivity of ANA (35–60%) and SSA (10–30%) in NMOSD patients, when sera were randomly tested. In a study of SLE patients with co-existing NMOSD, AQP4-Ab, ANA and dsDNA levels were raised during NMOSD attacks, suggesting polyclonal B-lymphocytes expansion.

Objective: To study the positivity of ANA, dsDNA and ENAs during NMOSD attacks in patients without co-existing SLE and Sjogren syndrome (SS).

Methods: Serum antibody profiles (AQP4-Ab, ANA, dsDNA, and ENAs) of 6 AQP4-seropositive NMOSD patients (without co-existing SLE and symptoms of SS) during or shortly after attacks were available for study.

Results: Sera of 5 patients (83%) were positive for ANA and SSA +/- SSB during or shortly after acute myelitis. The ANA titre ranged from 1:160 – 1:640 (all speckled pattern). All 5 patients had positive SSA +/- SSB, but not other ENAs: Sm, RNP, J01, Scl70; and negative for dsDNA. In fact, positive ANA and SSA +/- SSB predicted a positive AQP4 result, which usually returned later. The remaining 1 patient had low positive ANA (1:80, speckled) in 1 of myelitis exacerbations during steroids taper, but not in 2 other myelitis episodes, and were negative for ENAs and dsDNA. In contrast, 2 AQP4-seropositive NMOSD patients with co-existing SLE had positive dsDNA and ANA (homogenous pattern).

Conclusions: During or shortly after NMOSD attacks (at least in myelitis), ANA and SSA +/- SSB were very frequently positive, but not for dsDNA and other ENAs. Longitudinal study is needed to confirm this observation.
Rheumatoid Factor May Associated with Disability in Neuromyelitis Optica Spectrum Disorder


Department of Neurology, Korea University Guro Hospital, Korea University college of Medicine, Seoul, Korea

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

Neuroscience Center, Samsung Medical Center, Seoul, Korea

Department of Neurology, Soonchunhyang University Cheonan Hospital, Cheonan, Korea

Department of Neurology, Changwon Gyeongsang Institute of Health Science, Gyeongsang National University School of Medicine, Changwon, Korea

Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Korea

Department of Neurology, Severance hospital, Yonsei University College of Medicine, Seoul, Korea

Department of Neurology, Korea University Anam Hospital, College of Medicine, Seoul, Korea

Department of Neurology, Keimyung University School of Medicine, Daegu, Korea

Department of Neurology, College of Medicine, Chju National University, Chju, Korea

Department of Neurology, Eulji University College of Medicine, Seoul, Korea

Department of Neurology, College of Medicine, University of Ulsan, Asan Medical Center

Department of Neurology, Chungbuk National University College of Medicine, Cheongju, Korea

Department of Neurology, Konkuk University College of Medicine, Seoul, Korea

Department of Neurology, Kosin University College of Medicine, Busan, Korea

Department of Neurology, Dong-A University Hospital, Busan, Korea

Department of Neurology, Chungnam National University College of Medicine, Daejeon, Korea

Department of Neurology, Inje University College of Medicine, Ilsan

Department of Neurology, The Catholic University of Korea, College of Medicine, Bucheon St. Mary’s Hospital, Bucheon, Korea

Background: Neuromyelitis optica spectrum disorder (NMOSD) was rare neuroinflammatory disease, often coexists with autoantibodies such as anti-nucleotide antibody (ANA), anti-Sjogren’s syndrome A (SSA) antibody, anti-Sjogren’s syndrome B (SSB) antibody, and rheumatoid factor (RF). However, the relationship between autoantibodies and NMOSD is not clear.

Objective: We investigated the prevalence of autoantibodies and the associations between the existence of autoantibodies and disability in NMOSD patients.

Methods: We collected the clinical information and the profile of autoantibodies including ANA, SSA, SSB, anti-neutrophil cytoplasmic antibody (ANCA), anti-thyroperoxidase (TPO) antibody, anti-thyroglobulin (TG) antibody, and RF in NMOSD patients of 11 hospitals in Korea for 3 years (2014 Sep – 2016 Nov).

We evaluated the associations between the positivity of each autoantibody and the time from onset of NMOSD to a higher Expanded Disability Status Scale (EDSS) score (EDSS>6.0) using cox-regression analysis.

Results: A total of 159 patients were evaluated autoantibodies, the frequency of autoantibodies was ANA (33%), SSA (29%), TPO (15%), TG (12%), SSB (10%), RF (9%), and ANCA (2.4%). The median of EDSS was 3 (IQ 2-4), the mean of disease duration was 8.2 (SD 6.5) years. Higher EDSS was associated the elevation of RF (p=0.003) and the hazard ratio of RF was 7.9 (95% CI 2.0 – 31.1).

Conclusion: Autoantibodies possibly modulate the progression of disease in NMOSD. We confirmed that various autoantibodies were presented and suggested that the elevation of RF may be associated the higher disabilities in NMOSD patients.

Cerebrospinal Fluid-Actin Related Protein 2/3 Complex Subunit 4 as an Astrocytic Foot Process Damage Marker of Aquaporin-4-Igg Positive Neuromyelitis Optica Spectrum Disorders

Shuhei Nishiya,1 Tatsuro Misu,1 Ichiro Nakashima,2 Douglas Kazutoshi Sato,3 Kimihiko Kaneko,4 Ryo Ogawa,1 Hirohiko Ono,1 Kazuhiro Kurosawa,1 Yoshihki Takai,1 Toshiyuki Takahashi,2 Hiroshi Kuroda,1 Kazuo Fujihara,2 Masashi Aoki1

Department of Neurology, Tohoku University School of Medicine
Division of Neurology, Tohoku Medical and Pharmaceutical University
Department of Neurology, Niigata University School of Medicine
Department of Neurology, Yonezawa National Hospital
Department of Multiple Sclerosis and Therapeutics, Fukushima Medical University

Refer to O-15 in the Oral Presentation

Serum IL-27, IL-23 and IL-35 Levels in Neuromyelitis Optica Spectrum Disorders with Aquaporin-4 and Multiple Sclerosis

Egemen Idman,1 D Kaya,1 O Hasankoyoglu,2 A O Keskin,1 N Taydemir,2 Z Altun2

Department of Neurology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey
Geriatrics Medicine, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey
Department of Neurology, Dicle University Faculty of Medicine, Diyarbakir, Turkey
Department of Basic Oncology, Institute of Basic Oncology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

Background: The interleukin 12 (IL-12) family, namely IL-27, IL-23 and IL-35, has been reported to play important roles in autoimmune diseases such as neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis (MS).

Objective: To assess the role of IL-12 family members including IL-27, IL-23 and IL-35 in the pathogenesis of NMOSD and MS.

Methods: We determined their serum levels in patients with MS (n=29), NMOSD (n=30), and healthy control subjects (n=21) by ELISA and assessed potential correlations with clinical characteristics.
Results: There was no difference in regard to the serum levels of IL-23 and IL-27 among groups. It was shown that serum IL-35 levels in patients with NMOSD were higher than those with MS and healthy controls (both, p<0.001).

Conclusions: Our findings revealed that the increased IL-35 levels, but not IL-23 and IL-27, in NMOSD patients might be a biomarker and might represent potential therapeutic cytokine for treating the disease.

P-89
Study of The Placentae of Patients with Neuromyelitis Optica Spectrum Disorder
Yanyu Chang, Yaqing Shu, Xiaobo Sun, Tingting Lu, Chen Chen, Ling Fang, Dan He, Chengfang Xu, Zhengqi Lu, Xueqiang Hu, Lisheng Peng, Allan G Kermode, Wei Qiu
1Department of Neurology, The Third Affiliated Hospital of SUN Yat-sen University, Guangzhou, Guangdong, China
2Department of Pathology, The Third Affiliated Hospital of SUN Yat-sen University, Guangzhou, Guangdong, China
3Department of Obstetrics, The Third Affiliated Hospital of SUN Yat-sen University, Guangzhou, Guangdong, China
4Centre for Neuromuscular and Neurological Disorders, University of Western Australia, Department of Neurology, Sir Charles Gairdner Hospital, Queen Elizabeth II Medical Centre, Nedlands, Western Australia, Australia
5Institute of Immunology and Infectious Diseases, Murdoch University, Perth, Western Australia, Australia

Background: Previous studies have shown that circulating AQP4-IgG may lead to negative consequences during pregnancy in NMOSD patients.

Objectives: To explore whether AQP4-IgG influences pregnancy by affecting AQP4 expression and inducing placental inflammation in patients with neuromyelitis optica spectrum disorder (NMOSD).

Methods: We prospectively collected clinical data from six pregnant AQP4-IgG-seropositive NMOSD patients and their infants, and investigated AQP4 expression and placental inflammatory infiltration by comparing haematoxylin and eosin and immunohistochemical (AQP4, AQ P1, C5b-9, IgG, CD3, CD8, CD20, and CD68) staining results with a healthy control.

Results: Four patients were term pregnant, and their infants were normal for development; their serum AQP4-IgG was positive at birth, and three infants were negative for AQP4-IgG after 3 months. Two patients underwent induced abortion; one because of NMOSD relapse and another because of fetal malformation. Histological investigation showed normal structure of the chorionic villi, and no significant difference in the intensity of the immune histochemical staining for AQP1, AQP4, and inflammatory markers in placenta of patients and the control.

Conclusions: There was no decrease in placental AQP4 expression, and no obvious placental inflammation or signs of damage in term placenta of NMOSD patients seropositive for AQP4-IgG.

P-90
Association of Serum Cystatin C with Neuromyelitis Optica
Yaqing Shu, Chen Chen, Yanyu Chang, Haotian Wu, Jing Li, Lisheng Peng, Zhengqi Lu, Xueqiang Hu, Wei Qiu

Department of Neurology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China

Background: Cystatin C (CysC) is associated with many neurodegenerative disorders and autoimmune diseases, but its relationship with neuromyelitis optica (NMO) is unknown.

Methods: Serum levels of CysC were determined in 110 patients with NMO (57 NMO with relapse, 53 NMO with remission) and 115 healthy controls. Association of CysC with NMO and its clinical parameters were evaluated in the patients.

Results: The total serum levels of CysC were significantly higher in NMO patients than in healthy controls (p<0.05). Serum CysC levels in NMO with remission were respectively significantly higher than in NMO patients with relapse (p<0.001), healthy controls (p<0.001). Serum CysC levels were significantly positively associated with age.

Conclusion: Our results indicated an elevated serum level of CysC in NMO.

P-91
Neuroprotective Effect of Serum Creatinine in Korean Patients with Neuromyelitis Optica Spectrum Disorder
Dong Sun Kim, Seung Ju Kim, Byoung Joon Kim, Ju Hong Min
Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Background: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory disorder of CNS. The creatinine has a neuroprotective role in neurodegenerative disease. However, it is unclear that creatinine has a neuroprotective role in NMOSD.

Objective: In this study, we aimed to analyze the correlation of the disease severity of NMOSD and creatinine.

Method: 50 patients with NMOSD, who admitted our hospital were included. We analyzed creatinine (Cr) level in serum from NMOSD patients. Disease severity of NMOSD is measured by Expanded Disability Status Scale (EDSS) score, when the blood test was performed. The SPSS (version 18) was used for statistical analysis.

Results: The mean serum Cr was 0.628 ± 0.024 mg/dl. The mean EDSS was 4.32 ± 0.27. In the analysis, there was a significant correlation between serum Cr and bowel functional EDSS score (correlation coefficient = -0.250, p=0.025 on Kendall’s tau-b, correlation coefficient = -0.309, p=0.029 on Spearman’s rho), although other variables showed no statistically significant differences.

Conclusions: Our results showed that high level of Cr was associated with a better bladder and bowel function. Therefore, the Cr might be a predictive factor of bladder and bowel dysfunction in NMOSD patient, although Cr level is affected by general condition of patient and the bladder and bowel functions can be associated with other factors except the nervous system.

P-92
Hepatitis B Virus Infection in Patients with Neuromyelitis Optica Spectrum Disorder
Yanqiang Wang, Yuge Wang, Wei Qiu, Xueqiang Hu, Zhengqi Lu
Background: The exact cause and pathogenesis of autoimmune diseases are not completely understood. Hepatitis B virus (HBV) is notorious in its association with diverse autoimmune diseases, including Systemic lupus erythematosus, Rheumatoid arthritis, Type 1 diabetes, Thyroid disease. However, scientific data regarding the relationship between NMOSD and serum markers of HBV, is still lacking and which has yet to be studied and clarified.

Methods: 376 patients were included to this retrospective study. NMOSD (n = 102), MS (n = 78), Acute disseminated encephalomyelitis (n =46), other neurological disease (Myasthenia gravis (n = 28), Guillain-Barré syndrome (n = 21), Facial neuritis (n = 17), chronic inflammatory demyelinating polyneuropathy (n = 15), Parkinson’s disease (n = 43), tuberculous meningitis (n = 26)). The HBV markers were regularly tested, including HBsAg, HBsAb, HBeAg, HBeAb and HBcAb among NMOSD, MS and other neurological diseases (P> 0.05). HBeAb was statistically significant differences among these three groups (P <0.05).

Conclusions: The exact role of Hepatitis B virus in the pathogenesis of NMOSD needs to be studied further. And we suggest that HBV might not affect treatment delivery or outcomes in NMOSD, the diagnosis and treatment of the NMOSD has little effect on the immune protection. However, only a limited number of patients, the results of this study need to be further explored.

P-93
Intestinal Microbiota Distinguish Neuromyelitis Optica Patients from Healthy Individuals in a Chinese Pilot Study
Gong JL1,2#, Qiu W3#, Zen Q3#, Sun XB3, Li HJ3, Liu XY3, Yang Y3, Wu AM3, Bao J3, Wang YG3, Shu YQ1, Zhong SG1, Peng LS1, Lu YJ1,2, Lu ZQ2
1School of life sciences, Sun Yat-sen university, Guangzhou, 510275,China ; 2Department of Neurology, Third Affiliated Hospital, Sun Yat-sen University, Guangzhou Guangdong, China ; 3School of life sciences, Sun Yat-sen university, Changzhou, 510275,China ; 4Department of Clinical Immunology, Third Affiliated Hospital, Sun Yat-sen University, Guangzhou Guangdong, China

Poster Session 9
NMOSD Treatment

P-94
Establishment and Management of Neuromyelitis Optica (NMO) and NMO Spectrum Disorders (NMOSD) Nationwide Multicenter Registry in Korea
Hye Lim Lee1, Ju-Hong Min2*, Jin Myoung Seok1, Eun Bin Cho2, Ho Jin Kim2, Ha Young Shin2, Byung Jo Kim2, Seol-Hee Baek3, Hung Youl Seok4, Sa-Yoon Kang5, Oh-Hyun Kwon5, Kwang-Kuk Kim6, Young-Min Lim7, Sang-Soo Lee8, Jeeyoung Oh9, So-Young Huh10, Jong Kuk Kim11, Byeol-A Yoon11, Eun-Hee Sohn12, Joong-Yang Cho13, Hye Jin Cho14, Jong Seok Bae15, Byoung Joon Kim16,17
1Department of Neurology, Korean University Guro Hospital, Korea University College of Medicine, Seoul, Korea ; 2Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea ; 3Neuroscience Center, Samsung Medical Center, Seoul, Korea ; 4Department of Neurology, Soonchunhyang University Cheonan Hospital, Cheonan, Korea ; 5Department of Neurology, Changwon Gyeongsang Institute of Health Science, Gyeongsang National University School of Medicine, Changwon, Korea ; 6Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Korea ; 7Department of Neurology, Severance hospital, Yonsei University College of Medicine, Seoul, Korea ; 8Department of Neurology, Korea University Anam Hospital, College of Medicine, Seoul, Korea ; 9Department of Neurology, Korea University Anam Hospital, College of Medicine, Seoul, Korea ; 10Department of Neurology, Konkuk University College of Medicine, Seoul, Korea ; 11Department of Neurology, Kosin University College of Medicine, Busan, Korea ; 12Department of Neurology, Dong-A University Hospital, Busan, Korea ; 13Department of Neurology, Chungnam National University College of Medicine, Daejeon, Korea ; 14Department of Neurology, Inje University College of Medicine, Ilsan, Korea ; 15Department of Neurology, The Catholic University of Korea, College of Medicine, Bucheon St. Mary’s Hospital, Bucheon, Korea ; 16Department of Neurology, Department of Neurology, Gangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea

Background: Neuromyelitis optica (NMO) and NMO spectrum disorders (NMOSD) are uncommon neuroinflammatory syndrome. Rare diseases are necessary to established multicenter clinical consortium to facilitate clinical research.

Objective: We have plan to develop a national multicenter NMOSD clinical network (NMO NETWORK) and report clinical information of enrolled patients with NMO/NMOSD in Korea. We were supported by Korea centers for disease control and prevention.

Method: We constructed multi-center clinical network system, participating referral hospitals in Korea. We included the demyelinating disease and collected the clinical information, using the web-based clinical research and trial program. We gathered sera from participants and identified the presence of AQP4-ab of enrolled patients by cell based assay.

Result: A total of 22 hospitals attended in the NMO NETWORK in Korea and the 368 patients enrolled from Oct, 2014 to Nov, 2016. 74.7% (n=275) of enrolled patients were female and 45% (n=166)
patients had AQP4-ab. The mean age of enrollment was 44.7 years. The patients with optic neuropathy were 119, and the 259 patients had transverse myelitis, 82 patients had both of them. The median number of attacks was 3 (IQR, 1-5), 29.8% (n=110) patients showed the first event. The mean duration from disease onset to enrollment was 6.6 years and the median of score of EDSS was 3 (IQR, 2-4).

Conclusions: A nationwide clinical network to study NMO/NMOSD could facilitate the supply of accurate clinical information in epidemiology of NMO/NMOSD in Korea. We successfully established nationwide NMO/SD network, this consortium was expected a foundation for further studies.

P-95
Usefulness of PLEX Treatment Using Peripheral Venous Access in Patients with NMO
Sakamaki Masanori
Nippon Medical School Musashi Kosugi Hospital

Background: Plasma exchange (PLEX) has gained acceptance as an effective treatment for patients with neuromyelitis optica spectrum disorder (NMO). On the other hand, PLEX has many risks such as venous thrombosis or infection due to the central venous catheter. There are few studies that PLEX using peripheral venous access is more useful than PLEX using central venous access.

Objectives: to assess the usefulness of PLEX treatment using peripheral venous access in patients with NMO.

Methods: We collected data prospectively in patients with NMO or myasthenia gravis (MG) of treatment with PLEX at the Nippon Medical School Musashi Kosugi Hospital from May 2016 to September 2017. Peripheral venous access was performed using an 18-gauge dialysis cannula (HappyCath NEO; Togo Medikit, Tokyo, Japan) for draw and return access. Central venous access was performed using a 13-gauge dual-lumen catheter (GamCath Dolphin; Gambro, Hechingen, Germany). Central venous catheters were placed for patients who did not have adequate peripheral venous access.

Result: Three of 9 patients completed PLEX treatments using peripheral venous access. Although no patient had adverse events related to PLEX treatments using peripheral venous access, one patient had severe adverse events related to PLEX treatments using central venous access.

Discussion: No patient had adverse events related to PLEX treatments using peripheral venous access. But only thirty-three percent of patients completed PLEX treatments using peripheral venous access. PLEX by peripheral venous access requires good venous access that tolerates 18-gauge catheters.

Conclusions: PLEX via peripheral venous access is safe, cost benefit and effective in patients with NMO.

P-96
Evaluation of Classical Immunosuppressant Drugs-Cyclophosphamide, Methotrexate Among Patients with Neuromyelitis Optica Spectrum Disorder and Multiple Sclerosis
Yuge Wang*, Yanqiang Wang*, Wei Qiu*, Zhengqi Lu***

1Department of Neurology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) are the common inflammatory demyelinating diseases of the CNS. The cross-talk between nervous system and immune system is being studied thoroughly and is considered an important contributor of pathogenesis of these disorders resulting in immune related therapeutic strategies. However, recent advances in the pathogenesis of MS and NMOSD, and the emergence of new drugs. The classic immunosuppressant - MTX, CYC, has regarded as a second-line therapy. the current treatment guidelines for this, too much emphasis on the importance of follow the guidelines, clinical classification, the accumulation of side effects, and ignore individual differences and comprehensive assessment, clinical classification of, acute management and maintenance therapy for prevention of future relapse, race/ethnicity, geographical, risk/benefit difference. Mounting evidence indicates that non-organ-specific and organ-specific auto-mmune diseases are being recognized more frequently in NMOSD and MS, especially, have accompanied pre-existing NMOSD and MS. MTX has good tolerance and compliance, reduce recurrence rate, delay disease progression and improve quality of life, it may be used as auxiliary or drug combinations for those who cannot tolerate first-line drugs, frequent relapse, economic conditions. CTX is used as the main application of high-dose, reduce the recurrence and disability progress, and may be used as alternative or adjuvant therapy to select drugs for those who cannot tolerate interferon, biological agents, new immunosuppressive agents, invalid progressive and refractory disease. Low-dose pulsating applications may be beneficial for controlling the recurrence and progression of the lesion.

P-97
Bortezomib as Add-on Treatment for Highly Relapsing NMOSD Patients
C. Zhang1, D.C. Tian1, C.S. Yang1, B. Han1, J. Wang1, L. Yang1, F.-D. Shi1,2
1Departments of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin, China.
2Division of Neurology, Barrow Neurological Institute, St. Joseph’s Hospital and Medical Center, Phoenix, Arizona, USA.

Background: Neuromyelitis optica spectrum disorder (NMOSD) is a relatively rare autoimmune astrocytopathy resulting from aquaporin 4 antibody (AQP4-ab) mediated pathology. Peripheral plasma cells, which are closely related to AQP4-ab production, represent a novel therapeutic target.

Objective: To evaluate the safety and efficacy of bortezomib, a selective inhibitor of the 26S proteasome subunit targeting plasma cells, in patients with NMOSD.

Methods: Five Chinese NMOSD patients with AQP4-ab-seropositive who did not respond to previous medications were recruited. They received four cycles of 1 mg/m² body surface area bortezomib (Velcade®) subcutaneously administered as add-on treatment to their concurrent therapy. We evaluated the annualized relapse rate (ARR), the Expanded Disability Status Scale (EDSS). AQP4-ab titer was monitored by GFP-AQP4 fluorescence immunoprecipitation assays. This longitudinal study with a 12-month follow-up was registered with ClinicalTrials.gov, number NCT02893111.

PACTRIMS 2017 Programme & Abstracts | 57
Results: At the one-year follow up after initial administration of bortezomib, the mean ARR of the five patients decreased significantly from 3.0 (interquartile range, 3.0-3.5) to 0.0 (interquartile range, 0.0-0.5) (P = 0.039). The EDSS decreased from 5.50 (interquartile range, 3.75-6.25) to 3.50 (interquartile range, 0.75-4.25) (P = 0.043). The decline of serum AQP4-ab titer was statistically significant at the end of that one-year period (P = 0.043). Accordingly, bortezomib presumably caused gradual reduction in the number of peripheral blood CD19+ B cells and CD138+ plasma cells at the study’s one-year termination. Only a few mild and well-tolerated adverse effects were documented.

Conclusions: Bortezomib could serve as a promising escalation therapy for highly active NMOSD.

Poster Session 10
Myelitis, Optic Neuritis and MS MImics

P-98
CSF and MRI Findings of Acute Transverse Myelitis with Neuropathic Pain
Jun Hong Lee
Neurology, National Health Insurance Service Ilsan Hospital, Goyang-shi, South Korea

Purpose: We investigated CSF findings and follow up imaging features of acute transverse myelitis (ATM) with neuropathic pain patients in order to look at prognosis of ATM with neuropathic pain.

Method:
From January 2015 to December 2016, 21 patients were registered. The CSF findings on admission and follow up MRI imaging study were reviewed and analyzed.

Results:
Among 21 neuropathic pain patients of ATM, thirteen patients were male, the age is from 21 years old to 63 years old and average age was 48 years old. The location of lesions on MRI was cervical spine in 11 patients, thoracic spine in 9 patients and lumbar spine in 1 patient. The follow up period of MRI study was from 3 months to 48 month and average was 10 months. The WBC cell count of CSF study on admission was classified as follow: group A (> 5), B (1> and < 4), C (0). Among 5 patients of group A, the MRI lesions of 1 patients were disappeared, 1 patients were much improved, 2 patients were some improved, and 1 patients whose WBC count was 35, was aggravated. Among each 8 patients of group B and C, almost all patients were much or some improved.

Conclusion:
We reviewed clinical features of ATM with neuropathic pain. About the prognosis of ATM, about 57% of patients showed very good prognosis and 33% moderately good prognosis, but about 10% of patients showed poor prognosis. The WBC count of CSF study may give some information about prognosis.

P-99
Anti-neurofascin Antibodies in Patients with Acute Transverse Myelitis Combined with Peripheral Demyelination
Zhang Xu¹, PhD, Yang CS¹, MD, Zhang LJ², MD, LLM¹, MD, Yang L* MD, PhD

Objective: To detect anti-neurofascin antibodies and analyze clinical features of patients with acute transverse myelitis (ATM) combined with peripheral demyelination.

Methods: Fluorescence immunoprecipitation assay (FIPA) was used to detect the anti-neurofascin 155 and anti-neurofascin 186 antibodies in sera from 115 patients with ATM, including 35 patients with single longitudinal extensive transverse myelitis (LETM), 16 patients with short extensive transverse myelitis (SETM), 64 with neuromyelitis optica spectrum disorder (NMOSD) involved with LETM, and 26 healthy controls. All the positive results were further tested by Western Blot. The clinical features of the patients with anti-neurofascin antibodies and performed the nerve conduction study (NCS) during the acute phase were reported.

Results:
Six patients were positive for anti-neurofascin antibodies detected by FIPA. Two patients were positive for anti-neurofascin 155 antibodies and 2 patients were positive for anti-neurofascin 186 antibodies, other two patients with both anti neurofascin 155 and 186 antibodies. Western Blot further identified four double positive samples (two were consistent with FIPA). Through retrospective study, four of these six patients performed NCS test and proved peripheral demyelination, which mainly showed slow motor conduction velocity.

Conclusion:
The presence of anti-neurofascin antibodies may be a potential biomarker in some of the patients with ATM combined with peripheral demyelination and play an important role in the pathological process.

P-100
Diurnal Pattern of Initial Attack in Patients with Early Onset of Optic Neuritis
MJ Eslamí, S Ghorbani, M Etemadifar
Isfahan University of Medical Sciences, Hezar Jahab Avenue, Isfahan, Iran

Background: Optic neuritis is the first clinical manifestation of multiple sclerosis in 20% of patients. Though several studies implicate diurnal and nocturnal patterning in symptom intensity of many medical conditions, few studies explain a circadian rhythm in the relapses of multiple sclerosis and optic neuritis.

Objective: To evaluate the presence of diurnal patterning for initial attack in optic neuritis.

Method:
In this prospective cross sectional study that has been carried out in Isfahan, Iran, from March 2015 to March 2016, we asked about the time of first ON attack in 50 patients (43 female and 7 male) who have experienced their initial attack in optic neuritis.

Result:
41 patients (82%) reported their attacks between 6am to 12pm, 18 patients at 7am (36%), 2 patients (4%) between 6pm to 12am, 3 patients (6%) between 6pm to 12am and one (2%) between 12am to 6am. Visual symptoms in 29 patients (58%) involved left eye and 17 patients (34%) in right eye.
Conclusion: The data result implicate that most of attacks took place in the morning and wake up time and significantly suggests a diurnal patterning for initial attack times. Since the disease pathogenesis undergo an autoimmune mechanism and the immune system is under effect of some hormones and molecules that follow a circadian rhythm, it seems that some of these biomarkers that have a proved role in immune mechanisms are responsible to the diurnal patterning of disease initial symptoms.

P-101
Severe Optic Neuritis: 72 Cases from Turkey
Gülşen Akman Demir1, Gülşen Akdal2, Hülya Ertasoğlu Toydemir3, Burcu Altunrende1, İlksen Isikay1, Aylin Yaman1, Figen Gökçay6, Sebnem Bicakçı1, Meltem Soylev Bajan1, Nese Celebiosoy2, and Turkish Neurology Society, Neuro-ophthalmology/Neuro-otology Study Group
1Istanbul Bilim University Hospital Neurology Department, Istanbul, Turkey
2Dokuz Eylül University Hospital Neurology Department, Izmir, Turkey
3Bakırköy Dr. Sadi Konuk Teaching Hospital Department of Neurology, Istanbul Turkey
4Hacettepe University Hospital Neurology Department, Ankara, Turkey
5Dokuz Eylül University Hospital Ophthalmology Department, Izmir, Turkey
6Ege University Hospital Neurology Department, Izmir, Turkey
Purpose: Severe optic neuritis (ON), also considered as atypical ON, is characterized by aggressive course, lack of response to steroids, and recurrence during steroid tapering. Our aim was to evaluate the clinical features, laboratory findings, treatment modalities and outcomes of the patients with severe ON from Turkey, seen over the last 10 years.
Methods: Clinical files of 6 university hospitals were evaluated retrospectively to define cases with severe ON. Patients who show clinical involvement of other sites of the nervous system were excluded.
Results: There were 72 patients, aged 16 to 65 years (mean 38 ± 12): 52 (72%) were female, 18 had bilateral involvement, 37 (51%) had only one attack, 35 (49%) had 2 or more attacks. Anti-aquaporin-4 antibody was positive in only 4/72 (5.6%). Twelve patients were tested for MOG antibodies, and one was positive. All the patients received IV methylprednisolone (IVMP) for the acute attack, 9 had monthly IVMP; 8 had IVIg, and 20 patients who did not respond to corticosteroids had plasma exchange. Of the 35 with recurrence had 29 azathioprine, 2 had rituximab, 2 had methotrexate, and 2 had mycophenolate mofetil. Final outcome: 23/72 patients had no recovery of vision, 17 had full recovery, the other 22 had partial recovery.
Conclusion: It is important to recognize and treat severe ON early since prognosis can be poor, and treatment could lead to significant improvement. Plasma exchange should be considered in patients unresponsive to corticosteroids. IVIg could be an option in those patients who cannot receive plasma exchange.

P-102
Intravenous Immunoglobulin Treatment for Recurrent Optic Neuritis
B. Altunrende1, G. Akdal2, M. Soylev Bajan1, A. Yaman2, M. Kocaslan1, G. Akman-Demir1
1Istanbul Bilim University, Neurology, Istanbul, Turkey
2Dokuz Eylül University, Neurology, Izmir, Turkey
Purpose: Intravenous immunoglobulin (IVIg) treatment is used for many autoimmune inflammatory condition of unknown cause. Intravenous immunoglobulin (IVIg) treatment is used for many autoimmune disorders; however we do not have any information about its effect in rON, other than case reports.
Objective: We aimed to evaluate our patients with rON who were treated with IVIg.
Results: There were 72 patients, aged 16 to 65 years (mean 38 ± 12): 52 (72%) were female, 18 had bilateral involvement, 37 (51%) had only one attack, 35 (49%) had 2 or more attacks. Anti-aquaporin-4 antibody was positive in only 4/72 (5.6%). Twelve patients were tested for MOG antibodies, and one was positive. Under current treatments the patients had continued to have attacks, therefore monthly IVIg was given in addition to the existing immunosuppressant drug. The follow up duration was between 6 to 31 months. Three patients each suffered one relapse under IVIg treatment. Mean number of relapses in the year prior to treatment was 1.4±0.72, whereas it was 0.3±0.5 during the year after IVIg therapy. During follow-up with IVIg administration only one patient had fever and no other adverse events were reported.
Conclusion: Monthly IVIg is well-tolerated and safe and it seems to be effective in rON as an add on treatment. However, since our study is a retrospective case series, future randomized controlled trials with IVIG are needed.

P-103
Characteristics of Optic Neuropathy in Behçet’s Disease
Akman-Demir G1, Akdal G2, Ertasoglu Toydemir H1, Sağatç O7, Uygunoglu Uı, Altunrende Bı, Saip Sı, Yaman Aı, Keskinoglu Pı, Guven Yilmaz Sı, Tugal Tutkun İı, Bajin MSı, Siva Aı
1Bilim University, Faculty of Medicine, Department of Neurology, Istanbul/Turkey
2Dokuz Eylül University, Faculty of Medicine, Department of Neurology, İzmir/Turkey
3Bakırköy Dr. Sadi Konuk Training and Research Hospital, Department of Neurology, Istanbul/Turkey
4Dokuz Eylül University, Faculty of Medicine, Department of Ophthalmology, İzmir/Turkey
5Istanbul University, Cerrahpaşa Faculty of Medicine, Department of Neurology, Istanbul/Turkey
6Istanbul University, Faculty of Medicine, Department of Biostatistics, İzmir/Turkey
Purpose: Optic neuropathy (ON) has rarely been reported in Behçet’s disease (BD). Multicenter study presented here was aimed to show clinical profile, features and neuro-imaging findings of BD patients with ON.
Intracranial Hemorrhagic Lesion and Neurosarcoïdosis

Methods: Data from five different university hospitals were reviewed retrospectively, and patients with BD and ON were divided into 2 groups and their finding compared; (1) those already diagnosed with BD when ON developed (BD>ON group) and (2) those diagnosed with BD in further evaluation ON (ON>BD group).

Results: There were 25 BD patients with ON (13 males). Among these, 13 had ON>BD (6 males), and 12 had BD>ON (7 males). 17 patients had unilateral ON, and 7 patients had recurrent ON. BD>ON patients were significantly older. Disc edema was seen more in ON>BD patients (10 vs 3). 14 patients also had uveitis. There was other neurological involvement in 8 patients; in BD>ON group all 4 had MS-like disease. However, in ON>BD group, 3 had typical parenchymal involvement, and one had MS-like disease. All patients except one received immunosuppressive medications or corticosteroids or both. Prognosis was favourable in most: vision improved in 20 patients, more often in those receiving combined therapies.

Conclusion: BD may be diagnosed earlier if it is considered and investigated during the assessment of ON. Prognosis of ON related with BD might not be bad. Immunosuppressants should be given along with corticosteroids. MS-like presentations should also be kept in mind in patients with BD and ON.

P-104

Intracranial Hemorrhagic Lesion and Neurosarcoïdosis

Nishigori R, Warabi Y, Isozaki E
Department of Neurology, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan

Background: Neurosarcoïdosis and neuromyelitis optica spectrum disorders (NMOSD) are sometimes difficult to distinguish based on the magnetic resonance imaging (MRI) findings, especially in cases of longitudinally extensive myelitis.

Method: We retrospectively examined a series of neurosarcoïdosis or NMOSD patients admitted to our hospital between 2013 and 2017. Neurosarcoïdosis had been diagnosed in these patients based on the Japanese sarcoïdosis clinical or pathological criteria and the presence of spinal or cranial lesions. NMOSD was diagnosed based on the criteria for NMOSD with AQP4-IgG. The clinical characteri stics and head MRI findings of each group were analyzed and compared.

Result: Nine patients with neurosarcoïdosis and 26 patients with NMOSD underwent T2*-weighted imaging (T2*WI) of the head, which revealed an asymptomatic hemorrhagic lesion in six patients with neurosarcoïdosis. Five of these patients had a subcortical or brainstem microhemorrhage, and one patient had superficial siderosis. One NMOSD patient had an asymptomatic microhemorrhage in the left cerebellar hemisphere on T2*WI. The number of neurosarcoïdosis lesions on T2*WI was greater than that of NMOSD lesions (p<0.01; Fisher’s exact test).

Discussion: A dysfunction of the blood-brain-barrier (BBB) is thought to be involved in the development of central nervous lesions in sarcoïdosis. Our findings may therefore be related to the etiology of neurosarcoïdosis. Our study suggests that T2*WI of the head may be useful for distinguishing neurosarcoïdosis from NMOSD and even in myelitis cases, may reveal hemorrhagic brain lesions.

Conclusions: BBB leakage is thought to be involved in the development of central nervous lesions in sarcoïdosis.

P-105

Clinical Characteristics of Parenchymal Neuro-Behcet’s Disease in South Korea

SW Kim, YC Choi, SM Kim and HY Shin
Department of Neurology, Yonsei University College of Medicine, Seoul, Korea

Background: Neuro-Behcet’s disease (NBD) is a serious form of Behcet’s disease (BD). NBD can be categorized into parenchymal and non-parenchymal NBD, and parenchymal NBD can be further divided into acute parenchymal NBD (A-P-NBD) and chronic progressive parenchymal NBD (CP-P-NBD).

Objective: We analyzed the clinical and imaging characteristics of P-NBD patients and further compared the characteristics of A-P-NBD and CP-P-NBD.

Methods: We retrospectively reviewed the medical records of the patients diagnosed with BD in Severance Hospital between 1995 and 2017. The diagnosis of BD was based on international and Japanese BD criteria.

Results: 71 P-NBD patients (40 male and 31 females) were included. Symptoms of the patients included motor weakness (47.9%), dysarthria (43.7%), headache (40.8%), gait disturbance (26.8%), fever (25.4%) and sensory symptoms (22.5%). Site of MRI lesions included pons (53.5%), midbrain (50.7%), deep white matter (43.7%), internal capsule (33.8%) and basal ganglia (28.2%). Patients were treated with steroids in 51 (71.8%), azathioprine in 11 (15.5%) and cyclosporine in 6 (8.5%) patients. P-NBD patients were classified into 41 A-P-NBD and 30 CP-P-NBD patients. Brainstem and cerebral signs were more frequent in A-P-NBD patients (86.7% and 43.4%) than CP-P-NBD patients (46.3% and 14.6%, p<0.001 and p=0.007, respectively). The location of MRI lesion was not different between groups.

Conclusion: The present study demonstrates the clinical and MRI characteristics of P-NBD patients. This study is based on the largest number of MRI-confirmed P-NBD patients in South Korea and the findings well correspond to the previous reports.

P-106

Heterogeneity of Combined Central and Peripheral Demyelination: A Systematic Review

Jong Seok Bae, Jin Hyuck Yoo,
Department of Neurology, Kangdong Sacred Heart Hospital, Seoul, Republic of Korea

Background: Syndrome of combined central and peripheral demyelination (CCPD) is a syndrome, which is characterized by either simultaneous or sequential involvement of demyelinating lesions in both central and peripheral nervous systems.

Objective: To conceptualize and classify a CCPD or CCPD spectrum diseases

Methods: From 1977 to August 2017, we identified relevant studies regarding a CCPD or CCPD spectrum diseases through electronic searches of MEDLINE, PubMed, and EMBASE

Results: Until recently, two large scaled studies were identified. One is a nation-wide survey from Japan, and the other is a retrospective analysis from 2 European centers. Otherwise, most of literature are case reports or small sized case series. Some authors have defined CCPD as multiple sclerosis (MS) with peripheral demyelinating neuropathy, however others had a view of chronic inflammatory demyelinating polynuropathy (CIDP)
with central demyelination. However, considerable portion of CCPD could not be diagnosed with either MS or CIDP. Interestingly, several studies began to report that neurofascin (NF)-155 positive CIDP can manifest with various atypical features of CIDP, such as central demyelination. However, one case series identified that none of patients with CCPD had anti-NF155 antibodies.

Conclusions: CCPD is rather a broad concept which includes various conditions such as CIDP with central demyelination, MS with demyelinating polyneuropathy, or the other entity, not included by none of above. Therefore, the current diagnostic criteria for MS and CIDP are insufficient for diagnosis and recognition of CCPD. In addition, NF-155 antibody appears not to have a potential role in the pathophysiology of CCPD.

Poster Session 11
EAE

P-107
Oligodendroglia-Specific Connexin 47 Deletion Induced Relapse-Remitting EAE Model Mice
Ryo Yamasaki, Ekinan You, Hiro Yamaguchi, Jun-ichi Kira
Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University

Refer to O-17 in the Oral Presentation

P-108
The Antioxidant Properties and Anti-Inflammatory Effect of Sulforaphane in Mice with Experimental Autoimmune Encephalomyelitis
Suk-Won Ahn and Myung-Jin Kim
Department of Neurology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, South Korea

Background & Objective: Multiple sclerosis (MS) is a T-lymphocyte-mediated autoimmune disease which has occurrence of focal inflammatory demyelination lesion in central nervous system. Sulforaphane is an anti-oxidant phytochemical derived from broccoli and has neuroprotective effects in other diseases. We investigated the neuroprotective effect of sulforaphane in mouse model with experimental autoimmune encephalomyelitis (EAE).

Methods: Total 20 mice of C57BL/6 mice were participated in this study. Before EAE induction by autoimmunization, the sulforaphane (50mg/kg) was administrated daily in a sulforaphane-treated group (n=10) for 2 weeks, and the other C57BL/6 mice (n=10) were orally administrated with PBS as a control group. Two weeks later, the active induction of EAE was performed according to the manufacturer’s instructions. After auto-immunization, the sulforaphane or PBS was continuously administered in each group, and EAE scores were calculated according to a 0-5 scale.

Results: At 14 days after induction of EAE, all mice were sacrificed and harvested of spinal cords samples, and we investigated the western blots and immune-staining to compare the level of inflammation, demyelination and oxidative reaction in both sulforaphane-treated EAE group and control EAE group. The sulforaphane treated group exhibited a decline of CD68, GFAP and iNOS expression level. And the immune-staining and immunofluorescence data showed that infiltrating inflammatory cells and demyelinating lesions were decreased on the sulforaphane-treated group compared with control group.

Conclusions: These results indicate that oral administration of sulforaphane suppressed immune response and demyelinating process by anti-inflammatory and anti-oxidative effect.

P-109
Neutralization of the IL-19 Axis Diminishes Monocytes Invasion and Protects from Experimental Autoimmune Encephalomyelitis
Xiaoran Zhong, Zhiheng Mao, Junjie Yin, Wei Qiu, Zhengqi Lu, Xueqiang Hu
Department of Neurology, the Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou

Background: Initiation of EAE involves the activation of myelin-specific Th1 or Th17 cells, which in turn trigger the recruitment of blood-borne myelo-monocytic cells, including monocytes/macrophages. Th9 cells’ physiological roles have gradually expanded in EAE recently. We suppose neutralization of the IL-19 axis diminishes Ly6Chi inflammatory monocytes invasion and protects from EAE.

Objective: To observe the IL-9-monocytes axis in EAE.

Methods: Female C57BL/6 mice were randomly divided into 3 groups, MOG-induced EAE, EAE treated with anti-IL-9 antibody and EAE treated with IgG isotype controls.

Results: Anti-IL-9 Abs treatment delayed the onset of clinical disease, ameliorated the severity of EAE, and gained significantly more weight over 14 to 25, began to gain weight earlier than the other groups. Ly6Chi inflammatory monocytes expressed IL-9R and mainly by IL-2Rγ, where later neutrophils expressed only limited. After anti-IL-9 Abs treatment, significantly reduced the number of Ly6Chi inflammatory monocytes in vivo and vitro. The proportion of Ly6Clo macrophages increased in D15. In contrast, the amount of expression level of Dectin-1 was increased in D15 in anti-IL-9 Abs group, compared with IgG groups, p<0.05. The mRNA expression of CCL20 was obviously increased in mice treated with anti-IL-9 Abs compared with the isotype control group. However, CCL20 expressed very limited in monocytes. Anti-IL-9 antibody treatment reduced the STAT3 and increased the STAT5 mRNA, compared with IgG group in EAE.

Conclusions: Taken together, our study revealed that neutralization of the IL-19 axis diminishes monocytes invasion and protects from EAE.

P-110
Autoreactive CD8+ Central Memory T Cells Failed to Induce Experimental Autoimmune Encephalomyelitis
Hong Jiang, Ya-Juan Xiang, Pei-Ju Liu, Ting-Ting Yang, Shan-Shan Zhong, Yang-Yang Wang, He Yang, Bao-Lei Xu, Xu-Guang Gao, Liu Guang-Zhi

Department of Neurology, Peking University People’s Hospital 100044; Department of Neurology, Beijing Anzhen Hospital, Capital Medical University 100029 Beijing, China; Department of Neurology, Tsinghua Changgung Hospital, 100118, Beijing, China

Objective: The aim of this study is to investigate the pathogenic role of autoreactive CD8+ central memory T cells (TCM) in experimental autoimmune encephalomyelitis (EAE).

Methods: an EAE model was established after immunizing female C57BL/6 mice with myelin oligodendrocyte glycoprotein (MOG)35-55.
Poster Session 12

Case Report-1 MS

P-111
Fabry Disease or Multiple Sclerosis - Two Entities and Their Diagnostical and Treatment Challenges

P. Stourac1, J. Bednarova2
1Department of Neurology, University Hospital and Masaryk University Brno, Czech Republic
2Department of Clinical Microbiology, University Hospital Brno, Czech Republic

Objective: Fabry disease is an X- linked recessive lysosomal storage disorder resulting from the deficiency of alpha-galactosidase affecting multiple organ system including nervous system. Fabry disease can be misdiagnosed as multiple sclerosis due to its clinical symptoms and MRI white matter lesions. We present a case of 34-year female patient diagnosed as multiple sclerosis, then subsequently reconsidered as Fabry disease but the very rare concommitant occurence of these two entities cannot be excluded.

Methods: We present a case of a patient with the diagnosis of multiple sclerosis based on The International diagnostic criteria and subsequently confirmed as a carrier of a Fabry disease causing mutation in the GLA gene (Centogene AG, Germany).

Results: The patient suffered from diplopia, hypaesthesia, mild hemiparesis, bilateral ataxia, unstable walking, imperative micturition, fatigue and short - term memory. MRI revealed white matter lesions in frontal and temporal regions. In CSF analysis one oligoclonal IgG band was detected. Intravenously administered corticosteroids improved multiple sclerosis due to its clinical symptoms and MRI white matter lesions. We present a case of 34-year female patient diagnosed as multiple sclerosis, then subsequently reconsidered as Fabry disease but the very rare concommitant occurence of these two entities cannot be excluded.

Conclusion: The current clinical, radiological and laboratory results profile cannot definitely distinguish between these two diseases. Both diseases can be effectively treated and it poses a great diagnostic challenge.

P-112
A Patient Diagnosed as Multiple Sclerosis with Severe Brain Atrophy

Y Kim, M.D.1, HN Jung, M.D.2, HY Shin, M.D.2, SM Kim, M.D.2
1Department of Neurology, College of Medicine, Korea University Ansan Hospital
2Department of Neurology, Yonsei University College of Medicine, Seoul, Korea

Background: Multiple sclerosis(MS) is both an inflammatory and a neurodegenerative condition. We present here a patient diagnosed as relapsing-remittting multiple sclerosis with progressive brain atrophy.

Case: A 21-year-old female visited neurology department with tingling sensation on her left face and arm. Her first symptom was left hemibody tingling sense at the age of 19, which lasted for one week. On admission, neurologic exam was normal. Brain MRI showed multiple linear or ovoid T2 hyperintensities in the periventricular, juxtacortical areas and brainstem without enhancement. Cerebrospinal fluid was aseptic without any malignant cells, but the oligoclonal bands were positive. Her retinal nerve fiber layer showed thinning. Diagnosed as MS, the patient started interferon beta-1a.

Four months later, the vibration senses of bilateral lower extremities were mildly decreased. Six months later, the patient said she had trouble memorizing numbers. Follow-up MRI showed no new lesion.

After 1 year, with no symptom change, her brain MRI showed more widespread MS lesions, increased in numbers and sizes. Brain atrophy was prominent. Spine MRI showed multiple T2 high lesions. After 2 years, the visual acuity of the patient was slightly decreased. Brain MRI follow up showed more advanced atrophy. Her neuropsychological test revealed bilateral frontotemporal dysfunction. Other neurological abnormalities were mild dysmetria and mildly reduced visual acuity.

Conclusion: Bain atrophy is present in various MS subtypes. However, the attack rate or gadolinium enhancement might not be consistently associated with increased atrophy. The clinician should always consider the possibility of silent progression of brain atrophy.

P-113
Diffuse Lesion in Limbic System with Short-term Memory Loss in a Patient with Multiple Sclerosis

Department of Neurology, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan

Background: An overlap has been recognized between limbic encephalitis and demyelinating diseases. We report the case of a multiple sclerosis (MS) patient who presented diffuse lesion in limbic system with short-term memory loss.

Results: The mice were all sacrificed after their clinical symptoms peaked. Thereafter, mononuclear cells were obtained from their spleen and lymph nodes by density gradient centrifugation, followed by an isolation of CD8+ TCM (CD8+CCR7+CD44high) via a flow sorter. These CD8+ TCM were then injected intravenously into Rag-1-/- mice, whereas control mice were simultaneously injected with CD8+ terminal effector memory T cells (TEMRA) or PBS, respectively. In parallel with this, EAE-derived CD8+ T cells were also adoptively transferred into recipient Rag-1-/- mice. Thus, clinical assessment was performed for 40 days after the adoptive transfer, and pathological changes were detected in their brain and spinal cord by hematoxylin-eosin (HE) and Luxol fast blue (LFB) staining.

Results: After adoptive transfer of CD8+ T cells, all the Rag-1-/- mice exhibited hindquarter paralysis within 27~29 days as well as inflammatory infiltration and demyelination in brain or spinal cord. In contrast, neither of CD8+ TCM or CD8+ TEMRA produced clinical symptoms. The mice were all sacrificed after their clinical symptoms peaked. Thereafter, mononuclear cells were obtained from their spleen and lymph nodes by density gradient centrifugation, followed by an isolation of CD8+ TCM (CD8+CCR7+CD44high) via a flow sorter. These CD8+ TCM were then injected intravenously into Rag-1-/- mice, whereas control mice were simultaneously injected with CD8+ terminal effector memory T cells (TEMRA) or PBS, respectively. In parallel with this, EAE-derived CD8+ T cells were also adoptively transferred into recipient Rag-1-/- mice. Thus, clinical assessment was performed for 40 days after the adoptive transfer, and pathological changes were detected in their brain and spinal cord by hematoxylin-eosin (HE) and Luxol fast blue (LFB) staining.

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Case: Our patient developed numbness in the left upper extremity, which disappeared without treatment at 17 years of age. At 19 years of age, he subacutely developed loss of short-term memory, followed by paralysis and sensory disturbance in the left upper and lower extremities. MR brain FLAIR/T2W imaging demonstrated diffuse high-intensity lesions in the medial parts of both temporal lobes with spotty multiple lesions in the periventricular and subcortical white matter. Twenty days later, a new lesion appeared around the right putamen, while the temporal lesions disappeared. With gadolinium enhancement, a symptomatic cerebral lesion was found at C3, involving one vertebral segment. Cerebrospinal fluid (CSF) analysis revealed no pleocytosis or elevated protein level but showed oligoclonal IgG bands. There were no antibodies against aquaporin-4, myelin oligodendrocyte glycoprotein in the serum and anti-N-methyl-D-aspartate receptor (NMDAR) in the CSF samples. We diagnosed him as having MS, although diffuse lesion in limbic system with short-term memory loss was atypical for MS. Corticosteroid treatment had started. Brain magnetic resonance imagining (MRI) revealed left supratentorial hyperintense lesions in bilateral white matter in FLAIR sections. There was a juxtacortical lesion in left frontal region. These radiographic features are compatible with multiple sclerosis (MS) affecting cortical and subcortical structures. MS should be kept in mind in the etiology of epileptic seizures.

Conclusions: Demyelinating lesions can cause seizures by affecting cortical and subcortical structures. MS should be kept in mind in the etiology of epileptic seizures.

P-114
Epileptic Seizure as First Clinic Presentation of Multiple Sclerosis
Şeref Demirkaya, Ahmet Çetiz, Zafer Özkam
Gülhane Training and Research Hospital, Ankara, Turkey

Background: Epileptic seizures are rare in multiple sclerosis (MS) patients. Seizures are usually seen in the late period of the disease. Epileptic seizures seen as the first clinical sign in MS are even rarer.

Objective: In this case report we discussed a MS patient whose first clinical presentation is epileptic seizure.

Methods: Case report

Results: A 23-year-old female was admitted to our hospital because of seizure. Eight years ago, there was a similar complaint. Electroencephalography (EEG) revealed bilateral synchronous symmetrical generalized spike wave paroxysms. The patient’s seizure was generalized tonic clonic type and valproic acid treatment had started. Brain magnetic resonance imaging (MRI) revealed predominantly periventricular multiple ovoid hyperintense lesions in bilateral white matter in FLAIR sections. There was a juxtacortical lesion in left frontal region. These radiographic features are compatible with multiple sclerosis (McDonald Criteria 2010). Cerebrospinal fluid analysis revealed oligoclonal band as type 2 positive. The patient is followed up with valproic acid therapy.

Conclusions: Demyelinating lesions can cause seizures by affecting cortical and subcortical structures. MS should be kept in mind in the etiology of epileptic seizures.

P-115
Myelin Water Imaging in a Progressive Solitary Sclerosis Case
J.K. Chan, L.E. Lee, A. Trabousee, S.H. Kolind, R. Caruthers
University of British Columbia, Vancouver, Canada

Background: Progressive motor impairment due to a single demyelinating lesion along corticospinal tracts has recently been described in the literature and termed progressive solitary sclerosis (PSS). Unlike MS, these patients have no further demyelinating lesions and no additional clinical relapses. Myelin water imaging is an advanced magnetic resonance imaging (MRI) marker for measuring myelin damage and has shown reduced myelin water fraction (MWF) in normal appearing white matter (NAWM) in progressive MS.

Objectives: We investigate a single case of PSS using MRI-based myelin water imaging to gain further insight into the pathophysiology of this demyelinating disorder.

Methods: We identified a 51-year-old male at our center who met the criteria for PSS. He has a focal, T2 hyperintense lesion in the cervical cord with associated progressive right hemiparesis over 3 years. Two independent quantitative techniques for myelin water imaging, Multi-component driven equilibrium single pulse observation of T1/T2 (mcDESPOT) and multi-echo T2 relaxation gradient and spin echo (GRASE), were used to calculate MWF in NAWM at the corticospinal tracts using a 3T scanner. Our case was compared to four age and gender matched healthy controls.

Results: The MWF for our PSS case was 0.21 and 0.20 in the corticospinal tracts using mcDESPOT compared to 0.20 and 0.19 for the healthy controls. Using GRASE, MWF was 0.20 for both corticospinal tracts compared to 0.17 and 0.18 for the healthy controls.

Conclusion: There was no evidence of myelin loss in the NAWM along the corticospinal tracts in our PSS case, which differentiates PSS from progressive MS.

P-116
Condyloma Acuminata Aggravated in a Patient with Multiple Sclerosis after Fingolimod Therapy
Mesre Koseoglu Bittelü, Serkan Ozben, Gokcen Gozubatik Celik, Hande Sarıahmetoglu, Aysun Soysal, Dilek Atakılı
1Department of Neurology, Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery Diseases, Istanbul, Turkey
2Department of Neurology, Antalya Training and Research Hospital, Antalya, Turkey

Introduction: Condyloma acuminata is caused by Human Papilloma Virus (HPV). Lesions are usually present at the genital skin and/or the mucosa. Especially immunosuppressive patients are under risk for infection and progression. Fingolimod is the first novel oral disease-modifying drug approved for the treatment of relapsing-remitting multiple sclerosis (RRMS).

We present a case of progressive condyloma acuminata infection started 2 months after fingolimod therapy. Due to our literature review this side effect of fingolimod therapy has not been described previously.

Case: A 36-year-old female patient was under follow-up from our center for Relapsing Remitting Multiple Sclerosis (RRMS) since January 2011. After glatiramer acetate treatment due to occurrence of new lesions, she was switched to fingolimod therapy. The patient applied to our clinic with multiple (about 20) genital lesions, distinct in vulva. The patient was consulted to gynecology department and diagnosed as multiple condyloma acuminatum. Its occurrence and aggressive course was thought to be due to fingolimod treatment, and discontinuation of the treatment was...
recommended. Condyloma cauterization was applied under general anesthesia.

Discussion: Fingolimod is an oral agent with proven efficacy and safety. Due to fingolimod’s action on lymphopenia, side effects related to serious infections and cancer risk, possibly by interfering immune surveillance function of lymphocytes, are reported. Clinicians should be alert to the possibility of progressive genital lesions in patients under fingolimod therapy for RRMS. Evaluating patients who are on fingolimod therapy in this respect will make it possible to detect new cases in initial phases.

P-117
Induction Therapy with Cyclophosphamide and Rituximab followed by Fingolimod improves Outcomes in Fulminant Corticosteroid and Plasmapheresis Refractory Multiple Sclerosis
Tee SK1, Rose N, S1Viswanathan S1
1.Dept of Neurology, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia
2.Dept of Radiology, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia.

Background: Fulminant multiple sclerosis is subtype of fulminant demyelinating disease, associated with rapid progression to disability within several days to weeks. In refractory aggressive cases, cyclophosphamide and rituximab have been reported to produce good outcome as acute therapy when needed.

Objective: To illustrate a rare case of fulminant multiple sclerosis, treatment with induction therapy of IV cyclophosphamide/IV rituximab, followed by T.Fingolimod as maintenance therapy, keeps the patient in remission.

Results: This case report illustrate a rare case of fulminant multiple sclerosis in a 39 years old female with > than 4 attacks of MS in a year refractory to steroids and plasmapheresis with a highly active MRI brain and spine showing multiple T2WI and gadolinium enhancing lesions in the brainstem, cerebellum, cerebral subcortical white matter, thalam, hypothalamus and spinal cord. The aggressive use of IV cyclophosphamide and IV rituximab as induction therapy in this case followed by de-escalation to fingolimod successfully produced clinical remission over the last 3 years with the patient relapse free, EDSS improving from 8.5 to 4.5 and relatively stable MRI findings provided the patient is compliant.

Conclusion: Induction therapy in aggressive fulminant MS with cyclophosphamide followed by rituximab in selected cases followed by de-escalation to fingolimod with careful monitoring for side effects can produce good outcomes in terms of clinical relapses and disability in patients with fulminant MS. Though observational this case report provides helpful data on the management of this challenging area in the absence of more compelling level I evidence.

P-118
Fingolimod-Associated PML with Mild Immune Reconstitution Inflammatory Syndrome in Multiple Sclerosis
Shuhei Nishiya1ma, MD, PhD, Tatsuo Mitsu12, MD, PhD, Yukiko Shishido-Hara13, MD, PhD; Kazuo Nakamichi4, MD, PhD; Masayuki Saijo4, MD, PhD; Yoshiki Takai1, MD, PhD; Kentarou Takei1, MD; Naoki Yamamoto1, Hiroshi Kuroda1, MD, PhD; Ryuta Saito1, MD, PhD; Mika Watanabe6, MD, PhD; Teiji Tominaga7, MD, PhD; Ichiro Nakashima3, MD, PhD; Kazuo Fujihara8, MD, PhD; Masashi Aoki1, MD, PhD
1Department of Neurology, Tohoku University Graduate School of Medicine
2Department of Multiple Sclerosis Therapeutics, Tohoku University Graduate School of Medicine
3Department of Anatomic Pathology, Tokyo Medical University
4Laboratory of Neurovirology, Department of Virology 1, National Institute of Infectious Diseases
5Department of Neurosurgery, Tohoku University Graduate School of Medicine
6Department of Pathology, Tohoku University Graduate School of Medicine
7Department of Neurology, Tohoku Medical and Pharmaceutical University
8Department of Multiple Sclerosis Therapeutics, Fukushima Medical University

Induction therapy in aggressive fulminant MS with cyclophosphamide followed by rituximab in selected cases followed by de-escalation to fingolimod with careful monitoring for side effects can produce good outcomes in terms of clinical relapses and disability in patients with fulminant MS. Though observational this case report provides helpful data on the management of this challenging area in the absence of more compelling level I evidence.
plasma exchange. She was gradually improving and able to maintain alert for longer period afterwards.

**Conclusions:** Narcolepsy in NMO is linked with high expression of AQP4 in hypothalamic periventricular regions, therefore responsible for the symptom. This is an atypical presentation of NMO and sometimes mislead to other diagnosis, hamper appropriate treatment. Measuring CSF orexin level, which is currently not available in our country, may benefit for enhancing diagnosis.

**P-121**

**Difficulty in Differential Diagnosis of Recurrent Brainstem Syndrome; Rhombencephalitis or Neuromyelitis Optica?**

Su Jin Lee, M.D., Gina Choi, Hy-Eun Kim, M.D.  
*Department of Neurology, International St. Mary’s Hospital, Catholic Kwandong University*

**Background:** Acute brainstem syndrome may be the initial manifestation of various diseases such as multiple sclerosis (MS), neuromyelitis optica (NMO), encephalomyelitis. In the absence of autoantibodies including anti-aquaporin 4 (AQP4) antibody, to confirm a diagnosis is not easy.

**Objective:** Here, we present the case of a 45-year-old man who has not been confirmed diagnosis, but suspected have an autoimmune – mediated encephalitis or CNS vasculitis of unknown etiology.

**Patient and Methods:** He was first admitted to our hospital at age 44 due to headache and fever. The patient developed a tingling sensation in the upper extremities and gait disturbance. He was tentatively diagnosed with neuro-behçet’s disease or other vasculitis on the basis of T2 high signal intensity (HIS) lesion with patch Gd-enhancement in the brainstem. (and CSF results) His serum and CSF samples tested negative for auto antibodies including anti-NMDA receptor antibodies. Infectious etiology was excluded, Ig G index was normal and AQP4 antibodies were negative. After treatment with oral corticosteroids, there was recovery in the acute phase. Ten months later, he developed dysarthria and dysphagia abruptly. T2/FLAIR MRI images showed a HIS in the both cerebral peduncles to pons. He showed good recovery with steroid medication and immunosuppressive treatment was started since the recur.

**Conclusions:** Our patient had common features of both recurrent rhombencephalitis and NMO, illustrating that diagnostic characterization is not easy in spite of current criteria. Further, repeated investigations, and close observation of clinical course are required to clarify the definite diagnosis in our patient.

**P-122**

**Ectrodactyly in A Chinese Patient Born to A Mother with Neuromyelitis Optica Spectrum Disorder**

Chang Yanyu1, Shu Yaqing2, Sun Xiaobo3, Xu Chengfang4, He Dar5, Fang Ling6, Chen chen7, Hu Yueqiang6, Allan Kermode6,7, Qiu Wei6,8  
1Department of Neurology, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China  
2Department of Obstetrics, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China  
3Department of Pathology, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China  
4Centre for Neuromuscular and Neurological Disorders, University of Western Australia, Department of Neurology, Sir Charles Gairdner Hospital, Queen Elizabeth II Medical Centre, Nedlands, Perth, Western Australia, Australia  
5Institute of Immunology and Infectious Diseases, Murdoch University, Perth, Western Australia, Australia

**Background:** NMOSD develops primarily in women of childbearing age, and several previous studies have shown that the disorder may increase the risk of miscarriage.

**Objective:** To report a case of fetal malformation related to NMOSD.

**Methods:** We studied the case history a 30-year-old woman who was diagnosed with NMOSD who gave birth to an infant with ectrodactyly and the pathological manifestation of her placenta.

**Results:** The patient experienced recurrent neuritis and who was seropositive for AQP4-IgG. She became pregnant, and the fetus was found to have ectrodactyly. Histological analysis of the placenta showed moderate inflammatory infiltration.

**Conclusion:** It is important to be aware of NMOSD-related fetal malformation. Whether fetal malformation in NMOSD is related to inflammation and AQP4-IgG remains to be determined.

**P-123**

**Neuromyelitis Optica Spectrum Disorder and Sjögren’s Syndrome: A Rare Clinical Phenotype**

CF Ng, WZ Wan Asyraf, CS Khoo, R Rabani, WY Nafisah, HJ Tan, MI Norlinah  
*Neurology Unit, Department of Medicine, University Kebangsaan Malaysia Medical Centre, Cheras, Kuala Lumpur, Malaysia*

**Background and Objective:** Neuromyelitis optica (NMO) and Neuromyelitis optica spectrum disorders (NMOSD) are rare inflammatory demyelinating disorders of the central nervous system. NMOSD is a diverse disorder which is known in association with other connective tissue diseases.

**Methods:** We describe a case of NMOSD that initially presented with ischaemic stroke then progressed to longitudinally extensive transverse myelitis and subclinical optic neuropathy. Sjögren’s syndrome (SS) was only diagnosed one year later.

**Results:** A 60-year-old woman presented with sudden onset of right-sided body weakness. Computed tomography of the brain showed left internal capsule hypodensity and she was treated for left lacunar infarct. She returned one month later with urinary incontinence and persistent body weakness. Magnetic resonance imaging (MRI) of the spine showed enhancing intramedullary lesion from C2 to C6 segments. An ophthalmologic evaluation revealed right optic disc pallor. Serum Aquaporin-4 Antibody was positive. She was treated for NMO with oral prednisolone and azathioprine. One year after clinical remission, she developed dry eyes and left-sided body weakness. Schimer’s test was positive and Anti-Ro/La antibodies were detected. MRI brain showed multiple supratentorial white matter lesions. She was treated with intravenous methylprednisolone followed by cyclophosphamide and oral prednisolone. At three months review, she showed significant clinical improvement with near resolution of the limb weakness.

**Conclusion:** NMOSD has been reported in association with primary SS. Early recognition is crucial to determine the intensity of the treatment. This case illustrated an initial stable NMO that...
progressed to develop secondary SS, which necessitated the escalation of immunosuppressive therapy.

P-124
Neuromyelitis Optica Spectrum Disorder Presented with Pseudoathetosis
Hung Youl Seok,1 Mi-Yeon Eun,2 Seong Hwa Jang,1 Sooyeoun You1
1Department of Neurology, Keimyung University School of Medicine, Daegu, Korea
2Department of Neurology, Hanil General Hospital, Seoul, Korea

Background: Various conditions that involve the posterior column have been reported to cause spinal pseudoathetosis. However, neuromyelitis optica spectrum disorder (NMOSD) has not yet been reported as a cause of pseudoathetosis. We report a case that was diagnosed as pseudoathetosis caused by cervical myelitis associated with an aquaporin-4 antibody.

Case: A 69-year-old woman presented with abnormal movements in her hands. After 1 week, right leg weakness was noted. On admission, there was MRC grade 2 weakness in the right leg. A sensory examination revealed severe reduction in the joint position and vibration sense in hands and feet. She exhibited uncontrolled postures and movements of her fingers. The slow and involuntory movements were more obvious when she closed her eyes than when she opened her eyes. Spinal MRI showed a hyperintense posterior column lesion on T2-weighted images, extending from levels C1 to C8. The cerebrospinal fluid examination showed a slight increase in proteins, and oligoclonal bands were found. We also performed the serologic test for an aquaporin-4 antibody, and the antibody was detected. The patient was treated with high-dose methylprednisolone for 5 days. At 3-month follow-up her abnormal postures and movements of her fingers completely disappeared and right leg weakness improved to MRC grade 4.

Conclusion: To the best of our knowledge, this is the first report of pseudoathetosis caused by NMOSD. Our case suggests that pseudoathetosis can occur as the presenting symptom of NMOSD, and thus it should be taken into consideration as a differential diagnosis of pseudoathetosis.

P-125
A Case Report of Behavioral Symptoms and Multiple Cranial Neuropathies in MOG-IgG Positive Patient
K Choi1, SM Kim2, HK Song3, J Oh1
1Department of Neurology, Konkuk University Medical Center, Seoul, Republic of Korea
2Department of Neurology, Seoul National University Hospital, Seoul, Republic of Korea
3Department of Neurology, Kangdong Sacred Heart Hospital, Seoul, Republic of Korea

Background: Few early studies indicated that MOG antibodies are associated with more benign disease course than AQP4 antibodies, recent findings suggested broader clinical severity of MOG-IgG related central demyelinating disease.

Case reports: A 22-years old female admitted in March 2004 with complaints of paresthesia, weakness in the lower extremities and urinary retention. Paraparesis and sensory deficit were detected. MRI showed lesion extending from T5 level to conus medullaris. Cerebrospinal fluid(CSF) analysis revealed lymphocytic pleocytosis with negative oligoclonal bands(OCBs). She improved completely after IV methylprednisolone(IVMP). In her medical history, two steroid-responsive ON attacks were described. In October 2005, she had simultaneous bilateral ON and TM. Cranial MRI showed Gad-enhancing white matter lesions. She recovered with 1 gr/day IVMP. In January 2006, severe bilateral ON and TM occurred, EDSS reached 7.0. MRI showed atypical tumefactive frontal lesion which was biopsied and demyelination verified. After a course of plasmapheresis(PE) and monthly PE for 6 times, she improved completely. Her last attack was TM in December 2006. Although she refused long-term treatments, in 2017 EDSS is still 0.0 with no further attack. Anti-AQP4 antibody was always negative.
Conclusion: Although, relapsing NMO has poor prognosis without treatment, our patient can be an example for conversion to unusual benign course after catastrophic attacks.

P-127
B Cell Depleting Therapy for Multiple Sclerosis Overlapping with Neuromyelitis Optica Spectrum Disorder
Tingting Lu1, Yaqing Shu1, Yongqiang Dai2, Xu Liu1, Yanyu Chang3, Qiao Huang1,2, Allan Kermode4, Wei Qiu1
1Department of Neurology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China
2Department of Neurology, Zhaqong No. 2 People’s Hospital, Zhaqong, China
3Center for Neuromuscular and Neurological Disorders, University of Western Australia, Department of Neurology, Sir Charles Gairdner Hospital, Queen Elizabeth II Medical Centre, Australia
4Institute of Immunology and Infectious Diseases, Murdoch University, Australia
Background: Multiple sclerosis and neuromyelitis optica spectrum disorder and are currently thought to be independent entities. Some patients display intermediate manifestations that fit the criteria for both diseases without positive relevant serobiomarkers. An overall standard and consensus for the diagnosis and treatment of these overlapping patients have not been reached.
Objective: The aim of this study was to explore potential proper treatments for these patients.
Methods: We describe a patient with frequently relapsing demyelinating episodes and repeatedly adjusted treatment regimens due to diagnostic difficulties.
Results: The case was not well responsive to glucocorticoid plus azathoprine, or interferon. Benefits were obtained by using rituximab, a B cell scavenger targets humoral immunity.
Conclusions: Treatments targeting B cell mediated humoral immunity may be a safe and appropriate choice for the challenging demyelinating cases, especially in Asian population.

P-128
Acute Disseminated Encephalomyelitis in Post-Allogeneic Peripheral Blood Stem Cell Transplantation with Subclinical Cytomegalovirus Infection
CF Ng, WZ Wan Asyraf, CS Khoo, R Rabani, WY Nafisah, HJ Tan, ML Norlinah
Neurology Unit, Department of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Kuala Lumpur, Malaysia
Background and Objective: Acute disseminated encephalomyelitis (ADEM) is an autoimmune, inflammatory demyelinating disorder of the central nervous system. It is often triggered by infection and manifested as multifocal neurological deficits with rapid deterioration. It can be potentially fatal in immunosuppressed patients.
Method: We report a case of ADEM in post-allogeneic peripheral blood stem cell transplantation (PBSC) with Cytomegalovirus (CMV) antigenemia despite valganciclovir prophylaxis.
Results: A 63 year-old man with underlying chronic hepatitis B on treatment and acute myeloid leukaemia transformed from myelodysplastic syndrome, presented with acute confusion for two days on day-60 post-allogeneic PBSC. He acquired subclinical CMV antigenemia one month prior to the onset and had been on oral valganciclovir prophylaxis. On presentation, his Glasgow Coma Scale was E3V4M6 and there were right gaze palsy, brisk knee reflexes and sustained ankle clonus bilaterally. Magnetic resonance imaging of the brain showed multiple T2 hyperintense lesions over left thalamus, internal capsule and bilateral cerebellum with minimal contrast enhancement. Electroencephalography revealed diffuse generalised encephalopathy. Lumbar puncture was not performed due to severe thrombocytopenia. He was treated for ADEM and given intravenous methylprednisolone 500 mg daily for five days and intravenous ganciclovir. He improved on the fourth day of treatment and all his neurological symptoms were resolved.
Conclusion: ADEM is a life-threatening condition with high mortality if left untreated. In this patient, ADEM set in insidiously despite early antiviral prophylaxis for CMV antigenemia. Subclinical infection in immunosuppressed patients need to be identified and judiciously treated in order to reduce the risk of ADEM.

Poster Session 14
Case Report-3 MS Mimics

P-129
Susac’s Syndrome in a Patient Misdiagnosed with Multiple Sclerosis: A Case Report
Jong Sze Chin1; Sibi Sunny2; Raymond Seet Chee Seong2
1 Department of Internal Medicine, National University Hospital, Singapore
2 Department of Neurology, National University Hospital, Singapore
Refer to O-18 in the Oral Presentation

P-130
Susac Syndrome: Clinical Features, Laboratory Testing and Treatment Responses of 3 Cases
Mehmet OZMENOGLLI, Serap Zengin KARAHAN, Nuray Can USTA, Cavit BOZ
KTU Medical Faculty Farabi Hospital, Trabzon, Turkey
Background: Susac Syndrome (SS) is a rare, autoimmune angiopathy characterized by encephalopathy, hearing loss, and visual disturbance resulting from branch retinal artery occlusion.
Objective: The purpose of the study is to examine the demographics, clinical characteristics, treatment, and prognosis of 3 patients with Susac syndrome.
Case 1: A 27-year-old woman presented with vertigo, nausea, vomiting and change in behaviors that started 2 months prior to admission.
Case 2: A 19-year-old pregnant woman presented with headache and meaningless speech that started 1 month prior to admission.
Case 3: A 14-year-old female patient with a 2-year history of headaches was admitted with bilateral hearing loss. She also had visual complaints accompanied by clumsiness and difficulty walking for 3 months.
Results: All three cases’s brain MRI revealed multiple lesions in the corpus callosum and deep white matter. Fluorescein angiography revealed bilateral multiple branch retinal artery occlusion (BRAO). Audimetry showed bilateral sensorineural hearing loss. CSF analyses performed in 2 cases (case1, case 2) revealed elevated total protein but no OCB was detected. All patients have received pulse of high-dose intravenous
with foul smell after the events of her mother’s sudden death. LGI1 related autoimmune LE are once more stressed. This study, the clinical features, diagnosis and treatment of anti-symptoms, behavioral disorders and temporal lobe seizures. In characterized by memory deficits, various neuro-psychiatric autoimmune. Anti-leucine-rich glioma inactivated-1 (Anti-LGI1) affects the medial temporal and could be paraneoplastic or specific abnormal finding in ophthalmologic examinations. Left visual disturbance with left eyeball pain was rapidly developed a 64-year-old woman developed the left optic neuritis 3 times at 6-month intervals. She was diagnosed with Behcet disease 2 years ago. There was no developed the left optic neuritis 3 times at 6-month intervals. She disease were not well elucidated. A 64-year-old woman recurrently developed and respond well to steroid treatment. May suggest that optic neuritis in Behcet disease can be recurrently developed and respond well to steroid treatment. However, preventive therapy for the optic neuritis in patients with Behcet disease should be investigated in further study.

P-131
Recurrent Optic Neuritis in Patient with Behcet Disease
Kyong Jin Shin, Jong Kook Kim
Department of Neurology, Haeundae-Paik Hospital, Inje University College of Medicine
Department of Neurology, Dong-A University Hospital, Dong-A University College of Medicine.
Optic neuritis can recurrently developed in patients with multiple sclerosis and neuromyelitis optica. The severity and response to steroid of optic neuritis differ depending on the underlying cause. Recently, we experienced a patient with Behcet disease presenting recurrent optic neuritis. Clinical characteristics and treatment response of optic neuritis in patients with Behcet disease were not well elucidated. A 64-year-old woman recurrently after the discontinuation of steroid. Wave formation was not good and P100 latency was prolonged in the left full-field visual evoked potential. Cells were not found in optic neuritis occurred recurrently after the discontinuation of steroid. Cranial MR image was showed bilateral T2 and FLAIR hiperintensity on medial temporal lobes. In clinical follow-up, epileptic seizures were observed and generalized slow-wave activity was detected on EEG. After intravenous immunoglobulins treatment all symptoms declined vastly and autoimmune panel anti-LGI1 was found positive. Treatment should be start rapidly when anti-LGI1 autoantibody is positive.

P-132
Anti-LGI1 Auto-Antibody Related Limbic Encephalitis: A Case Report
Ufuk Emre*, Çağla Şişman*, Tuğçe Guven*, Yeşim Karagöz**
Health Sciences University, Istanbul Research and Training Hospital Neurology Clinic*, Radiology Clinic**
Background: Limbic encephalitis (LE) is a disease that generally affects the medial temporal and could be paraneoplastic or autoimmune. Anti-leucine-rich glioma inactivated-1 (Anti-LGI1) auto-antibody related limbic encephalitis is a rare autoimmune LE, characterized by memory deficits, various neuro-psychiatric symptoms, behavioral disorders and temporal lobe seizures. In this study, the clinical features, diagnosis and treatment of anti-LGI1 related autoimmune LE are once more stressed.

Case: A 32 year old woman presented with psychiatric symptoms, cognitive impairment, disorientation and seizures accompanied with foul smell after the events of her mother’s sudden death. Cranial MR image was showed bilateral T2 and FLAIR hiperintensity on medial temporal lobes. In clinical follow-up,
Case: A 36-year-old woman presented with progressive dysarthria and cognitive dysfunction after emotional stress during 3 months. She also complained of dysphagia and uncontrolled mood instability. Brain MRI showed striking diffuse white matter lesions on T2 and diffusion-weight imaging with bilateral putaminal enhancement. Anti-double-stranded DNA (anti-dsDNA) antibody was positive (228.5 IU/mL) and anti-smooth muscle antibody was also positive (>1:80). Anti-nuclear antibody was strong positive. C3 and C4 complement had dropped to 41.9 and 3.1 mg/dL. Cerebrospinal fluid (CSF) was normal and CSF John Cunningham (JC) virus antibody was negative. She was diagnosed as SLE with CNS involvement and started to methylprednisolone pulse therapy. After steroid treatment, her symptoms were dramatically improved. But, monthly follow-up MRI was not significant improvement during 3 months.

Continuing steroid and other immunosuppressive drugs (azathioprine and tacrolimus), anti-dsDNA antibody titer was improved (13.53 IU/mL for last follow-up). After 15 months later, follow-up MRI showed significant reduced lesions at bilateral temporal, crus cerebri and left frontal regions.

Conclusions: Although this patient has a good prognosis unlike diffuse lesions, other cases suggested its fatal clinical course though appropriate treatment. Early recognize a disease entity and aggressive treatment is very important, regardless of immunopathologic mechanisms may be different (vasogenic edema with perivascular lymphocytic infiltration; microinfarction; plaque-like demyelination; vacuolar demyelination).

P-135
Acute Toxic Hepatitis after Steroid Pulse Therapy in Myelopathy
Hye Joo Rha, Jung Im Seok
Department of Neurology, Catholic University of Daegu, School of Medicine

Background & Significance: Steroid pulse therapy is used in various inflammatory and autoimmune conditions. Although steroid has several side effects, toxic hepatitis is a rare complication of steroid treatment. We introduce 2 cases of acute hepatitis after steroid pulse therapy.

Case: A 37-year-old female presented with a 2-month history of paresthesia on left side (arm and leg). Cervical spine Magnetic Resonance Imaging (MRI) showed focal spinal cord edema at C4 level. She was treated with steroid pulse therapy (methylprednisolone 1g/day for 3 days). The next day after therapy, she complained of right upper quadrant (RUQ) pain. In laboratory findings, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were elevated up to 39 and 108 U/L (normal <35 U/L) respectively.

A 32-year-old female presented with a 3-month history of paresthesia below the neck and weakness in left arm and leg. Cervical spine MRI revealed syringomyelia at C4-6 level. She was treated with steroid pulse therapy (methylprednisolone 500mg/day for 3 days). The next day after therapy, she complained of RUQ pain and AST and ALT were elevated up to 824 and 863 U/L respectively.

In both cases, the abdomen CT and hepatobiliary ultrasound showed gallbladder wall thickening. Abdominal pain subsided and abnormal laboratory finding normalized within several days of conservative treatment.

Conclusions or Comments: Monitoring of AST and ALT following steroid pulse therapy should be considered.

P-136
Optic Neuritis: A Complication of ZIKA Virus Infection in An Adult
ST Lam1, SH Vigneshwari1, AS Bhave1, CWT Tan2, PA Tambyah2, D Soon1
1Yong Loo Lin School of Medicine, National University of Singapore
2National University Health System, Singapore

Introduction: Zika Virus (ZIKV) is a flavivirus transmitted through Aedes mosquitoes and endemic in Africa, Asia and South America. In 2016, an increase in ZIKV-associated congenital defects was observed in South America. A wide range of neurological complications have since been reported in association with ZIKV, including Guillain-Barre syndrome, encephalitis and transverse myelitis.

Clinical Description: An 18-year-old Singaporean gentleman presented with 4 days of malaise and lethargy, associated with sore throat and erythematous rash. Blood tests indicated mild dengue infection, and urinary PCR confirmed the presence of ZIKV-specific RNA.

2 weeks later, he reported bilateral retro-orbital pain, exacerbated by eye movement. Visual evoked potentials revealed bilaterally prolonged latencies, indicating optic neuritis. As no compromise of visual acuity was detected clinically, corticosteroids were not administered at the time. The patient’s symptoms resolved and he declined further testing.

Discussion: We describe optic neuritis as a complication of adult ZIKV infection. To date, much of the ophthalmic complications described with ZIKV have been in the context of congenital infections. Optic neuritis represents a hitherto unreported complication of adult ZIKV infection. The pathogenesis in our case is also unclear. While ZIKV has been isolated in lacrimal fluid (suggesting a direct viral attack), the onset of optic neuritis 2 weeks following the acute infection in our case also raises the possibility of a post-infectious process. Further observational and prospective studies will help to elucidate the incidence and nature of ZIKV associated ophthalmic complications.

P-137
Progressive Multifocal Leukoencephalopathy after Liver Transplantation
Y Kim, M.D.1, HN Jung, M.D.2, HY Shin, M.D. 2, SM Kim, M.D. 2
1Department of Neurology, College of Medicine, Korea University Arsan Hospital
2Department of Neurology, Yonsei University College of Medicine, Seoul, Korea

Background: Progressive multifocal leukoencephalopathy (PML) is an opportunistic demyelinating encephalopathy which invariably affects immunosuppressed patients. We present a patient who developed PML after liver transplantation (LT).

Case: A 77-year-old male with history of thyroid cancer, cholecystectomy and secondary biliary cirrhosis received LT. Tacrolimus was prescribed for immunosuppression. After 2 months, patient felt slight right hand clumsiness. After 5 months, tacrolimus was changed to cyclosporine because of the itching sense. After 1 week, patient insidiously developed fever, malaise, right side weakness and aphasia. On outside brain MRI, an ill-
defined high signal intensity was in left frontal lobe around precentral gyrus on diffusion weighted image. Follow-up MRI was done, and the patient visited Severance hospital. On admission, the patient was alert but had global aphasia. He had right visual field defect. His right side motor grade was Medical Research Council (MRC) grade 0 to III. The patient was on tacrolimus at the time. On cerebrospinal fluid (CSF) examination, John Cunningham (JC) virus was positive and we diagnosed PML. We tapered tacrolimus and started mirtazapine and cidofovir. 1 month after admission, tacrolimus was stopped. However, follow-up MRI showed more enlarged brain lesion on previous area. After 3 months of admission, liver sonography implied liver rejection. The patient died 4 months after diagnosis of PML.

Conclusion: PML occurs in transplant recipients. It is caused by oligodendrocyte destruction by JC virus. It can be mistaken as stroke or any other diseases. If clinically suspected, CSF JC virus test must be done. Treating PML is difficult and needs careful approach.

P-138
Central Pontine Myelinolysis without Rapid Correction of Hyperosmolar Hyperglycemia
Jae Young An, Kwang Soo Lee
Department of Neurology, College of Medicine, The Catholic University of Korea

Introduction: The osmotic demyelination syndrome (ODS) is well recognized to occur in a variety of clinical settings, particularly following rapid correction of severe hyponatraemia. Although the rapid correction of hyponatraemia is a dominate cause of ODS, a variety of other medical conditions have been associated with the development of ODS, independent of changes in serum sodium in recent years. Most ODS cases with hyperosmolar hyperglycemia are related with acute correction of hyperglycemia.

Case: A 48-year-old woman with liver cirrhosis and diabetes developed dysarthria, dysphagia and paraparesis. In ER, the serum glucose was 788 mg/dl, sodium 126 mEq/L, potassium 4.3 mEq/L, BUN 18.6 mg/dl and calculated osmolality 312 mOsm/kg. There was no ketoacidosis, consistent with a hyperosmolar hyperglycemic state. Neurological examination showed the findings of gait ataxia and paraparesis (MRC grade IV) and also revealed mild dysarthria and dysphagia. The other examination was unremarkable. Diffusion MRI of the brain performed on the same day demonstrated a region of high signal in the pons with decreased ADC value. These findings were consistent with ODS. Conclusion: The ODS associated with the rapid development of severe serum hyperosmolality in the absence of rapid correction of preceding hyponatremia is very rare. Proposed mechanism between oligodendrocyte shrinkage and myelinolysis may be more faster hypertonia than the rate of compensation of brain cells can result in ODS.
EUROPEAN CHARCOT FOUNDATION SYMPOSIUM

How to Improve Recovery in MS
Chairperson: William Carroll (Australia)

Remyelination Strategy: Its Basic Science and Clinical Application
Hans-Peter Hartung (Germany)
Information not available at time of printing.

Symptomatic Treatment
Kazuo Fujihara (Japan)
Information not available at time of printing.

New Strategies for Rehabilitation
Giancarlo Comi (Italy)
Information not available at time of printing.

Neuromodulation to Enhance Recovery in MS
Letizia Leocani (Italy)
Information not available at time of printing.
PHARMA EDUCATIONAL SEMINAR

Merck

Changing the Paradigm in the Treatment of MS in Asia Pacific
Chairperson: Ching-Piao Tsai (Taiwan) & William Carroll (Australia)
Thursday, 23 November 2017, 17:30-19:00

MS in Asian Population and Its Unique Clinical Features
Alexander Lau (Hong Kong)
Assistant Professor, Department of Medicine & Therapeutics; Associate Director and Convener (Neuroscience), Hong Kong Institute of Integrative Medicine; Faculty of Medicine, The Chinese University of Hong Kong; Specialist in Neurology, Prince of Wales Hospital

Multiple sclerosis (MS) is regarded as a relatively uncommon yet debilitating condition in Asia Pacific. Current estimates indicate that the prevalence is between 2 and 8 per 100,000 patients with increasing trends observed more recently, particularly in Taiwan, Japan and Korea, respectively. In terms of demographics, women appear to have a greater predisposition to MS, with a high female to male ratio. In addition, symptoms are likely to appear around the age of 30 years, which is a time of life that a person is economically active and starting a family. Consequently, the socio-economic implications of this disease are long-lasting and immense.

To improve timely diagnosis and outcomes for Asian patients with MS, there is a need to recognize and address barriers to treatment so as to provide an optimal framework for the management of those individuals afflicted by the condition. This review highlights the current unmet needs for MS across Asia Pacific with the aim of raising awareness of the disease, increasing the quality of life (QoL) of patients and improving accessibility to healthcare resources.

How RWE Can Help Physicians to Understand Disease and Optimize Treatment Options
Helmut Butzkueven (Australia)
Professor, Department of Medicine, University of Melbourne; Joint Director of the MS Service at The Royal Melbourne Hospital; Director of the MS service at Box Hill Hospital, Melbourne, Australia; Deputy Director of the MBC-RMH; Chairman of the MS Base Foundation

RWE (Real-World Evidence) can help physicians to understand disease and optimize treatment options by providing insights into the real-world efficacy and safety of treatments in specific populations. This is particularly important in the context of MS, where treatment approaches need to be tailored to the unique clinical features of the disease in Asian populations.

T-/B-cells Pathogenesis in MS, Selective Immune Reconstitution Therapy
Per Soelberg Sorensen (Denmark)
Director of Danish Multiple Sclerosis Center, Department of Neurology, Rigshospitalet, Copenhagen (since 1995); Professor of Neurology, University of Copenhagen (since 1998); Senior Consultant, Department of Neurology, Neuroscience Centre, Copenhagen; University Hospital Rigshospitalet, Copenhagen (since 1985)

In MS, the long-term goal of treatment is to control disease activity and prevent disability progression. In current practice this is often linked to NEDA; no relapses, confirmed disability progression or MRI activity as defined by clinical assessment. With the newer treatment available, should the focus be on achieving long-term remission? Remission is not currently defined in the context of MS. Overall, there are two basic groups of disease-modifying drugs, chronic therapies that impact the immune system only during active treatment – with our suggested classification as ‘Maintenance/Escalation Therapies’ and secondly, short-term therapies that ‘reconstitute’ the immune system with long-term changes in immune function with the suggested label as Immune Reconstitution Therapies. The maintenance therapy category consists of disease-modifying drugs that work by continuous immunosuppression or immunomodulation that need to be given continuously to have an effect. The suggested new category of immune reconstitution therapy or ‘IRT’ encompasses some of the newer disease-modifying drugs, and would consist of those treatments that could be given for a short time only but would have a long-term effect on the immune system; transient reduction in function followed by qualitative changes.
Sanofi Genzyme

New Treatment Options for Multiple Sclerosis – How to Find the Right Approach for Each Patient?
Chairperson: Ho Jin Kim (Republic of Korea)
Friday, 24 November 2017, 8:30-10:00

The Evolving Understanding of MS Pathophysiology and its Implications for Patient Care
Anat Achiron (Israel)
Sheba Medical Center, Tel-Hashomer/Multiple Sclerosis Center, Tel Aviv, Israel
Multiple sclerosis (MS) is a chronic, CNS-specific, autoimmune demyelinating disease affecting people in their most productive years and a leading cause of disability. Although MS is less frequent in Asia compared with the western world, latest estimates indicate a prevalence of several hundred thousand people suffering from MS in this region. For every individual with MS, there will also be an effect on family, care partners, and healthcare resources.

T and B lymphocytes are critical mediators of inflammatory processes in MS. The inflammatory component of the disease has been recognized and, even today, we see patients treated with purely anti-inflammatory strategies (ie, corticosteroids as monotherapy). Meanwhile, we know that more specific, targeted disease-modifying treatments that have anti-inflammatory effects AND reduce axonal damage can affect disease progression more effectively long-term. This goes hand-in-hand with our expanding understanding of the neurodegenerative component of the disease, while modern MRI techniques help quantify effects of therapeutic interventions on brain atrophy and other surrogate markers.

Increasingly, the spotlight is moving towards other important outcomes, such as fatigue or cognitive function. In the recent vsMS survey among RMS patients for instance, over 3/4 of respondents felt fatigue limited their daily activities, even when they had enough sleep. Over half of respondents also said their ability to process information had slowed down since their diagnosis.

During this presentation, the evolving pathophysiological concept of MS is discussed and linked to outcome measures. Finally, imperatives for optimal patient care based on personal experience are discussed.

The Evolving Spectrum of New Oral Treatment Options – Opportunities and Risks
Regina Berkovich (USA)
Keck Hospital, University of California, Los Angeles, USA
Based on experience from more than two decades, injectable interferon beta and glatiramer acetate are seen as the standard of care of disease-modifying therapies in MS – at least for patients with mild to moderate disease. However, there is a need for customized treatment approaches based on disease prognosis, individual patient needs/risk tolerance, and adherence to therapy. With the introduction of new oral treatment alternatives – teriflunomide, fingolimod, and dimethyl fumarate – choices for neurologists and patients expand. Each of these new compounds has a specific mode of action, efficacy, and safety and tolerability profile, with implications for benefit/risk assessment and the appropriate patient profile.

During this presentation, key clinical data for the new oral MS treatments will be introduced, risks and opportunities discussed, and optimal patient profiles derived. Several case studies will help to illustrate the clinical decision-making processes in real-world conditions.

The Evolving Spectrum of High-Efficacy Monoclonal Antibodies – Setting New Treatment Goals
Simon Broadley (Australia)
Department of Neurology, Gold Coast University Hospital, Gold Coast, Australia
From clinical experience, we know that some patients with MS show signs of active disease even during treatment with injectable or oral disease-modifying therapies. These patients are in need of higher efficacy treatment options.

In previous years, the armamentarium of high-efficacy monoclonal antibodies targeting different receptors on T and/or B cells to treat MS has expanded significantly. Among them, alemtuzumab, natalizumab, and ocrelizumab need to be mentioned in particular. Higher efficacy often comes with a balance of risk, which (beside patient access issues) seems to have limited the use of these drugs so far in large parts of Asia. However, the safety of high-efficacy monoclonal antibodies is also related to the effectiveness of the risk management plan in place. When potential side effects are detectable and treatable, more patients with a poor prognosis could benefit from these treatment options, allowing a profound impact on the disease course, particularly on the accumulation of disability and transition to secondary progressive MS.

During this presentation, key clinical data for the above high-efficacy monoclonal antibodies will be introduced, potential safety issues and mitigation strategies discussed, and optimal patient profiles derived. Several case studies will help to illustrate relevant steps in clinical decision-making.
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