8th Congress of the Pan-Asian Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS)

Thursday 19 - Saturday 21 November 2015, Seoul, Republic of Korea
WELCOME NOTE

Dear colleagues and delegates,

Welcome to the eighth annual meeting of PACTRIMS to be held in Seoul, Republic of Korea. The PACTRIMS region is home to 60% of the world’s population and represents many and varied cultures, customs and cuisines. In Seoul you will find a fascinating blend of old and new, a unique history and a modern story set among soaring architecture and Buddhist temples and home to some 10 million people.

The Scientific Program Committee chaired by Professor Jun-ichi Kira and comprising members from all the PACTRIMS regions have prepared an exciting and informative program highlighting topics of importance to all clinicians, researchers and students involved in MS as well as people living with MS and other related demyelinating disorders in the PACTRIMS region and elsewhere. The topics explore the major challenges currently facing researchers and clinicians as well as updating the key advances in the understanding and treatment of these conditions. Among the topics selected for the eighth PACTRIMS meeting, there will be invited lectures and symposia exploring the mechanism of axonal injury in MS, the role of photoimmunology in demyelinating diseases, the immunopathological distinction between MS and NMOSD, the difficult overlap between NMOSD and MS in the Asian region, understanding the newly described variants of NMOSD, new treatments for NMOSD and a critique on the effectiveness of current MS treatments as well as the use of biomarkers and imaging in demyelinating diseases in Asia.

Among the galaxy of invited speakers, PACTRIMS is delighted to have distinguished guests such as Takahashi Yamamura, Sasitorn Siritho, Moses Rodriguez, Douglas Sato and Martin Kerschensteiner as well as experts from India, Japan, Korea, China and Australia. This eighth PACTRIMS meeting is again proud to host the European Charcot Foundation symposium in conjunction with PACTRIMS led by Professor Kazuo Fujihara.

The Presidential symposium, parallel sessions featuring young investigators and posters also add to the exciting and interesting programme together with the PACTRIMS and Multiple Sclerosis Journal awards and Pharma sponsored educational symposia.

Continuing to reflect the close ties between PACTRIMS and the Multiple Sclerosis Journal, the abstracts are published in MSJ and delegates will also be offered free, all issues of MSJ for the next 12 months as well as those from the past 12 months.

A social programme to complement the scientific meeting and which facilitates colleagues to mingle and interact is also not to be missed on the Thursday and Friday evenings. Join us in taking in the sights of Seoul, the capital of the Republic of Korea, surrounded by mountains and with the Han River running through from East to West. A modern city dotted with historical reminders of its storied past awaits.

We are indebted to those who have worked tirelessly to prepare this meeting for us, especially Kays Asia, Pharma and industry and the PACTRIMS subcommittees and on behalf of all we wish you a most enjoyable, satisfying and memorable meeting.

Sincerely,

Takahiko Saida
President

William Carroll
Vice President & Treasurer

Kwang-Kuk Kim
Local Organising Chairman
PACTRIMS 2015 COMMITTEES

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Deputy Secretary
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Members
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Professor Kwang-Ho Lee
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Professor Xianhao Xu

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Professor Xian-Hao Xu
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Hong Kong
Professor Patrick Li
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Professor Ernest Willoughby
Singapore
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Taiwan
Professor Ching-Piao Tsai
Thailand
A/Professor Naraporn Prayoonwiwat

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Professor Kwang-Kuk Kim (Korea)
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Professor Byung-Jo Kim (Korea)
Professor Qi Cheng (China)
Professor Xian-Hao Xu (China)
Professor Fu-Dong Shi (China)
Professor Ching-Piao Tsai (Taiwan)
Professor Chih-Chao Yong (Taiwan)
South-East Asia (Vietnam to Iran)
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A/Professor Naraporn Prayoonwiwat (Thailand)
Professor Bhimsen Singhal (India)
Professor Lekha Pandit (India)
Professor Benjamin Ong (Singapore)
Dr Alvin Seah (Singapore)
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Professor Masoud Etemadifar (Iran)
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A/Professor Helmut Butzkueven (Australia)
Dr Ian Sutton (Australia)
Professor Ernest Willoughby (New Zealand)
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Professor Kwang-Kuk Kim (Republic of Korea)
Europe
Professor Alan J Thompson (UK)
Treatment for Immune neurological diseases

Immunoadsorption Column

Indication
Neurological diseases
(e.g., Myasthenia gravis (MG), Guillain-Barré syndrome (GBS), Chronic inflammatory demyelinating polyneuropathy (CIDP), Multiple sclerosis (MS))

Features of IMMUSORBA TR-350(L)
- Therapeutic plasmapheresis by removing pathogenic substances (anti-acetylcholine receptor antibodies and immune complexes) from patient’s plasma by selective adsorption.
- No need for the replacement of plasma, minimizing the risk of infection with hepatitis, AIDS, etc.
- Applicable to patients with protein allergy.
# PROGRAMME OVERVIEW

## Thursday, 19 November 2015

### Grand Ballroom

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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| 13:00-14:30 | **European Charcot Foundation Symposium**  
             *Looking into The Future of MS and NMOSD*  
             Chairperson: Kazuo Fujihara (Japan) and Jacqueline Palace (UK)  
             1. New Insights on Molecular Pathogenesis of NMOSD  
                — Kazuo Fujihara (Japan)  
             2. MS Therapies on the Horizon and Beyond  
                — William Carroll (Australia)  
             3. ADEM and NMOSD: Which Treatments Work and for Which Patients?  
                — Jacqueline Palace (UK)  |
| 14:30-15:00 | Coffee Break                                                                            |
| 15:00-15:15 | **Opening Ceremony**                                                                     |
|             | 1. Welcome Address by the Chairman, 2015 Local Organising Committee  
             — Kwang-Kuk Kim (Republic of Korea)  
             2. Opening Address by the President, PACTRIMS  
                — Takahiko Saida (Japan)  
             3. Special Remarks by the Vice Mayor of Seoul  
                — Jong Seok Im (Republic of Korea)  |
| 15:15-15:45 | **Opening Lecture**                                                                     |
|             | Chairperson: Kwang-Ho Lee (Republic of Korea)  
             Anti-IL6 Receptor Monoclonal Antibody Therapy in NMO  
             — Takashi Yamamura (Japan)  |
| 15:45-16:30 | **PACTRIMS Basic Science Lecture**                                                      |
|             | Chairperson: Jun-ichi Kira (Japan)  
             In Vivo Analysis of Axon Damage in Multiple Sclerosis Models  
             — Martin Kerschensteiner (Germany)  |
| 16:30-17:00 | **PACTRIMS Educational Lecture**                                                       |
|             | Chairperson: William Carroll (Australia)  
             NMO-IgG Negative Idiopathic Recurrent Transverse Myelitis  
             — Kwang-Kuk Kim (Republic of Korea)  |
| 17:00-17:30 | Coffee Break                                                                            |
| 17:30-19:00 | **UCB Sponsored Symposium**                                                             |
|             | What Matters Most – Functional and Long Term Outcomes in Multiple Sclerosis            |
| 19:30-21:00 | **Welcome Reception @ 37 Grill & Bar, 37F, Conrad Seoul**                               |
# Programme Overview

**Friday, 20 November 2015**

**Grand Ballroom**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>8:30-10:00</td>
<td>Teva Sponsored Symposium: The Story of Copaxone: An Approach to the Treatment of Multiple Sclerosis</td>
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<tr>
<td>10:00-10:20</td>
<td>Coffee Break &amp; Poster Viewing</td>
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<tr>
<td>10:20-12:15</td>
<td><strong>Main Symposium-1</strong>&lt;br&gt;Early Aggressive Treatment versus Cell/Neuroprotection Therapy in MS and NMO&lt;br&gt;Chairperson: Ohyun Kwon (Republic of Korea) &amp; Fu-Dong Shi (China)&lt;br&gt;1. Keynote Lecture: Does Early Aggressive Treatment of MS Prevent Progression?&lt;br&gt;   — Michael Barnett (Australia)&lt;br&gt;2. Human Recombinant Monoclonal Antibodies as Therapy for Demyelinating and Degenerative CNS Disorders&lt;br&gt;   — Moses Rodriguez (USA)&lt;br&gt;3. Real-World Evidence for Treatment Effectiveness and Treatment Sequences in MS&lt;br&gt;   — Helmut Butzkueven (Australia)&lt;br&gt;4. Autologous MSCT as a Therapy in NMO&lt;br&gt;   — Ying Fu (China)</td>
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<tr>
<td>12:15-13:15</td>
<td>Lunch &amp; Poster Viewing</td>
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<tr>
<td>13:15-14:45</td>
<td><strong>PACTRIMS Presidential Symposium</strong>&lt;br&gt;Distinct and Common Aspects of Multiple Sclerosis and Neuromyelitis Optica&lt;br&gt;Chairperson: Kwang-Kuk Kim (Republic of Korea) &amp; Helmut Butzkueven (Australia)&lt;br&gt;1. Distinguishing NMOSD from MS: Current and Future Neuroimaging Perspectives&lt;br&gt;   — Ho Jin Kim (Republic of Korea)&lt;br&gt;2. Anti-MOG Antibody in NMO and Other Demyelinating Diseases&lt;br&gt;   — Douglas Kazutoshi Sato (Japan)&lt;br&gt;3. Common and Distinct Features of Immunopathology between MS and NMO&lt;br&gt;   — Katsuhisa Masaki (Japan)</td>
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<tr>
<td>14:45-15:15</td>
<td>Coffee Break &amp; Poster Viewing</td>
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<tr>
<td>15:15-16:45</td>
<td><strong>Main Symposium-2</strong>&lt;br&gt;Environmental Influences in MS and NMOSD&lt;br&gt;Chairperson: Allan Kermode (Australia) &amp; Masoud Etemadifar (Iran)&lt;br&gt;1. Environmental Influences on Demyelinating Disease in Caucasians&lt;br&gt;   — Bruce Taylor (Australia)&lt;br&gt;2. Photo-Immunology in Demyelinating Disease&lt;br&gt;   — Scott Byrne (Australia)&lt;br&gt;3. Environmental Influences on Demyelinating Disease in Asians&lt;br&gt;   — Jun-ichi Kira (Japan)</td>
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<tr>
<td>16:45-17:00</td>
<td>Coffee Break</td>
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<tr>
<td>17:00-18:30</td>
<td><strong>Genzyme Sponsored Symposium</strong>&lt;br&gt;Reshaping MS with Alemtuzumab</td>
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<tr>
<td>20:00-22:00</td>
<td>Presidential Dinner @ Convention Hall, 2F, Some Gavit, Some Sevit</td>
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</tbody>
</table>
### Oral Session-1: NMO (10:20-11:20)

Chairperson: Lehka Pandit (India) & Akio Suzumura (Japan)


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

(O-2) (12 min) Characterization of Anti MOG and Anti AQP4 Antibody Associated NMOSD in a South Indian Cohort — Pandit L, Sato D, Mustafa S, Fujihara K, Takahashi T, D’Cunha A, Malii C, Ramesh A

*Department of Neurology, KS Hegde Medical College, Nitte University, Mangalore, India; †Department of Neurology / Multiple Sclerosis Therapeutics, Tokohu University Graduate School of Medicine, Sendai, Miyagi, Japan

(O-3) (12 min) Antibody to Myelin Oligodendrocyte Glycoprotein in Adults with Inflammatory Demyelinating Disease of the CNS — SM Kim†, JS Kim†, BJ Bae†, SH Baek†, SY Sohn†, M. Woodhall‡, JS Kim‡, SJ Kim‡, KS Park§, A. Vincentt, KW Lee†, P. Waters‡

†Department of Neurology, College of Medicine, Seoul National University, Seoul, Republic of Korea; ‡Muffield Department of Clinical Neurosciences, John Radcliffe Hospital, Oxford, UK; §Department of Ophthalmology, College of Medicine, Seoul National University, Seoul; †Department of Neurology, Seoul National University Bundang Hospital, Gyeonggi, Republic of Korea; §Department of Neurology, Republic of Korea University Guro Hospital, Seoul, Republic of Korea

(O-4) (12 min) Development of Auaporin Antibody Binding Inhibitor: A Preliminary Data — E-L Ju†, SY Cheon*, SK Yeon*, JS Kim†, BJ Kim*, SH Baek*, SY Sohn*, SW Kim*, OH Kwom, KD Park*, SM Kim*

†Center for Neuro-Medicine, Republic of Korea Institute of Science and Technology, Republic of Korea; *Department of Neurology, College of Medicine, Seoul National University, Seoul, Republic of Korea; †Department of Anatomy, College of Medicine, Inha University, Incheon, Republic of Korea; ‡Department of Neurology, College of Medicine, Eulji University, Daegom, Republic of Korea

(O-5) (12 min) Astrocyte Injury and Secondary Demyelination Induced by Intracerebral Injection of AQP4-IgG and Complement in Mouse Brain — Yoshiaki Takai†, Yoichiro Abe†, Tasturo Misu*, Kazuhiro Kurosawa*, Yoshiyuki Takahashi†, Hiroshi Kuroda†, Ichiro Nakashima†, Shuhei Nishiyama*, Masato Yasu†, Kazuo Fujihara*, Masashi Aoki†

†Department of Biomedicine, University Hospital Basel, Basel, Switzerland; ‡Department of Multiple Sclerosis Therapeutics, Tokohu University School of Medicine, Sendai, Japan; †Department of Pharmacology, Keio University School of Medicine, Tokyo, Japan

### Oral Session-2: Neuroimaging (11:20-12:20)

Chairperson: Chong-Tin Tan (Malaysia) & Riwanti Estasari (Indonesia)

(O-6) (12 min) Structural MRI Substrates of Cognitive Impairment in Neuromyelitis Optica — Yao Liu†, Ying Fu*, Menno M. Schoonheim*, Nan Zhang†, Moli Fan†, Lei Su†, Yi Shen†, Yaping Yan†, Li Yang†, Qihui Wang†

†Department of Neurology and Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin, 300052, P. R. China; ‡Department of Radiology and Nuclear Medicine, Neuroscience Campus Amsterdam, VU University Medical Center, Amsterdam 1007 MB, The Netherlands


Department of Neurology, Mental Health Clinic, †Department of Radiology, ‡Biometric Research Branch, Research Institute and Hospital of National Cancer Center, Republic of Korea; †Department of Biomedical Engineering, Hanyang University, Republic of Korea

(O-8) (12 min) Comparison of Myelin Water Fraction Values in White Matter Lesions Between Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder — In Hye Jeong*, Joon Yul Choi*, Su-Hyun Kim†, Jae-Won Hyun*, AeRan Joung†, Jongho Lee*, Ho Jin Kim†

Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Republic of Korea; †Department of Electrical and Computer Engineering, Seoul National University, Seoul, Republic of Korea

(O-9) (12 min) Differences and Similarities in Brain MRI Features between Japanese and Caucasian Patients with Multiple Sclerosis and Their Impact on Disability Progression — Nakamura Y†, Alternatt A†, Matsushita T†, Gaetano L†, Sprenger T†, Radue EW†, Bauer L†, Saida T‡, Kappos L‡, Kira J‡

†Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; ‡Medical Image Analysis Center (MIAC), University Hospital Basel, Basel, Switzerland; †DKD Helis Klinik Wiesbaden, Wiesbaden, Germany; §Neurology and Biomedicine, University Hospital Basel, Basel, Switzerland; ¶Institute of Neurotherapeutics, Kyoto, Japan; †Department of Neurology, Kyoto Min-ken-Central Hospital, Kyoto, Japan; Kyoto University Hospital, Kyoto, Japan

(O-10) (12 min) Teriflunomide Slows Brain Volume Loss in Relapsing MS: A SIEVA Analysis of the TEMSO MRI Dataset — E-W Radue†, T Sprenger†, L Gaetano†, N Mueller-Lenke†, J Wuerfel†, JS Wolinsky†, K Thangavelu†, S Cavalier†

†Medical Image Analysis Centre (MIAC AG), Basel, Switzerland; †University Hospital Basel, Basel, Switzerland; †DKD Helis Klinik, Wiesbaden, Germany; †University of Texas Health Science Center at Houston, Houston, TX, USA; †Genzyme, a Sanofi company, Cambridge, MA, USA; †equal contribution

### Lunch & Poster Viewing (12:20-13:15)
Oral Session-3: MS Genetics (13:15-13:51)
Chairperson: Michael Barnett (Australia) & Makoto Matsui (Japan)

(O-11) (12 min) Association of Genetic Variant Rs763361 on CD226 Gene in Relapsing Remitting Multiple Sclerosis (RRMS) Patients Compared to Control Group
1Isfahan University of Medical Sciences, Applied Physiology Research Center (APRC); 2Tarbiat Modares University, Tehran, IRAN

(O-12) (12 min) Latitude and HLA-DRB1 Alleles Affect Emergence of CSF IgG Abnormalities in MS
Authors: Masaaki Nino1, Shinya Sato1, Toshiyuki Fukazawa2, Satoshi Yoshimura3, Shin Hisahara4, Takuya Matsushita5, Yurik Nakamura6, Noriko Isobe7, Kazuto Yoshida7, Ken Yamamoto7, Ken Nakamura7, Jun-ichi Kira7
1Hokkaido Medical Center, Sapporo, Japan; 2Kyushu University, Fukuoka, Japan; 3Asahikawa Red Cross Hospital, Asahikawa, Japan; 4Obihiro Kosei General Hospital, Obihiro, Japan

(O-13) (12 min) Genome-Wide Association Study (GWAS) for Clinical Phenotypes of Multiple Sclerosis in The Japanese
Authors: Takuya Matsushita1, Shinya Sato1, Ken Yamamoto2, Yuri Nakamura1, Jun-ichi Kira1, the Japan Multiple Sclerosis Genetics Consortium
1Department of Neurology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; 2Department of Medical Chemistry, School of Medicine, Kurume University, Kurume, Japan

Oral Session-4: MS Treatment (13:51-14:43)
Chairperson: Allan Kermode (Australia) & Alexandra Seewann (Australia)

(O-14) (13 min) Durable Effect of Alemtuzumab on Clinical Outcomes Over 5 years in Treatment-Naive Patients With Active Relapsing-Remitting Multiple Sclerosis Despite Most Patients Not Receiving Treatment for 4 Years: CARE-MS I Extension Study
Authors: PA McCombe1, H-P Hartung2, E Havrdova3, KW Selma4, DH Margolin5, L Kasten6, DAS Compston7
1The University of Queensland, Brisbane, Australia; 2Heinrich-Heine University, Düsseldorf, Germany; 3First Medical Faculty, Charles University in Prague, Prague, Czech Republic; 4Medical University of Lodz, Lodz, Poland; 5Genzyme, a Sanofi company, Cambridge, MA, USA; 6PROMETRIKA, LLC, Cambridge, MA, USA; 7University of Cambridge, Cambridge, UK

(O-15) (13 min) Alemtuzumab Has Durable Efficacy on MRI Outcomes and Brain Atrophy Over 5 Years With Most Patients Free From Treatment for 4 Years: CARE-MS II Extension Study
Authors: J King1, A Traboulsee2, DAS Compston3, H-P Hartung4, E Havrdova5, KW Selma6, DH Margolin7, K Thangavelu8, F Barkhof9
1Royal Melbourne Hospital, Melbourne, Australia; 2The University of British Columbia, Vancouver, British Columbia, Canada; 3University of Cambridge, Cambridge, UK; 4Heinrich-Heine University, Düsseldorf, Germany; 5First Medical Faculty, Charles University in Prague, Prague, Czech Republic; 6Medical University of Lodz, Lodz, Poland; 7Genzyme, a Sanofi company, Cambridge, MA, USA; 8VU University Medical Centre, Amsterdam, The Netherlands

(O-16) (13 min) Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis in A Western Australian Cohort
Authors: MJ Fabis-Pedrini1, D Hall2,3, G Cul7,8, BM Augustson2,3, S Walters1, C Crosbie2, WM Carroll4, AG Kermode1
1Centre for Neuromuscular and Neurological Disorders, Western Australian Neuroscience Research Institute, Perth, University of Western Australia; 2Haematology Care Centre, Sir Charles Gardiner Hospital, Queen Elizabeth II Medical Centre, Perth, Western Australia; 3PathWest Laboratory Medicine, Queen Elizabeth II Medical Centre, Perth, Western Australia; 4Department of Neurology, Sir Charles Gardiner Hospital, Queen Elizabeth II Medical Centre, Perth, Western Australia; 5Institute of Immunology and Infectious Diseases, Murdoch University, Perth, Western Australia

(O-17) (13 min) The Role of α4 Integrins on Theiler’s Murine Encephalomyelitis Virus (TMEV) Induced Demyelinating Disease, An Infectious Animal Model for Multiple Sclerosis (MS)
Authors: Hirono Y1, Kobayashi K1, Tomiki H1, Ichikawa M1 and Koh CS2
1Department of Biomedical Laboratory Sciences, Graduate School of Medicine, Shinshu University, Matsumoto, 390-8621, Nagano, Japan

14:43-15:15 Coffee Break & Poster Viewing

PACTRIMS Teaching Course
How to Diagnose and Treat Indistinguishable Early Cases of Inflammatory CNS Disease in Asians
Chairperson: Kazuo Fujihara (Japan) & Byung-Jo Kim (Republic of Korea)

1. New Diagnostic Criteria for NMOSD
   Kazuo Fujihara (Japan)
2. Clinical Spectrum of a Gray Zone between MS and NMO in Asians
   Sasitorn Siritho (Thailand)
3. Management of Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorders in Resource Poor Settings
   Lekha Pandit (India)

16:45-17:00 Coffee Break
# PROGRAMME OVERVIEW

**Saturday, 21 November 2015**

**Grand Ballroom**

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<td>10:00-10:30</td>
<td><strong>Coffee Break &amp; Poster Viewing</strong></td>
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<tr>
<td>10:30-12:30</td>
<td><strong>Main Symposium-3</strong>&lt;br&gt;<strong>Update on Biomarkers for Diagnosis and Monitoring of MS</strong>&lt;br&gt;Chairperson: Ernest Willoughby (New Zealand) &amp; Naraporn Prayoonwiwat (Thailand)&lt;br&gt;1. The Use of MRI in the Diagnosis, Management and Research of MS&lt;br&gt;— Alexandra Seewann (Australia)&lt;br&gt;2. Can OCT Really be a Monitor of Global Axonal Loss in MS?&lt;br&gt;— Anneke van der Walt (Australia)&lt;br&gt;3. Potential Biomarkers for MS in Asians&lt;br&gt;— Takuya Matsushita (Japan)&lt;br&gt;4. How to Use Biomarkers for Diagnosis and Monitoring of MS in Asians&lt;br&gt;— Ching-Piao Tsai (Taiwan)</td>
</tr>
<tr>
<td>12:30-12:45</td>
<td><strong>Closing and Award Ceremony</strong>&lt;br&gt;1. Award Ceremony&lt;br&gt;— Jun-ichi Kira (Japan)&lt;br&gt;2. Remarks by the Chairman, 2016 Local Organising Committee&lt;br&gt;— Naraporn Prayoonwiwat (Thailand)&lt;br&gt;3. Closing Remarks by the Chairman, 2015 Local Organising Committee&lt;br&gt;— Kwang-Kuk Kim (Republic of Korea)</td>
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32ND CONGRESS
OF THE EUROPEAN COMMITTEE
FOR TREATMENT AND RESEARCH
IN MULTIPLE SCLEROSIS

AND

21ST ANNUAL CONFERENCE
OF REHABILITATION IN MS

14–17 SEPTEMBER 2016
LONDON, UNITED KINGDOM
Anti-IL6 Receptor Monoclonal Antibody Therapy in NMO

Takashi Yamamura (Japan)
Department of Immunology, National Institute of Neuroscience, NCNP
Multiple Sclerosis Center, NCNP, Tokyo, Japan

Neuromyelitis optica (NMO) is an autoimmune disease of the central nervous system, associated with elevation of anti-aquaporin 4 (AQP4) antibodies. We reported previously that patients with NMO have an increased number of plasmablasts (PBs) producing anti-AQP4 antibodies in the peripheral blood (Chihara et al. PNAS 2011). Increased PBs are also detected in the cerebrospinal fluid of NMO during relapse (Chihara et al. PLoS One 2013). Given that survival of PBs and anti-AQP4 antibody production would depend on IL-6 signaling, we applied anti-IL-6 receptor antibody tocilizumab (TCZ) for treatment of NMO. This trial has been successful in reducing relapses and neurogenic pain in serious cases with NMO and opened the way to efficient control of NMO by blocking IL-6 receptors (Araki et al. Mod Rheumatol 2012; Neurrol 2014). The results also pointed to the central role of IL6 in the pathogenesis of NMO. TCZ treatment was found to induce regulatory cell populations including CD56 high NK cells and foxp3+ regulatory T cells in the peripheral blood, which may partly account for the mechanism for the efficacy of TCZ.

INVITED LECTURE

Opening Lecture

L-1
Anti-IL6 Receptor Monoclonal Antibody Therapy in NMO

Takashi Yamamura (Japan)
Department of Immunology, National Institute of Neuroscience, NCNP
Multiple Sclerosis Center, NCNP, Tokyo, Japan

Neuromyelitis optica (NMO) is an autoimmune disease of the central nervous system, associated with elevation of anti-aquaporin 4 (AQP4) antibodies. We reported previously that patients with NMO have an increased number of plasmablasts (PBs) producing anti-AQP4 antibodies in the peripheral blood (Chihara et al. PNAS 2011). Increased PBs are also detected in the cerebrospinal fluid of NMO during relapse (Chihara et al. PLoS One 2013). Given that survival of PBs and anti-AQP4 antibody production would depend on IL-6 signaling, we applied anti-IL-6 receptor antibody tocilizumab (TCZ) for treatment of NMO. This trial has been successful in reducing relapses and neurogenic pain in serious cases with NMO and opened the way to efficient control of NMO by blocking IL-6 receptors (Araki et al. Mod Rheumatol 2012; Neurrol 2014). The results also pointed to the central role of IL6 in the pathogenesis of NMO. TCZ treatment was found to induce regulatory cell populations including CD56 high NK cells and foxp3+ regulatory T cells in the peripheral blood, which may partly account for the mechanism for the efficacy of TCZ.

PACTRIMS Basic Science Lecture

L-2
In Vivo Analysis of Axon Damage in Multiple Sclerosis Models

Martin Kerschensteiner (Germany)
Institute of Clinical Neuroimmunology, Hospital of the Ludwig-Maximilians University, Munich, Germany

Here, I want to discuss how advances in in vivo microscopy and mouse genetics can improve our understanding of the cellular, subcellular and molecular mechanisms that mediate neuroinflammatory tissue damage. To illustrate this approach I will use our recent insights into the in vivo pathogenesis of immune-mediated axon damage as an example. Immune-mediated axon damage plays a crucial role in inflammatory diseases of the central nervous system (CNS) like multiple sclerosis (MS), as we know by now that the number of axons damaged by immune cells critically determines the clinical disability of MS patients. However we still understand very little about the process that leads to axon damage.

In the past years we have used an in vivo imaging approach to investigate the pathogenesis of immune-mediated axon damage in an animal model of multiple sclerosis. By time-lapse imaging of fluorescently labeled axons we could follow the slow and spatially restricted degeneration of axons in inflammatory CNS lesions. This “focal axonal degeneration” appears to be a novel type of axonal degeneration that is characterized by intermediated stages that can persist for several days and progress either to the degeneration or full recovery of the affected axons.

To better understand the relation between structural and functional axon damage in neuroinflammatory lesions, we have now directly measured axonal transport of fluorescently labelled organelles such as mitochondria in neuroinflammatory lesions. These studies revealed a pervasive state of axonal dysfunction in acute neuroinflammatory lesions. This state is characterized by transport arrest that occurs in the absence of structural alterations of axon morphology, myelin sheaths and microtubule tracks. While such transport deficits recover within in days in acute MS models they persist long-term in chronic neuroinflammatory lesions where they cause distal organelle depletion and axon dystrophy.

Using these examples, I hope to illustrate how recent advances in light microscopy can help us to reveal and mechanistically dissect neuroinflammatory tissue damage as it happens in the living CNS.

PACTRIMS Educational Lecture

L-3
NMO-IgG Negative Idiopathic Recurrent Transverse Myelitis

Kwang-Kuk Kim (Republic of Korea)
Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Objective: To determine characteristics of the clinical profile and magnetic resonance imaging of NMO-IgG(-) idiopathic recurrent transverse myelitis (iRTM).

Design: A retrospective analysis of 81 cases was conducted. Patients were classified as having NMO-IgG(-) iRTM on the basis of clinical manifestations of myelopathy, brain and spinal cord MRI findings and seronegative NMO-IgG antibody study.

Setting: Asan Medical Center, Seoul, South Korea, from January 1, 2000, through December 31, 2013.

Main outcome Measures: Presenting symptoms and clinical manifestations, relapsing times, relapsing interval, MRI features, IgG index and oligoclonal bands in cerebrospinal fluid, and other vasculitis-related antibody.

Result: NMO-IgG(-) iRTM occurred predominantly in male patients and presented more often with acute transverse myelitis with long cord lesions (more than 3 vertebral bodies) (45.6%) than did second myelitis (23.4%). More than 2 relapses occurred in 18 cases (22.2%) of NMO-IgG(-) iRTM. The involved long segments of spinal cord on T2-weighted images were 45.6%, 23.4% and 44.4% each in 1st attack, 2nd attack and 3rd attack. But partial long cord lesions also detected in 34.9% of total long cord lesions. Relapsing interval time within 1 year was 61%. Enhancing lesions appeared mostly in posterior columns, the spinothalamic tract and spinocerebellar tracts of white matter. Additionally, almost all patients with NMO-IgG(-) iRTM had normal cerebrospinal fluid indexes.

Conclusion: NMO-IgG(-)RTM might be a disease entity distinct from NMO-IgG(+)NOMOSD, or multiple sclerosis-associated RTM, differing in its male predominance, absence of oligoclonal bands, frequent presentation as acute transverse myelitis with partial long cord lesions and normal brain MRI.

Main symposium-1

Early Aggressive Treatment versus Cell/Neuroprotection Therapy in MS and NMO
L-4
Keynote Lecture: Does Early Aggressive Treatment of MS Prevent Progression?
Michael Barnett (Australia)
Information not available at time of printing.

L-5
Human Recombinant Monoclonal Antibodies as Therapy for Demyelinating and Degenerative CNS Disorders
Moses Rodriguez (USA)
Departments of Neurology and Immunology, Mayo Clinic, Minnesota, USA
Our laboratory has identified human monoclonal antibodies from patients with serum gammopathies that bind to central nervous system (CNS) cells and promote CNS repair. All of these antibodies have been shown to cross the blood brain barrier. The antibodies bind to antigens on lipid rafts of oligodendrocytes or neurons to induce calcium influx and signal transduction to enhance either proliferation of progenitor oligodendroglia or promote neurite extension of neurons. Antibody rHIgM22, which binds to oligodendrocytes, has already completed Phase I clinical trials and shown absolutely no toxicity in 72 patients and a hint of efficacy in patients with long term fixed neurologic deficits in multiple sclerosis. A clinical trial testing the antibody in patients following an acute exacerbation in multiples sclerosis patients is being planned. Antibody rHIgM12 has resulted in increase in survival in patients with serum gammopathies that bind to central nervous system (CNS) cells and promote CNS repair. All of these antibodies have provided validation of registry-based comparative treatment outcomes analyses by replicating several Phase 3 trial results using propensity matching procedures in lieu of randomization. Recent publications from the MSBase registry have demonstrated the superiority of either natalizumab or fingolimod over interferon-beta or glatiramer as a switching choice after on –treatment relapse, and further demonstrated the relative superiority of natalizumab over fingolimod in the same scenario. Long-term outcome modeling using the same registry dataset is evolving, but several analyses have no conclusively demonstrated the beneficial effect of disease-modifying drug treatment in reducing disability accumulation in relapsing-remitting MS.

L-6
Real-World Evidence for Treatment Effectiveness and Treatment Sequences in MS
Helmut Butzkueven (Australia)
Department of Medicine, Melbourne Brain Centre at the Royal Melbourne Hospital, University of Melbourne, Victoria, Australia
The term ‘Real-world evidence’ in Multiple Sclerosis encompasses a wide variety of different data collection methodologies. Registries can provide structured, prospectively collected real-world evidence for analysis of treatment efficacy, treatment sequencing outcomes and serious adverse event identity and frequency. The information from multiple centres is collected prospectively using a minimum agreed dataset and observation frequency. The major barrier to participation is cost and time. Therefore, data collection systems ideally should provide resources and other value-adds to clinicians in return for this considerable burden. The globally operative MSBase is a very successful collaborative, prospective Multiple Sclerosis registry. It has attracted over 35,000 patient records at more than 200 MS centres, and its median recorded visit density is, at 5.5 months, better than most sponsored Phase IV studies. Registry analysts

L-7
Autologous MSCT as a Therapy in NMO
Ying Fu (China)
Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin, China
Objective: This clinical trial was carried out to evaluate safety and efficacy of autologous bone marrow-derived mesenchymal stem cells (MSC) as a potential treatment for neuromyelitis optica spectrum disorder (NMOSD).
Methods: Patients with NMOSD were recruited. All patients received a single intravenous infusion of $1.0 \times 10^8$ autologous MSC within 3-4 derivation generated from bone–marrow. The primary endpoints of the study were efficacy as reflected by reduction of annualized relapse rates (ARR) and inflammatory lesions observed by MRI. Secondary outcomes were recovery by assessing the Expanded Disability Status Scale (EDSS), visual acuity, retinal nerve fiber layer thickness, optic nerve area diameter and upper cervical cord area.
Results: At 12 months after MSC infusion, the mean ARR was reduced (1.1 vs 0.3, $p = 0.002$), and the T2 or gadolinium-enhancing T1 lesions decreased in the optic nerve and spinal cord. Disability in these patients was reduced (EDSS, 4.3 vs 4.9, $p = 0.021$; Visual acuity, 0.4 vs 0.5, $p = 0.007$). The patients had an increase in retinal nerve fiber layer thickness (73 vs 81 μm, $p < 0.001$), optic nerve diameters (2.3 vs 2.6 mm, $p < 0.001$) and upper cervical cord area ( 69 vs 73 mm², $p < 0.001$). We did not identify any serious MSC-related adverse events.
Conclusion: MSC infusion is safe and this treatment dramatically reduces the relapse frequency, and mitigates neurological disability with neural structures in the optic nerve and spinal cord recover.

PACTRIMS Presidential Symposium
Distinct and Common Aspects of Multiple Sclerosis and Neuromyelitis Optica

L-8
Distinguishing NMOSD from MS: Current and Future Neuroimaging Perspectives
Ho Jin Kim (Republic of Korea)
Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Republic of Korea
Magnetic resonance imaging (MRI) markers have become important for both distinguishing neuromyelitis optica spectrums disorder (NMOSD) from multiple sclerosis (MS) and elucidating
the different pathophysiology between the two diseases. Differentiating these conditions is of prime importance because early initiation of effective immunosuppressive therapy is the key to preventing attack-related disability in NMO, whereas some disease-modifying drugs for MS may exacerbate the disease.

Recently revised diagnostic criteria by the International Panel for NMO diagnosis included more detailed neuroimaging characteristics of NMO. Detection of a longitudinally extensive spinal cord lesion associated with acute myelitis is the most specific neuroimaging characteristic of NMO and is very uncommon in adult MS. Brain lesions in patients with NMO are common on conventional MRI and some may be relatively unique by virtue of localization and configuration which can be helpful in the diagnosis of NMO.

In addition to these conventional MRI findings, advanced quantitative imaging measures, including proton MR spectroscopy, diffusion tensor imaging, magnetization transfer imaging, quantitative MR volumetry, and ultrahigh-field strength MRI are beginning to offer new insights into the pathophysiolo gy of NMO and MS and further differentiates these two diseases. Careful inspection of near-microscopic lesions using ultra high-field MRI can help in differentiating NMO from MS and findings from diffusion tensor imaging and brain volumetry studies suggest widespread brain injury in NMO that are not identified using conventional MRI. Although studies of NMO using advanced MRI techniques are still scarce and further confirmation studies are needed, the integration and combination of results from different imaging modalities might provide a new way to improve the diagnostic accuracy and to better understand the pathomechanisms of NMO.

L-9 Anti-MOG Antibody in NMO and Other Demyelinating Diseases
Douglas Kazutoshi Sato (Japan)
Tohoku University School of Medicine, Sendai, Japan
Neuromyelitis optica spectrum disorders (NMO) are characterized by severe optic neuritis and/or longitudinally extensive transverse myelitis, and some brain lesions are also unique to NMO. Serum autoantibodies against aquaporin-4 (AQP4) are detected in most cases of NMO. However, some patients with NMO remain seronegative despite repetitive testing during attacks with highly sensitive cell-based assays. The differential diagnosis of NMO is not restricted to multiple sclerosis and it includes many diseases that can produce longitudinally extensive myelitis and/or optic neuritis. Some clinical features, imaging, and laboratory findings can be helpful to distinguish NMO patients with AQP4 antibodies from those who are negative. More recently, we found also that a fraction of seronegative NMO patients had antibodies against myelin oligodendrocyte glycoprotein (MOG), and these patients seem to have a more limited phenotype with single or low number of attacks. However, MOG antibodies are not limited to patients with NMO phenotype, so the clinical spectrum associated to MOG antibodies include acute disseminated encephalomyelitis and pediatric cases with demyelinating lesions.

Katsuhisa Masaki (Japan)
Department of Neurological Therapeutics, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
Multiple sclerosis (MS) and neuromyelitis optica (NMO) are inflammatory demyelinating diseases of the CNS. The pathological hallmark of MS is sharply demarcated demyelinating plaques with relative axonal preservation. In contrast, NMO severely affects both axons and myelin of the optic nerves and spinal cord, resulting in necrotic cavitation. The discovery of anti-aquaporin-4 (AQP4) antibody indicates that NMO is distinct from MS with a different etiology.

Pathological studies demonstrated that astrocytes were selectively targeted in NMO as evidenced by the extensive loss of AQP4 and gial fibrillary acidic protein, as well as perivascular deposition of immunoglobulins and activated complement within lesions with a relative preservation of myelin. We have demonstrated an extensive loss of AQP4 in active lesions of Baló’s disease and loss of AQP4 and connexin 43 (Cx43) in actively demyelinating lesions of MS and NMO. Moreover, we and others recently reported that early NMO lesions showed oligodendrocyte apoptosis associated with a selective loss of myelin-associated glycoprotein (distal oligodendrogliopathy) in addition to typical NMO features, such as a loss of AQP4. Such pathological features resembled those of MS lesion patterns II and III.

Although the pathomechanism of distal oligodendrogliopathy could be occurred in MS and NMO is still remain unknown, extensive loss of astrocytic Cx43 may induce secondary damage for oligodendrocytes/myelin due to disconnection of heterotypic Cx43/Cx47 gap junctions in the affected white matter. Now, we undertake a neuropathological study about the expression of glucose and lactate transporters in the lesions of MS and NMO because energy failure caused by insufficient transport of nutritional substances may facilitate the extension of demyelinating lesions.

In this session, I would like to introduce the common and distinct pathological features with our data in MS and NMO, such as Cx43/AQP4 astrocytopathy, distal oligodendrogliopathy and energy transporters.

Main symposium-2 Environmental Influences in MS and NMO
L-11 Environmental Influences on Demyelinating Disease in Caucasians
Bruce Taylor (Australia)
Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia
Multiple sclerosis (MS) is a complex disorder of the central nervous system with both inflammatory and neurodegenerative characteristics. MS risk is influenced by several well described environmental, genetic and personal factors. Including latitude of residence and birth, sun exposure particularly in adolescence, vitamin D levels and intake particularly in adolescence and early adult life, adolescent obesity and smoking. In addition nearly 200 genetic variables have been described as associated with MS risk. Exposure to, and the timing of exposure to the Epstein Barr virus significantly influences...
the risk of developing MS. However the factors that are associated with the risk of developing MS are not necessarily the same as the factors that are associated with progression of MS. Understanding how these factors influence MS risk and interact with genetic and personal factors can provide important information that may allow public health interventions to reduce population risk of MS and also personal risk of MS in those at greatest risk (first degree relatives). Additionally delineating the potentially modifiable factors that drive MS progression may again allow non-pharmacological interventions to be combined with disease modifying therapies to modify outcomes.

Understanding environmental factors that influence risk and progression of NMO spectrum disorder is a developing field and these factors may not be the same as those that influence MS. This presentation will evaluate the evidence for environmental factors in MS and related disorders onset and progression as well as the areas of future research that may allow us to understand and modify MS risk.

L-12

Photo-Immunology in Demyelinating Disease
Scott Byrne (Australia)
The University of Sydney, New South Wales, Australia

Living on a sun-drenched planet has traditionally required adaption to and protection from the harmful effects of solar ultraviolet (UV) radiation. This has been (and continues to be) necessary to combat the rising incidence of skin cancer. However, convincing epidemiological and recent empirical evidence also supports a Vitamin D-independent protective effect of sunlight against a range of diseases including asthma, colitis, liver inflammation, obesity, diabetes, and cardiovascular disease. Central Nervous System (CNS)-autoimmune diseases such as multiple sclerosis (MS) show the most striking inverse correlation with UV. Indeed, higher amounts of UV reduce the incidence of a patient’s first clinical diagnosis of CNS demyelination, many of whom will develop clinically confirmed MS. This is important because it shows that UV is able to prevent both the development and progression of MS. However, despite intense community interest in understanding how increasing the amount of UV we receive leads to a reduction in autoimmune diseases, the mechanisms by which UV provides this protection remains unknown. We have used the murine CNS autoimmune model, experimental autoimmune encephalomyelitis (EAE) to investigate the cellular and molecular mechanisms by which UV protects the host from autoimmune disease. Others have demonstrated that this protection from EAE is not mediated by UV-induced Vitamin D3 suggesting another UV-induced event is responsible for protection from autoimmune disease. We hypothesise that activation of immunoregulatory pathways may explain how sunlight protects us from a CNS-targeted autoimmune attack.

Understanding the cellular and molecular mechanisms by which UV suppresses adaptive immune responses will allow us to design novel therapeutic strategies to prevent and treat autoimmunity.

Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.

The number of multiple sclerosis (MS) patients in Asia has steadily increased, although the environmental influence on MS remains to be established. In Japan, results from four nationwide surveys of MS conducted between 1972 and 2004 revealed a four-fold increase in the estimated number of MS patients in 2003 compared with 1972; a shift in the peak age at onset from early 30s in 1989 to early 20s in 2003; and an increase in the number of MS patients with brain lesions that fulfilled the Barkhof criteria (Barkhof brain lesions) with advancing birth year. The changes in MS epidemiology and features have coincided with Japan’s rapid modernization. We have explored the factors contributing to these changes.

1) Genetic background: We reported that HLA-DRB1*04:05 is the most common susceptibility allele for MS in Japan, and that DRB1*0405 carriers comprise >40% of all Japanese MS patients. HLA-DRB1*0405-positive MS patients present at a younger age at onset and have fewer brain lesions, a lower frequency of CSF IgG abnormalities, and a slower progression. We also determined gene dosage effects of DRB1*04:05 in MS Severity Score (MSSS); MSSS decreased by 0.57 per DRB1*04:05 allele. The recent increase in the number of MS patients in this subgroup may explain the decreased age at onset, as shown by the fourth nationwide survey in Japanese MS patients. Among the HLA-DRB1*0405-negative MS patients, DRB1*1501 is a risk factor for MS and DRB1*1501 carriers exhibit high frequencies of Barkhof brain lesions and CSF IgG abnormalities.

2) Infection: HLA-DRB1*0405-negative MS patients have higher frequencies of Epstein–Barr virus infection, while both HLA-DRB1*0405-positive and -negative MS patients have a lower frequency of Helicobacter pylori infection, which reflects improved sanitation in childhood. We also found that Chlamydia pneumoniae infection confers CSF IgG abnormalities.

3) Latitude: Higher latitude correlated with increased susceptibility to MS in the Japanese population. Multivariate analysis revealed that latitude and DRB1*04:05 had an independent negative association with MSSS, and that latitude was positively associated with Barkhof brain lesions and CSF IgG abnormalities.

4) Vitamin D: We also found that serum 25(OH) vitamin D and 1,25(OH)2 vitamin D levels were lower in Japanese patients with MS, especially in secondary progressive MS patients, compared with healthy controls.

Environmental and genetic factors differentially contribute to MS susceptibility, disability progression, brain MRI lesions, and CSF IgG abnormalities in Asians.

L-13

Environmental Influences on Demyelinating Disease in Asians
Jun-ichi Kira (Japan)

PACTRIMS Teaching Course
How to Diagnose and Treat Indistinguishable Early Cases of Inflammatory CNS Disease in Asians

L-14

New Diagnostic Criteria for NMO
Kazu Fujiwara (Japan)
Department of Multiple Sclerosis Therapeutics, Tohoku University Graduate School of Medicine, Sendai, Japan
More than a century has passed since the first report of neuromyelitis optica (NMO). The discovery of NMO-specific aquaporin-4 (AQP4)-IgG has truly accelerated clinical and research efforts towards understanding the disease, the diagnostic criteria of NMO have evolved. The International Panel on NMO Diagnosis has recently published the new diagnostic criteria of NMOSD (NMOSD is the unifying term.). The new criteria are essentially based on AQP4-IgG serostatus (1. NMOSD with AQP4-IgG and 2. NMOSD without AQP4-IgG or with unknown serostatus) and core clinical characteristics of NMOSD, namely, optic neuritis, acute myelitis, and area postrema and some other brain syndromes, although alternative diagnoses should be carefully ruled out. Unlike AQP4-IgG-positive NMOSD requiring only one core clinical feature, two or more clinical characteristics are needed for diagnosing NMOSD in cases without AQP4-IgG or those with unknown serostatus, but we need to be careful that this group may be heterogeneous. In fact, a fraction of patients with seronegative NMOSD are positive for myelin oligodendrocyte glycoprotein (MOG)-IgG and have some unique clinical, MRI and laboratory features. We anticipate that the new diagnostic criteria of NMOSD will facilitate the early diagnosis and treatment decision, but allow for future revisions, especially in seronegative NMOSD.

L-15
Clinical Spectrum of a Gray Zone between MS and NMO in Asians
Sasitorn Siritho (Thailand)
Siriraj Hospital, Mahidol University, Bangkok, Thailand
Acquired idiopathic inflammatory central nervous system (CNS) disorders encompasses heterogeneous groups of diseases i.e. Multiple Sclerosis (MS), neuromyelitis optica spectrum disorders (NMOSD), acute disseminated encephalomyelitis (ADEM), and others. NMO Diagnostic criteria 2006 mandates that a patient exhibits both optic neuritis and transverse myelitis, together with 2 out of the 3 supportive criteria; spinal cord involvement equal to or longer than 3 vertebral segments (VBs), a negative brain MRI at onset and the presence of AQP4-antibody. The term “neuromyelitis optica spectrum disorder” (NMOSD) has been proposed to refer to the spectrum of AQP4-antibody related diseases, including definite NMO. However, some patients with the clinical characteristics of NMO/NMOSD are AQP4-negative despite the use of highly sensitive cell-based assays. Recently, the 2015 International consensus diagnostic criteria for NMOSD had been proposed. The new criteria unify the terms NMO and NMOSD and categorize it to seropositive and seronegative NMOSD. On the other hand, diagnosis of MS, based on the 2010 Revised McDonald Diagnostic Criteria, comprised of dissemination in time and space of the clinical manifestations suggestive of MS and no better explanation. When patients come with first demyelinating event i.e. optic neuritis or myelitis or with non-typical clinical and radiological characteristics of each disease, it could be a challenge to distinguish those two apart. Since the prevalence of NMOSD is high Among Asian countries and the treatment differs therefore it is crucial to distinguish early on between the two diseases to ensure appropriate treatment. Hereby some clinical points have been mentioned regarding those issues.

L-16
Management of Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorders in Resource Poor Settings
Lekha Pandit (India)
Nitte University, Mangalore, Karnataka, India
Multiple sclerosis (MS) and Neuromyelitis optica spectrum disorders (NMOSD) are prevalent in every region of the world. The estimated number of people with MS alone, has increased from 2.1 million in 2008 to 2.3 million in 2013 (Atlas of MS,2013). Significant global inequalities exist in the availability of specialist care and access to diagnosis and treatment of these disorders. The lack of universal health coverage and non-availability of free/ subsidized disease modifying therapies further reduce the number of patients who can be brought under the umbrella of comprehensive care.

In this background management strategies in resource poor settings should include the creation of disease registries in teaching/academic centers. The latter most often have access to subsidized inpatient care and multidisciplinary treatment. In house protocols for magnetic resonance imaging and AQP4-antibody assays and the use of generic drugs bring down cost of acute care. The generous use of cheap and easily available immunosuppressants such as Azathioprine and Mycophenolate mofetil supported by oral steroids form the back bone of therapy particularly for NMOS disorders. Strategies that include the use of first line disease modifying drugs for induction of remission followed by oral immunosuppressants for maintenance therapy are useful in the management of MS. Long term care can be achieved through active participation of sensitized community physicians and telephonic follow-up with the help of trained nurse/ coordinators at primary sites. Using a south Indian demyelinating disease registry as a model these strategies will be discussed in detail.

Main symposium-3
Update on Biomarkers for Diagnosis and Monitoring of MS

L-17
The Use of MRI in the Diagnosis, Management and Research of MS
Alexandra Seewann (Australia)
Western Australian Neuroscience Research Institute, Perth, Australia
Brain and spinal cord MRI are the most important paraclinical tools for the diagnosis and management of MS. Presently, several choices for disease modifying therapy are available, but it cannot be reliably predicted how an individual patient will respond to a particular therapy. Therefore, MRI has become an integral component of therapy selection and monitoring by assessing the number and volume of white matter lesions. However, both counting, and volume assessment of white matter lesions correlate relatively weakly with clinical measures. This so-called clinico-radiological paradox has several explanations. First, conventional MRI is sensitive for MS related changes, but lacks pathological specificity; lesions are heterogeneous, and may
reflect very different tissue damage, which is neglected when only number and volume of lesions are measured. Second, these measures do not take into account the relevance of the location where lesions occur. Third, a vast majority of MS related damage, such as cortical lesions and diffuse changes in the white and grey matter go undetected with conventional MRI. New imaging techniques can detect pathology which is unseen with conventional MRI. Furthermore, they allow the detection of dynamic changes of the pathological process; therewith MRI contributes to our understanding how MS pathology evolves. This presentation will review some of the new MRI techniques currently used for clinical studies and research, and explain MRI-histopathological correlations. The main focus is therewith on understanding what can and what cannot be seen with the individual MRI techniques.

L-18
Can OCT Really be a Monitor of Global Axonal Loss in MS?
Anneke van der Walt (Australia)
Melbourne Brain Centre, Department of Medicine, University of Melbourne, Victoria, Australia

Optical coherence tomography (OCT) is a noninvasive, high-resolution technique that uses near-infrared light to generate cross-sectional tomographic images of retinal tissues, including the retinal nerve fiber layer (RNFL). The ability to measure the RNFL allows for an unique window into axonal changes in an unmyelinated part of the central nervous system and, over past 15 years, the application of OCT technology has yielded valuable insights into the neurodegenerative processes occurring in MS. Studies focusing on RNFL loss after acute and chronic optic neuritis and in extant multiple sclerosis have shown correlations with clinical, electrophysiological and MRI measures. RNFL thinning can be caused by retrograde degeneration of axons after ON but possibly also by trans-synaptic degeneration due to chronic lesions in the posterior optic pathways. Furthermore, improvements in the technology and a focus on retinal ganglion cell layer (RGCL) loss at the macula has made it possible to detect axonal loss early after optic neuritis in addition to different subtypes of MS. Indeed, OCT-derived outcome measures of axonal loss have become biomarker endpoints in several phase II studies of putative neuroprotective treatments for MS. This talk will review the current literature on the use of OCT in optic neuritis and MS, and provide insights into the correlation of a retinal pathology markers with outcomes in these conditions. The impact of newer technologies on OCT measurements will be reviewed. The limitations of OCT as a single global measurement of MS axonal loss will be discussed to highlight firstly the complexity of defining neurodegeneration in MS, and, secondly, to discuss the need for multi-modal assessment.

L-19
Potential Biomarkers for MS in Asians
Takuya Matsushita (Japan)
Department of Neurology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Multiple sclerosis (MS) has a heterogeneous phenotype and disease course. It is very important to identify a good biomarker, which can distinguish between MS and other neuroinflammatory diseases and detect inflammatory activity and the degree of neurodegeneration as well as effectiveness of the treatments. However, validated and clinically useful biomarkers have not been identified. Thus, current diagnostic criteria are based on the combination of clinical manifestations, magnetic resonance imaging (MRI) findings, and CSF IgG abnormalities that are not specific for MS. Diagnosis of MS in Asians is relatively difficult because the abnormalities in Asians are less common than in people of European descent. The disease course is also different from MS of European descent. The appropriate biomarkers for Asians have been desired for a long time. Recent studies have revealed several biomarkers for diagnosis, disease activity and response to the therapy in Asian. Findings of genome-wide association study in the Japanese suggest that lipid metabolism affects the clinical course. A lipoprotein and leptin are possible biomarkers for the disability progression. We will discuss potential biomarkers in MS of Asian referring to recent studies. The application of reliable biomarkers could totally alter the management of MS and help refine treatment strategies for preventing progression of neurological disability.

L-20
How to Use Biomarkers for Diagnosis and Monitoring of MS in Asians
Ching-Piao Tsai (Taiwan)
Taipei Veterans General Hospital, and National Yang-Ming University, Taipei, Taiwan

Multiple Sclerosis (MS) is an important inflammatory demyelinating neurological disease with broad heterogeneity in clinical, histopathological and immunological phenotypes, therefore, reliable and more accurate biological markers that reflect the disease progression and allow the prediction of disease course is urgent need. Serious efforts are made in the field of biomarkers to improve the diagnostic discrimination, despite the broad range of biomarker studies, only oligoclonal bands (OCB) are used routinely in differential diagnosis of MS so far, although Epstein Barr Virus (EBV) and anti-myelin antibodies failed when tested, neurofilament and GFAP, the monocyte macrophage marker CD163, the glial activation marker YKL-40, the B cell chemo attractant CXCL13, etc., performed in a promising way. NMO patients often suffered from severe inflammatory events, despite of current available treatments, leading to permanent disable. Hence, the early detection will be the necessity for the clinician to take more aggressive treatment to lessen the inflammatory storm in the early stage. Besides aquaporin-4 antibody detection, T helper (Th)17 and astrocytic damages, Glial fibrillary acidic protein (GFAP) in CSF, CSF haptoglobin concentration/haptoglobin index and EDSS demonstrates good correlations with clinical severity of NMO relapses which highlights the potential of haptoglobin as a biomarker of NMO. We also survey the serum marker changes including anti-AQP4 antibody titer, cytokines and the level of high-mobility group box 1 protein in NMO groups during the disease course, trying to find out the possible early signal for the NMO relapsing.
We seek a place beyond imagination
where fertile soil nourishes seeds of change.
We pursue talent and technology
beyond cultural and national boundaries.
We disrupt common paradigms.
And if there are a million people
with the same disease,
we’ll find a million individual ways to treat them.
Together with the medical community,
we strive to deliver hope and relief to those who suffer.
And, when the world says there’s no cure,
we don’t give up until we find one.

INNOVATION BEYOND IMAGINATION
Innovation all for the patients
CHUGAI PHARMACEUTICAL CO., LTD.
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O-2 Characterization Of Anti MOG and Anti AQP4 Antibody Associated NMOS in A South Indian Cohort

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Background: Neuromyelitis optica spectrum disorders (NMOSD) represented approximately 20% of all demyelinating disorders seen in this south Indian registry. Less than 50% of these patients were positive for anti aquaporin antibody (anti AQP4- Ab) by commercially available cell based assay.

Objective: To detect seropositive patients with anti AQP4 and anti MOG- Ab using a sensitive (live cell based) assay and to characterize them clinically.

Materials and Methods: 125 consecutive patients including 17 children were included. Clinical and demographic features were characterized. A previously validated cell based assay (CBA) was used to detect serum anti MOG and anti AQP4 – Ab. Antibody status was correlated with clinical features, course and disease outcome.

Results: 30.4% of patients were positive for anti AQP4- Ab, 20 % for anti MOG –Ab and 49.6 % were seronegative for both antibodies. Anti MOG -Ab positive patients constituted 28.7% (25/87) of seronegative NMOSD. Compared to anti AQP4 – Ab positive patients, anti MOG-Ab positive patients were commonly male (P< 0.001), had less frequent attacks (p<0.001) and milder disability on EDSS scale (p <0.001). Seronegative patients were more often males, 36% (9/25) were monophasic LETM and disability was comparable with anti AQP4-Ab positive patients (p<0.02). Lumbar cord involvement was significant in anti MOG- Ab and seronegative (p < 0.01) cases, while cervical cord was more affected in anti AQP4-Ab positive patients (p< 0.001).

Conclusion: Live cell based assay improved detection of patients with anti AQP4 antibody and for the first time diagnosed Indian patients with anti MOG antibody. Nearly 50% of NMOSD in our cohort were seronegative. Distinct clinical and radiological features distinguished patients with anti MOG& anti AQP4 antibody.

O-3 Antibody to Myelin Oligodendrocyte Glycoprotein in Adults with Inflammatory Demyelinating Disease of The CNS

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Background: Several recent studies have shown the presence of myelin-oligodendrocyte glycoprotein antibody (MOG-Ab) in the serum of adult patients with the NMOSD (neuromyelitis optica spectrum disorder) phenotype. However, the clinical relevance of MOG-Ab’s among adult patients with IDD (inflammatory demyelinating disease) is not yet clear.

Objective: To evaluate the clinical relevance of MOG-Ab in a large cohort of consecutive adult patients with IDD of the CNS (central nervous system).

Methods: Live cell based assays for antibodies to MOG-Ab and AQP4-Ab were performed in a cohort of 288 adult IDD patients and in 72 controls.
Results: Eighteen patients with IDD (6.3%) had MOG-Ab (MOG group) and fifty patients (17.4%) had AQP4-Ab; none had both antibodies. The MOG group tended to manifest as a symptoms of isolated optic neuritis (15/18, 83%). All relapses in MOG group involved only the optic nerve within 1 year of disease onset. At onset, MRI in the MOG group uniquely demonstrated extensive peri-neurial enhancement (6/18; 33%). There was no female bias in the MOG group and none of them met the criteria for definite NMO. In MOG group, 3/13 monophasic patients suffered a poor visual outcome (<0.2) or paraplegia from the initial attack, while 1/5 relapsing patient suffered poor visual outcome due to repeated optic neuritis.

Conclusions: MOG-Ab may be a disease specific biomarker in adult patients with IDD who have a disease distinct from NMO or MS. Some patients with MOG-Ab may be left with severe disability, suggesting the need for early active immune modulating or suppressing treatment.

O-4
Development of Aquaporin4 Antibody Binding Inhibitor: A Preliminary Data

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Background: Neuromyelitis Optica (NMO) is a demyelinating autoimmune disease of optic nerve and spinal cord, triggered by antibodies of NMO-IgG in the astrocyte and subsequent disruption of the blood brain barrier.

Objective: To clarify the mechanisms of demyelination in NMO from the aspect of astrocyte dysfunction and tissue inflammation.

Methods: We created an NMO mouse model by directly injecting anti-mouseAQP4 monoclonal antibody and human complement into the mouse brain. We evaluated astrocytes destruction, secondary demyelination and inflammatory cell infiltration of NMO-like lesions in this model by immunohistochemistry using markers of astrocytes (AQP4/ GFAP/ EAAT2/ Cx43), myelins (MBP and Kluver-Barrera’s stain), and inflammatory cells (CD3/CD68).

Results: One day after injection, we could detect astrocyte destructive lesions without demyelination or inflammatory cell infiltration. Those lesions lacked immunoreactivities of AQP4, GFAP, EAAT2 and Cx43. Four or seven days after injection, demyelination was observed at the center of the lesions with astrocyte loss. The size of demyelinating lesions correlated with infiltration of macrophages. Moreover, injection of recombinant C5a, a chemotactic factor, with AQP4 antibody and complement, resulted in more remarkable infiltration of macrophages and enlargement of demyelinating lesions. On the other hand, in the absence of inflammation, demyelination did not expand at the periphery of the lesions with loss of EAAT2 and Cx43.

Conclusions: Inflammation leading to astrocyte injury rather than downregulation of cellular molecules causing astrocytic dysfunction may be associated with demyelination in NMO.

Oral Session 2

Neuroimaging

O-6
Structural MRI Substrates of Cognitive Impairment in Neuromyelitis Optica

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NMOSD. Although not statistically significant, a similar trend was observed in the comparison of CC lesions.

Conclusion: To the best of our knowledge, this is the first study comparing the lesion MWF between MS and NMOSD. We demonstrated that WM lesions exhibit more severe myelin loss in MS than in NMOSD.

O-9 Differences and Similarities in Brain MRI Features between Japanese and Caucasian Patients with Multiple Sclerosis and Their Impact on Disability Progression

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Background: The appearance of multiple sclerosis (MS) in Asians is reported to be different from Caucasians.

Objective: To identify differences of MS-related MRI features between Japanese and Caucasian MS patients by analysing and comparing baseline data from phase II fingolimod trials in both populations.

Methods: Ninety-eight Japanese and 276 Caucasian patients with MS with Expanded Disability Status Scale score of 0 to 6 were enrolled. T2-weighted MRI images of the brain acquired at study baseline were used to evaluate the number and volume of MS lesions.

Results: Japanese patients had a younger age at onset (mean age 27.0 vs. 29.2 years, p=0.0243) and lower Multiple Sclerosis Severity Score (MSSS) (mean 3.29 vs. 4.00, p = 0.0035) than Caucasian patients. Japanese patients had numerically higher T2 lesion volumes than Caucasian patients (median 7401 mm³ vs. 5242 mm³, mean 11432 mm³ vs. 9289 mm³; p=0.0742). There was no significant difference in the number of T2 lesions between both populations. Logistic regression analysis on contributing factors for MSSS revealed that race (lower in Japanese) and age at onset (lower in younger onset) were significant contributions, but neither T2 lesion numbers nor volumes were significantly different.

Conclusions: T2 lesion volume was numerically higher in Japanese patients than in Caucasian patients, although the former were younger and had lower MSSS than the latter. Racial differences may have greater impact on disability than T2 lesion load.

O-10 Teriflunomide Slows Brain Volume Loss in Relapsing MS: A SIENA Analysis of the TEMSO MRI Dataset

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Background: Two phase 3 studies, TEMSO (NCT00134563) and TOWER (NCT00751881), showed significant effects of teriflunomide on slowing disability progression in patients with relapsing MS (RMS). In TEMSO there were significant effects of teriflunomide on MRI disease markers, but no significant attenuation in brain volume loss (BVL) (measured by brain parenchymal fraction). Given associations of BVL and long-term disability, a blinded independent analysis of TEMSO MRI data was warranted using a validated alternative method of measuring brain tissue loss.

Objective: To assess effects of teriflunomide on BVL utilizing SIENA (structural image evaluation using normalization of atrophy).

Methods: Median annualized percentage change in brain volume from baseline was calculated (SIENA). Treatment groups were compared by rank ANCOVA, adjusted for region, age, EDSS strata, and normalized brain volume (SIENAX) at baseline.

Results: 969 patients were included. Median percentage reduction from baseline in brain volume at Months 12 and 24 for placebo was 0.61 and 1.29. For teriflunomide 14mg and 7mg these reductions were 0.39 and 0.90, and 0.40 and 0.94. BVL was lower(229,568),(568,577) for both teriflunomide groups vs placebo at Months 12 and 24: 14mg (36.9%, P=0.0001); 7mg (34.4%, P=0.0011); and 30.6% (P=0.0001) for 14mg; 27.6% (P=0.0019) for 7mg.

Conclusions: This blinded analysis demonstrates teriflunomide was associated with significant reductions in BVL vs placebo over 2 years. These findings, using SIENA, an established measure of brain tissue loss, are consistent with the effects of teriflunomide on delaying disability progression observed across studies in patients with RMS.

Oral Session 3

MS Genetics

O-11 Association of Genetic Variant Rs763361 on CD226 Gene in Relapsing Remitting Multiple Sclerosis (RRMS) Patients Compared to Control Group

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Materials and Methods: Blood samples from 200 patients with RRMS (180 females and 20 male; mean age=31.65±8.3) and 203 age and sex matched healthy subjects (163 females and 40 male; mean age=31.74±7.75) were collected. DNA was extracted from whole blood. SNP analysis was performed using HRM Real Time PCR.

Results: Our results showed that Allele frequency T, rs763361 polymorphism in patients with RRMS compared to the control group showed significant differences (P=0.035, OR =0.64). Also the frequency distribution of genotypes TT, CT, CC is different
between cases and controls (P = 0.014). CT + TT genotype in patients was higher than the control group (P = 0.007, OR = 1.80).

**Dissuasion:** Our results indicated CD226 rs763631 variant gene could be the risk factor of MS disease in the studied population.

**O-12**

**Latitude and HLA-DRB1 Alleles Affect Emergence of CSF IgG Abnormalities in MS**

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**Background:** Although a north–south gradient of MS prevalence rates is seen in Japan, it is unclear whether the prevalence of oligoclonal IgG bands (OCBs) in MS differs between the northern and southern regions of Japan.

**Objectives:** It was investigated whether the rates of OCB positivity and an elevated IgG index in Japanese MS patients are different between the Japanese islands of Hokkaido (north) and Kyushu (south), which exhibit a latitude difference of 10°. We also investigated whether any differences in OCB positivity and the elevated IgG index in MS patients from these islands were affected by HLA-DRB1*04:05 and *15:01 alleles.

**Methods:** This study included 180 MS patients from Hokkaido and 184 patients from Kyushu. The IgG index was considered increased if it was >0.658. The presence of OCBs and/or an increased IgG index were defined as positive CSF findings.

**Results:** Positive CSF findings and OCB positivity were significantly more frequent in MS patients from Hokkaido than in those from Kyushu (73.9% vs. 43.5% for CSF positivity, 63.3% vs. 41.4% for OCB positivity). Logistic regression analysis revealed that adjusting for covariates possibly related to abnormal CSF IgG production, Hokkaido showed odds ratios of 4.08 and 2.57 for positive CSF findings and OCB positivity, respectively, while those from Kyushu (73.9% vs. 43.5% for CSF positivity, 63.3% vs. 41.4% for OCB positivity) were significantly more frequent in MS patients from Hokkaido than in those from Kyushu.

**Conclusions:** A north–south gradient in OCB positivity in MS patients may be common in Japan and Western countries. The HLA-DRB1*04:05 allele is protective for abnormal IgG production in Japanese MS patients, regardless of latitude.

**O-13**

**Genome-Wide Association Study (GWAS) for Clinical Phenotypes of Multiple Sclerosis in The Japanese.**

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**Objective:** To clarify genetic factors associated with clinical phenotypes of multiple sclerosis (MS) in Japanese population.

**Method:** Genome-wide 600,000 SNPs were genotyped in Japanese MS. Allelic effects for age of onset, MS severity score (MSSS) and positivity of IgG oligoclonal bands (OCB) were calculated based on a linear or logistic regression model including age of onset or gender as covariates. Quartiles of MSSS were used for the phenotypic values.

**Results:** 553 cases were available for the analyses. rs13202636 (lipoprotein(a)) in chromosome 6 and rs74731427 (leptin) in chromosome 7 were associated with MSSS (p = 3.04e-7 and 2.07e-6 respectively). Lipoprotein(a) (LPA) was measured by means of latex agglutination turbidimetry and leptin was measured by ELISA in 182 sera from case subjects that had been genotyped in this analysis. The number of the risk allele of rs13202636 was negatively correlated with concentrations of LPA. Individuals homozygous for the risk allele had a lower concentration of LPA than individuals without the risk allele (p = 0.011). There was no correlation between the number of rs74731427 allele and concentrations of leptin. rs2808707 (Neurotrophic Tyrosine Kinase, Receptor, Type 2 gene) was associated with age of onset (p = 2.37e-7). Several SNPs in MHC region were also associated with the positivity of OCB.

**Conclusion:** Genetic loci relating to lipid metabolisms were associated with disability progression of Japanese MS. CSF IgG abnormality was associated with MHC in the Japanese like MS of European descent.

**Oral Session 4**

**MS Treatment**

**O-14**

**Durable Effect of Alemtuzumab on Clinical Outcomes Over 5 years in Treatment-Naive Patients With Active Relapsing-Remitting Multiple Sclerosis Despite Most Patients Not Receiving Treatment for 4 Years: CARE-MS I Extension Study**

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**Background:** In CARE-MS I (NCT00530348), alemtuzumab significantly reduced annualised relapse rate (ARR) versus SC IFNB-1a by 55% over 2 years in treatment-naive patients with active RRMS.

**Objective:** Examine 5-year clinical efficacy/safety in CARE-MS I alemtuzumab-treated patients.

**Methods:** Alemtuzumab-treated patients received 2 annual courses (12 mg) and, in the extension study (NCT00930553), as-needed alemtuzumab retreatment or other disease-modifying therapy (DMT). Endpoints: ARR, sustained accumulation of disability (SAD); ≥1-point EDSS decrease over 6 months, sustained reduction in preexisting disability (SRD); ≥1-point EDSS decrease over 6 months), no evidence of disease activity (NEDA; no relapse, SAD, new/enlarging T2, or gadolinium-enhancing lesions).

**Results:** The extension enrolled 349 (95%) CARE-MS I alemtuzumab-treated patients; 91% remained on study, 68% received no alemtuzumab after Month 12, 2% received another DMT. Low ARR was maintained from Year 3 (0.19) through 5 (0.15). Through Year 5, 80% were SAD-free and 33% achieved SRD. In Year 5, 62% achieved NEDA. Of patients who only received the initial 2
courses, 56% achieved sustained NEDA during extension (3 years). Infusion-associated reaction and infection incidences decreased over time. Thyroid adverse events (AEs) peaked at Year 3, declining thereafter. Incidence of serious AEs was low.

Conclusions: Alemtuzumab's efficacy was maintained over 5 years, despite most patients not receiving retreatment over the previous 4 years. Most patients who only received the initial 2 treatment courses were disease activity-free in absence of any additional treatment. This durable effect of the initial 2 courses may result from immunomodulatory effects of the distinct lymphocyte repopulation pattern following treatment.

O-15

Alemtuzumab Has Durable Efficacy on MRI Outcomes and Brain Atrophy Over 5 Years with Most Patients Free From Treatment for 4 Years: CARE-MS II Extension Study

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Background: In CARE-MS II (NCT00548405), in active relapsing-remitting multiple sclerosis (RRMS) patients with inadequate response (≥1 relapse) to prior therapy, alemtuzumab significantly improved magnetic resonance imaging (MRI) outcomes and slowed brain volume (BV) loss over 2 years versus subcutaneous interferon beta-1a.

Objective: Examine 5-year MRI and brain atrophy outcomes in CARE-MS II alemtuzumab-treated patients.

Methods: Alemtuzumab-treated patients received 2 annual courses (12 mg) in the core study, and as-needed retreatment based on evidence of disease activity, or other disease-modifying therapy, in an ongoing extension (NCT00930553). Baseline and annual MRI scans were collected. MRI activity was defined as new gadolinium (Gd)-enhancing and new/enlarging T2-hyperintense lesions; BV loss was measured by brain parenchymal fraction change.

Results: The extension study enrolled 93% of CARE-MS II alemtuzumab-treated patients. Of those, 93% remained on study and 60% received no alemtuzumab since Month 12. Proportions of lesion-free patients in Year 5 were similar to core study Year 2 (Gd: 89.7% vs 91.3%; T2; 67.9% vs 76.3%; T1: 87.5% vs 92.8%). Proportion MRI activity-free in Year 5 was similar to Year 2 (67.7% vs 76.1%). Median yearly rate of BV loss slowed over 3 years and remained low in Years 4 and 5 (Years 1–5: –0.48%, –0.22%, –0.10%, –0.19%, –0.07%).

Conclusions: Alemtuzumab's effect on MRI outcomes and brain atrophy was maintained over 5 years, despite most patients not receiving retreatment since Month 12. Durable efficacy may result from immunomodulatory effects of the distinct lymphocyte repopulation pattern following treatment, representing a novel treatment approach for RRMS.

O-16

Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis in A Western Australian Cohort

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Background: Autologous hematopoietic stem cell transplantation (AHSCT) has shown promise as a treatment strategy for multiple sclerosis (MS), possibly by eradicating self-reactive immune cells and resetting the immune repertoire upon post-transplant reconstitution. However, the precise mechanism is unclear and we undertook a detailed analysis of lymphocyte subsets following AHSCT for MS.

Objective: To review the outcome of AHSCT for multiple sclerosis in Western Australian cohort.

Methods: Fourteen patients with aggressive MS unresponsive to other therapies underwent AHSCT. Stem cell mobilization was with cyclophosphamide 2g/m2 and granulocyte-colony stimulating factor 5ug/kg bd. Conditioning chemotherapy was with cyclophosphamide 50mg/kg and rabbit antithymocyte globulin 1mg/kg days -5 to -2. Lymphocyte subsets including CD4, CD8, naïve T-cells, recent thymic emigrants, T-regulatory cells, TH1, TH2 and TH17 cells were assessed by flow cytometry for 2 years following AHSCT. Eleven healthy volunteers were used as controls.

Results: In the first 2 years after AHSCT following intensive physiotherapy some patients noticed minor improvement in walking distance or bladder function. However, most patients remained stable with neither improvement nor deterioration and some patients reported worsening of the disease over a minimum 2-year interval. In the lymphocytes subsets, in the short term there was a clear shift in favour of CD8 cells and Th1 cells. Naïve T-cells and RTEs fall initially but re-establish by 12 months. TH17 cells appear to emerge with time.

Conclusions: In this group of patients with advanced MS, neurological function 24 months post-AHSCT was essentially stable in half the cohort while the remainder experienced clinical progression.

O-17

The Role of α4 Integrins on Thieier’s Murine Encephalomyelitis Virus (TMEV) –Induced Demyelinating Disease, An Infectious Animal Model for Multiple Sclerosis (MS)

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Background: The interactions of α4 integrins and vascular-cell adhesion molecule 1 (VCAM-1) are required for lymphocytes to
enter the central nervous system (CNS) in Experimental autoimmune encephalomyelitis.

Objective: In this study, we investigated the role of α4 integrin and the therapeutic effect of HCA3551, a newly synthesized, orally active small molecule α4 integrin antagonist, in the development of TMEV-induced demyelinating disease (TMEV-IDD).

Methods: TMEV was infected into six-week-old female SJL/J mice intracerebrally at day 0. Mice were treated with 0.05% Methocel/H2O as vehicle or 100 mg/kg HCA3551 twice a day via oral gavage from day 11 to 41. Spinal cords and brain were analysed immunologically and histologically.

Results: The expression of α4 integrin mRNA was significantly increased in the CNS of mice with TMEV-IDD compared with naïve mice (*p<0.05). HCA3551 treatment significantly suppressed the disease development of TMEV-IDD both clinically and histologically. The number of infiltrating mononuclear inflammatory cells in the CNS was significantly decreased in mice treated with HCA3551 (*p<0.05). Flow cytometric analysis of cytokine staining revealed that absolute cell numbers of TNF-α-producing CD4+ and IFN-γ-producing CD8+ T cells were significantly decreased in the CNS of mice treated with HCA3551 (*p<0.05).

Conclusion: HCA3551 treatment may ameliorate TMEV-IDD by inhibiting α4 integrin accompanied with decreasing the number of MNCs and pro-inflammatory cytokine producing cells in the CNS. Therefore, The interactions of α4 integrin and VCAM-1 are required for lymphocytes to enter the CNS in TMEV-IDD and HCA3551 could be used as a novel therapeutic treatment of MS.

Poster Session 1

MS Epidemiology & Clinical Manifestation

P-1
Clinical and Demographic Profile of Demyelinating Disease of the Central Nervous System in National Hospital Ciptomangunkusumo, Jakarta, Indonesia
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Background: Demyelinating disease of the central nervous system (CNS) happens when the myelin sheath of neurons is damaged. So far, data on demyelinating disease of the CNS in Indonesia has not been recorded properly. Clinical and demographic profile in these patients is also not known with certainty.

Objective: To study the clinical and demographic profile of demyelinating diseases of the CNS in National Hospital Ciptomangunkusumo (NHCM), Jakarta, Indonesia

Methods: The data was retrieved from medical records in patients with demyelinating disease of the CNS in NHCM in the period of January 2014-June 2015.

Results: From all the 35 cases obtained, there are 14 patients (40%) with MS (multiple sclerosis) (12 with the diagnosis of RRMS (Relapsing Remitting MS), one with PPMS (Primary Progressive MS), and one with tumefactive MS; 8 patients were positive for oligoclonal band in the cerebrospinal fluid), two patients (6%) with myelitis, five patients (14%) with optic neuritis, and ten patients (29%) with neuromyelitis optica. Four patients (11%) have their cerebrospinal fluid positively tested for virus. One with cytomegalovirus and three other with varicella zoster virus.

Conclusions: In patients with demyelinating diseases of the CNS in NHCM, the majority were found to have MS. Analysis of cerebrospinal fluid in some patients showed that viral infections may be the causative agent of the disease.

P-2
Survey of Multiple Sclerosis in Indonesia: Diagnostic Approach and Treatment Selection
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Background: Multiple Sclerosis in Indonesia is still considered a rare disease that is difficult to diagnose and treat. Neurologists in Indonesia is also still rarely use the DMTs.

Objective: To understand how neurologists make decisions regarding diagnostic approach and the prescription of DMTs for patients with MS.

Methods: In Neurology workshop and symposium held on March 2015 in Jakarta, a MS questionnaire is given to all participants. A total of 239 neurologists, 55 residents and 27 general practitioners completed the survey. Only 8.4% participants that never deal with the patients with suspected MS. Most of the participants (54.2%) have both magnetic resonance imaging (MRI) and Visual Evoked Potential (VEP) at the hospital in their province. In diagnostic approach, 53% never done a lumbar puncture in MS patients and only 32.7% that always ask an oligoclonal band examination. Multiple sclerosis (72.6%) and Neuritis Optic (53%) are the most common demyelination disease they met in daily practice. Relapsing Remitting MS (79.9%) is the most common type of MS.
Most of the participants (67.3%) never prescribe interferon as the only DMTs available in Indonesia; they only give methylprednisolone (74.1%) as an alternative.

**Conclusion:** Our survey results showed the MS diagnostic approach in Indonesia still faces many obstacles like facilities support. Most of MS patients did not received any DMTs, probably because it is very expensive and not covered by the National Health Insurance.

**P-3**

**Multiple Sclerosis in Nepal: a Retrospective Clinical Analysis**

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**Background:** Multiple sclerosis (MS), a central demyelinating disease (CDD), among South Asian populations has been regarded as a rare disease. No previous MS studies have been reported from Nepal.

**Objective:** The study was conducted to analyze the clinical manifestations of MS in Nepal.

**Methods:** We respectively studied all the patients with CDD admitted to Neurology department, Tribhuvan University teaching hospital, Nepal from January 2014 to June 2016. McDonald Criteria 2010 was used for the diagnosis of MS.

**Results:** Out of 25 CDD patients, 3 patients were diagnosed with MS (mean age 35.7±10.0 years (Range=26-45); male=1(33.3%), female=2(66.7%)). According to Mcdonald criteria 2010, definite MS comprised of two patients and remaining one patient was probable. 2 patients presented with limb weakness as well as sensory symptoms, out of which one patient had visual impairment; remaining 1 patient had progressive cerebellar features. Relapsing and remitting course was found in two patients and primary progressive in one patient. Oligoclonal bands were positive in all the patients and raised Immunoglobulin was found in two patients. Magnetic Resonance Imaging (MRI) brain showed typical lesions in all the cases and one patient had lesion in spinal cord too. Neuromyelitis Optica (NMO) was found to be more common than MS in our study; 5 patients (mean age=29.2±10.3 years (Range=21-41)); male=3 (60.0%), female=2(40.0%).

**Conclusions:** Lack of Neurologists, MRI, VEP and laboratory facilities in most of the hospitals might be the reason for low number of diagnosed MS patients in Nepal.

**P-4**

**Short Term Fasting and Multiple Sclerosis**

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**Background:** Fasting during Ramadan causes many physiological and biochemical change that may have an effect on MS disease course; however the role of fasting on MS disease parameter is still much debated. Leptin plays a role in Th-1 immune response by acting as a proinflammatory cytokine, the role of this substance in In EAE (experimental autoimmune encephalomyelitis) has been demonstrated however the role in MS disease course has not been fully elucidated.

**Objective:** Here we try to shed light on effect of fasting on MS disease parameters (EDSS, Relapse rate) six month after Ramadan and also serum leptin levels and its relation with fasting and MS disease course in MS patients.

**Method:** This study is a prospective randomized study which was conducted on 25 patients with definite diagnosis of MS and EDSS<6 who reside in Isfahan, Iran. Our study population was divided into two groups: fasting and non-fasting, patient were followed 6 month after Ramadan to access the change in their EDSS and number of clinical relapse. Plasma leptin level was measured at the end of Ramadan.

**Results:** our study demonstrated no significant difference between EDSS and Relapse rate six month after Ramadan in Fasting and non-Fasting MS patients (P value>0.05) Also no correlation between Plasma Leptin level and MS disease parameter was found. (P value>0.05) however leptin levels were significantly higher in Females compared to males.

**Conclusion:** Fasting and serum leptin levels have no unfavorable short term effect on MS disease course; however larger study for longer duration needs to be conducted.

**P-5**

**Patterns of the Oro-facial Neural Manifestations in Multiple Sclerosis Patients in Kerman (Iran)**

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**Aims:** Studies have shown an increase in the incidence of multiple sclerosis (MS) in recent years. This medical condition exhibits motor–sensory manifestations in the oral cavity and face. The aim of the present study was to evaluate the prevalence of these manifestations in patients with MS in Kerman Province, Iran, in 2013.

**Methods:** A total of 100 patients with MS, based on McDonald’s 2010 Diagnostic Criteria, were selected by simple sampling technique for the purpose of the present cross-sectional study. All the subjects received treatment in the Department of Neurology in Kerman Shafa Hospital.

**Results:** Eighty patients were female and the mean age of the subjects was 36.4 years; 33% and 43% of the subjects had dysphagia and a feeling of an unpleasant taste in the oral cavity or a history of facial pains, respectively.

**Conclusion:** Based on the results of the present study, it is recommended that dentists take account of the oral problems of these patients with MS due to the sensory problems of these patients.

**P-6**

**Tumefactive Demyelinating Lesions: Clinical, Laboratory, and Neuroimaging Characteristics**

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**Background:** Tumefactive demyelinating lesions (TDLs) are major diagnostic challenge, because their clinical and radiographic features are often indistinguishable from brain tumors.

**Aims:** To present clinical, laboratory, and neuroimaging characteristics of six patients with TLDs in the Republic of Korea.

**Methods:** The study was conducted to analyze the clinical manifestations of MS in Nepal.
Objectives: The purpose of this study is to evaluate the clinical, laboratory, and radiographic features of TDLs.

Methods: All patients met the following criteria: 1) acute or subacute onset of neurologic symptoms and signs; 2) at least 1 brain lesion with the longest diameter ≥2cm seen on brain MRI; 3) no evidence of systemic illness, vasculitis, toxic or metabolic disease, or CNS infection. The final diagnosis of TDLs was made on the basis of histopathologic findings or a strong clinical suspicion supported by the patient’s clinical course and the follow-up MRI findings.

Results: Twenty-nine patients (12 women and 17 men) were included. Twenty-three patients (79.3%) had monophasic clinical course, and five (17.2%) had relapsing. One patient had chronic progressive deterioration. Mean Expanded Disability Status Scale were 1.88 (range, 0-9.5). Cerebrospinal fluid analyses were usually normal and negative for oligoclonal bands, although 6 patients showed mild elevation of CSF lymphocytes or protein. Mean IgG index was 0.55. There was perilesional edema or mass effect in seven patients (24%). Contrast-enhancement was observed in 19 (65.5%). Fourteen patients underwent brain biopsy. All of them showed reactive gliosis and various degree of inflammatory cell infiltration with relative axonal preservation, which compatible with inflammatory demyelinating disease.

Conclusions: Based on our results, TDL is usually monophasic and responds favorably to steroid treatment. However, relapsing and clinical deterioration is observed in some cases and brain biopsy is required for precise diagnosis.

Poster Session 2

MS Emotion and Higher Brain Function

P-7

The Relationship between Balance and Depression in Patients with Multiple Sclerosis

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Introduction: Depression is a common symptom in patients with multiple sclerosis (MS). Its prevalence has been reported about 50 percent throughout their lifetime. Several factors contribute to depression in these patients; in this regard, the motor disability and inability to perform daily living activities can be pointed that Balance is one of the most influential factors. So, the aim of this study was to investigate the relationship between balance and depression in patients with MS.

Methods: This cross-sectional study was conducted on multiple sclerosis patients who referred to hospitals. Population were selected by convenience sampling and according to the inclusion and exclusion criteria from the 95 patients, 35 patients were entered in the study. After recording demographic data, for measuring the balance and depression, Berg Balance Scale and Beck depression questionnaire were used.

Results: participants were included 29 women and 6 men with an age range of 20-60 (32±8.92). Borg scale scores was 45.14 ± 10.12 and the Beck Inventory score was 17.74 ± 9.65. Statistical analysis showed that there was a significant relationship between balance and Depression (r= -0.485, p= 0.004).

Conclusion: According to the balance disorders and depression which appeared in the participations, the balance and depression-related interventions are essential in the rehabilitation process. Since, a significant correlation was seen between these two variables, the balance interventions may have a positive effect on the depression of patients with MS.

P-8

Effect of Disease Duration on Personality Type in Multiple Sclerosis Patients and Healthy Individual

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Background: Multiple sclerosis have profound emotional consequences. The relation between psychological and physical factors could lead patients toward unforeseen disease. This study focuses on multiple sclerosis (MS) disease duration on personality type A and B in relation to individuals’ behaviors.

Materials and Methods: This descriptive-analytical study was conducted in Isfahan Alzahra hospital in 2013. Three hundred MS patients and 100 healthy individuals were determined. The distributed questionnaires related to MS patients and considering the descriptive statistics such as demographic variables. Data were analyzed by SPSS software (version 18) based on Chi-square test and independent T-test.

Results: Disease duration varied between 1 to 38 years: 30% (1–4 years), 39% (5–10 years), 20% (10–20 years), and 12% (more than 20 years). Significant relationship was observed between disease duration and tendency to type A (higher stress). This relation was positive and significant in Relapsing Remitting MS patients; but negative correlation was seen in Secondary Progressive MS patients. These patients tended to type B (lower stress) when disease duration increased.

Conclusions: Individuals with disease duration of one year and less than one year tend to type A personality, while patients with increment of disease duration have tendency to type B.

P-9

Evaluating the Relationship between Emotional Intelligence and Cognitive Disorders in MS Patients

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Association between Multiple Sclerosis and Dementia in Korea: A National Population-based Study

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Background: Cognitive deficits are among the most common complications in patients with multiple sclerosis (MS). However, the prevalence and risk factors of dementia in MS patients are uncertain.

Objectives: We aimed to estimate the prevalence and risk factors of dementia in patients with MS in Korea using the National Health Insurance (NHI) data.

Methods: Population-based data were obtained by using the annual outpatient claims and hospitalization discharge claims for 2005 – 2014 from the Bureau of NHI. The cases of MS and dementia were identified according to the International Classification of Diseases, tenth revision (ICD-10), and additional requirements for the operational definition of the disease.

Results: The prevalence of dementia in MS patients was significantly higher than people without MS. Among the variables, hypertension and hyperlipidemia were significant risk factors for dementia in MS patients. The hazard ratio with 95% confidence interval was 3.27 for hypertension and 2.42 for hyperlipidemia. After adjustment for age, sex, income, and place of living, they were 2.12 and 2.31, respectively.

Conclusions: This is the first study for the association of dementia in patient having MS in Korea utilizing the NHI database as a main data source. Hypertension and hyperlipidemia were major risk factors for developing dementia in Korean MS patients.

Cognitive Profile in Neuromyelitis Optica Spectrum Disorder

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Background: Cognitive impairment in Neuromyelitis Optica Spectrum Disorder (NMOSD) can be seen however the features and influencing factors of cognitive impairment of Turkish NMOSD patients are unclear.

Objective: To investigate cognitive function in a cohort of 22 Turkish patients with NMOSD.

Methods: 22 patients with the diagnosis of NMOSD, underwent neuropsychological tests (Brief Repeatable Battery-Neuropsychology (BRB-N), Addenbrooke’s Cognitive Examination (ACE-R) and Beck Depression Inventory (BDI)). Cognitive impairment was considered if at least two cognitive domains were inferior to the 5th percentile for normal values for BRB-N test. The specificity and sensitivity of ACE-R test on detecting cognitive impairment were assessed through ACE-R test results.

Results: The mean age of the patients was 42.86±10.98 (25-65), 45.5% (n=10) of the patients had cognitive impairment and 50% (n=11) had depression. The mostly affected cognitive profile was found to be memory impairment, attention and processing dysfunction. The group with cognitive impairment had significantly older age, lower educational status, higher EDSS and BDI scores (p<0,05). The diagnostic level of ACE_R test was found to be statistically good since it can detect cognitive impairment with a sensitivity of 88% and specificity of 75% on a cut off level of 82.5.

Conclusions: In our study, approximately half of the patients had depression or cognitive impairment. It has been concluded that ACE-R test can be used to detect cognitive impairment in NMOSD patients. Since cognitive impairment and depression are frequent in NMOSD patients, for their quality of life, it is important to evaluate these aspects of the disease.

Multiplying 10 by 10 Grid of Number Clue to Find Attention Impairment in Multiple Sclerosis Patients

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Background: Cognitive impairment occurs in 40-65% of patients with Multiple Sclerosis (MS). Impaired attention and cognitive information processing are more prominent in MS. They sometimes have little or no relation to Mini Mental State Examination (MMSE) scores. To check them, Symbol Digit Modalities Test (SDMT) is often used. Although SDMT is useful, much brief cognitive tests to monitor are needed.
Objective: To examine multiplying 10 by 10 grid of number (10 X 10 scores) as brief cognitive screening tests.

Methods: Performance on 10 X 10 scores, SDMT, MMSE were assessed in 6 Relapsing Remitting MS patients. 4 females and 2 males. Average age was 41.3. Mean disease duration was 9.6. Average EDSS was 5.25. Average MMSE was 25.3. Magnetic Resonance Image was also used to measure 3rd ventricular space which reflects thalamic atrophy.

Results: 3 out of 6 showed low SDMT scores and low 10 X 10 scores. 2 out of the 3 had low MMSE scores. 1 out of the 3 had intermediate MMSE score. 2 out of the 3 had long disease duration and dilated 3rd ventricular space. One patient had high MMSE score and high SDMT scores with long disease duration and dilated 3rd ventricular space.

Conclusion: Multiplying 10 by 10 grid of number could be useful to screen attention impairment in Multiple Sclerosis patients.

Poster Session 3
MS Genetics

P-13
Same as O-13

P-14
Same as O-11

P-15
Association between the CTLA-4 +49 A/G Polymorphism and Susceptibility to Multiple Sclerosis: A Meta-Analysis
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Objective: To explore the association between the cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) +49A/G polymorphism and susceptibility to multiple sclerosis (MS).

Methods: The literature was searched using the PubMed database from the establishment of database till September 2013 to identify studies in which the CTLA-4 polymorphism was analyzed in MS patients. A meta-analysis was conducted on the associations between CTLA-4 +49A/G polymorphism and MS. Pooled OR value and 95% CI were calculated for each study by using RevMan 4.2 software.

Results: A total of 25 studies including were included in this meta-analysis. Ethnicity-specific meta-analysis was performed on Caucasian and Asian populations. Pooled data results showed the OR value of G/A + GG+GA/AA + GG/GA+AA were 1.00 (95% CI: 0.96–1.06) + 1.01 (95% CI: 0.93–1.10) + 0.73 (95% CI: 0.68–0.88) + 1.00 (95% CI: 0.88–1.10) + 0.81 , respectively. In subgroup analysis, pooled data results of Caucasians showed the OR value of G/A + GG+GA/AA + GG/GA+AA were 1.00 (95%: 0.94–1.06) + 1.01 (95%: 0.93–1.10) + 0.73 (95%: 0.68–0.88), respectively. In Chinese populations, the OR value of G/A + GG+GA/AA + GG/GA+AA were 1.00 (95%: 0.94–1.06) + 1.01 (95%: 0.93–1.10) + 0.73 (95%: 0.68–0.88), respectively. In Asian populations, the OR value of G/A + GG+GA/AA + GG/GA+AA were 1.00 (95%: 0.94–1.06) + 1.01 (95%: 0.93–1.10) + 0.73 (95%: 0.68–0.88), respectively. In African populations, the OR value of G/A + GG+GA/AA + GG/GA+AA were 1.00 (95%: 0.94–1.06) + 1.01 (95%: 0.93–1.10) + 0.73 (95%: 0.68–0.88), respectively.

Conclusions: There was no evidence for association of CTLA-4 +49A/G gene polymorphisms and susceptibility to multiple sclerosis.

P-16
Same as O-12

P-17
Relationship between HLA-DRB1 Genotype and Clinical Response to Interferon-Beta among Iranian Multiple Sclerosis Patients
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Objective: To evaluate the relationship between HLA-DRB1 genotype, which has been proved to be more common in Iranian MS patients, and clinical response to interferon-beta, which is the most common immunotherapy for RRMS.

Design and Setting: 68 Iranian patients with confirmed diagnosis of RRMS were selected from “December 2010 until May 2011” and patients were followed prospectively for 2 years and clinical data, including EDSS scores were recorded every 3 months. At the end of the following period each patient was to be classified as responder or non-responder. Since there is not any common and international criteria to define response to IFNβ, in this study we used Rio et al (2006) that is a stringent criteria in which patient is considered as non-responder when there is at least 1 point increase in his/her EDSS confirmed for 6-months of follow-up or when at least 1 relapse occurs during the follow-up period which must be two years.

Methods: The HLA-DRB1 genetic polymorphism was determined by DNA amplification with PCR and hybridized by specific sequence oligonucleotide primers using R.O.S.E.

Results: Total number of individuals was 68 Iranian MS patients with 53(77.9%) female and 15(22.1%) male, mean aged of onset in years 20.1±5, mean disease duration in years 6.8±5. EDSS at entry was1.9(±0.8) and relapse no.2 years before starting INFβ was1.7(±0.7). There were 47(69.1%) responders and 21(30.9%) non-responders. Fisher’s exact test did not show any difference between HLA-DRB1 allele frequencies in responders and non-responders. Since there is not any common and non-responders. Since there is not any common and international criteria to define response to IFNβ, in this study we used Rio et al (2006) that is a stringent criteria in which patient is considered as non-responder when there is at least 1 point increase in his/her EDSS confirmed for 6-months of follow-up or when at least 1 relapse occurs during the follow-up period which must be two years.

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Conclusions: We concluded that currently available data do not support a role for HLA class II genes as modifiers of response to immunotherapy.

Poster Session 4
MS Neuroimaging

P-18
Magnetic Resonance Imaging (MRI) Atrophy Measurements in Multiple Sclerosis – An Overview
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Multiple Sclerosis (MS) is an inflammatory and neurodegenerative disease which is associated with marked brain and spinal cord atrophy. It occurs early in MS, progresses throughout the course of disease and affects both gray matter (GM) and white matter (WM).

Advances in MRI techniques and image processing software improve data quality and allow new outcome measures, such as whole brain, spinal cord, and local atrophy measurements within acceptable image processing times.

Different methods for the detection of atrophy will be discussed. Methods for whole brain atrophy, as well as methods for tissue specific, e.g. cortical GM and deep GM atrophy, will be shown. We will give an overview on the assets and drawbacks of the different imaging modalities focusing on the well known pitfalls of state of the art techniques such as Siena and SienaX, FSLs FIRST or Voxel-based Morphometry.

New methods for detecting cerebellar and spinal cord atrophy will be introduced. Finally, the talk will discuss the clinical relevance of the above mentioned techniques in the context of disability progression and cognitive decline.

P-19
Same as O-9

P-20
Graph Analysis of Resting State Functional MRI in Chinese with RRMS
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Resting state functional magnetic resonance imaging (R-fMRI) exploits the blood-oxygen-level dependent signal to detect intrinsic brain activity, allowing investigations in functional connectivity of anatomically separate brain regions. R-fMRI data can be analysed using graph theory to describe the overall organisation of the brain network. In this cross-sectional study, we compare the topological differences in the functional brain network of Hong Kong Chinese patients with relapse-remitting multiple sclerosis (RRMS) and matched healthy controls (HC). R-fMRI examinations were acquired on a 3T scanner, and binary matrices were obtained to represent whole brain functional connectivity per subject. Graph metrics describing regional and global network characteristics were compared between RRMS and HC cohorts, with significance at p<0.05. We enrolled 20 consecutive patients with median age 32 years (18-52), median disease duration since diagnosis of 1.5 years (range 0.0-13.0), and median end-stage disability score of 1 (range 0-6.5). All patients had supratentorial lesions on MRI, and 5 had enhancing lesions at the time of scan. Graph analysis showed significantly reduced clustering coefficient but shorter characteristic path length in RRMS patients, with preservation of small world architecture. Notably, the RRMS cohort exhibited significantly decreased local efficiency but increased global efficiency, despite loss of hubs in the superior parietal lobule, pre-central gyrus, superior frontal gyrus (orbital part), and middle temporal lobe. Our results imply enhanced functional integration in RRMS, which may be a functional adaptation in early disease and reflect cortical reorganisation or brain plasticity.

P-21
Same as O-8

P-22
Detection of Myelin Changes in Vivo Using High Field MRI
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Objective: To detect changes in myelin content we have applied a segmented Magnetization Prepared Rapid Acquisition Gradient Echo (MP-RAGE) MRI technique for mouse brain MR imaging at high field (9.4T) along with a very sensitive rf cryo-coil. A cuprinoze mouse model of MS was used.

Results: High resolution T1-weighted MR images were obtained. T1 components of the brain structures with different myelin content were identified and quantified. The results showed that the MP-RAGE sequence used with cryo-coil at 9.4T, allows high resolution images of the mouse brain in vivo and allows detections of changes in diseased animals. Varying pulse sequence parameters, such as inversion time, allowed tunable, thus optimal white/grey matter contrast.

Conclusions: The proposed MP-RAGE technique, when applied with a cryo-coil may be suitable for early diagnosis of myelin related brain pathologies such as MS or AD.

Poster Session 5
MS Laboratory Test

P-23
The Effect of Aquatic Exercise on Ground Reaction Forces during Gait of Patients with Multiple Sclerosis
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Background: Rehabilitation of Multiple sclerosis (MS) is necessary.
Objective: The objectives of this study were to evaluate the effect of aquatic exercise on ground reaction forces during gait in two different clinical forms of MS.

Methods: 21 women patients with MS (n=11 with ataxia syndrome and n=10 with spasticity syndrome) (EDSS>4) and 10 normal subjects participated in this study voluntarily. A Kistler force plate was used to measure the ground reaction forces (GRFs) during the gait. All patients participated in exercise (24 sessions). All tests repeated after exercise. For statistical analysis, General linear model (repeated measures), Post-hoc Tukey analysis was used (P-value<0.05).

Results: Fz2 (valley force) and Fz3 (second peak) of vertical GRF, and the shear GRF in the antero-posterior were significantly reduced in both groups of patients (P<0.001). Aquatic exercise improved the rate of reaction forces (P<0.01). The Fz2 and anterior shear GRF had significant difference with healthy subjects after exercise (P<0.02), which represents a significant drop in GRF of in these patients. Ataxia group had weaker performance in some other reaction forces in compared to spastic group (P<0.01).

Conclusions: The decreased GRF in MS patients might be due to the reduction of the walking speed. This pattern may result in a muscle weakness in long term. In the early stages of rehabilitation for MS patients, 20 to 30 training sessions in water can prepare them for practice in land. It is recommended that MS patient perform aquatic exercise aside from drug therapy to maintain and improved their performance.

P-24 Tests of The Autonomic Nervous System Dysfunction of Patients with Multiple Sclerosis

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The aim of this study was to compare the effectiveness of autonomic tests and to examine autonomic nervous system (ANS) dysfunction in patients with multiple sclerosis. We studied 47 patients (mean age 33 years, 21 females and 26 males) and 36 age-matched healthy subjects (mean age 34 years, 19 females and 17 males). Non-invasive the head-up tilt test, the sympathetic skin response (SSR), and the heart rate interval variation (RRIV) were studied using electromyogram (EMG) in all the subjects. The mean values of "30/15" head-up tilt test (0.53±0.98 vs. 1.12±2.30 in patients and controls respectively) was significantly lower compared with the controls (p<0.05). The mean values of RRIV in patients during at rest (mean RRIV in patients, 51.30±27.13 % vs. controls, 31.73±6.97 % [p<0.005]) was significantly prolonged compared with the controls. The mean latency of SSR in patients (mean SSR latency in patients, 1.53±0.23 milliseconds vs controls, 1.36±0.42 milliseconds [p<0.05]) was significantly prolonged compared with the controls. Abnormal head-up tilt test was more pronounced in patients with clinical orthostatic functional abnormalities than those without orthostatic functional abnormalities.

We conclude that RRIV, SSR and head-up tilt test which can be easily and rapidly performed in an EMG laboratory can provide useful, objective information. RRIV during deep breathing is more sensitive than others tests but combined use of these three tests are more effective.

P-25 Association of Serum Bilirubin Levels With Relapsing Remitting Multiple Sclerosis

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Introduction: Bilirubin is a strong antioxidant with effective protects against lipid peroxidation, so plays an important role in neuroprotection. Previous studies in animal model of multiple sclerosis have shown that bilirubin has beneficial effect in amelioration of disease episodes. However few studies have investigated the relationship between bilirubin and multiple sclerosis (MS).

Objective: The aim of present study was to determine serum bilirubin concentration in relapsing remitting (RR) MS patients compared to healthy control subjects (HCs).

Methods: Serum samples were collected from participants who attended to Kashani MS clinic in Isfahan. A total of 80 RRMS patients (67 females and 13 males) and 94 HC (62 female and 32 male) enrolled in this study and bilirubin levels were measured in all subjects. Patients didn’t receive immunosuppressive or interferon medication at least 6 months prior to study entry.

Result: The level of direct bilirubin (Dbil) was significantly lower in MS patients compared with HCs (P < 0.00). Otherwise the serum concentration of total bilirubin (Tbil) and indirect bilirubin (Ibil) were higher in MS patients. Bilirubin level was decreased in females compared to males in both study groups. There was a negative correlation between Extended Disability Status Scale (EDSS) and bilirubin levels in MS patients, but it was not statistically significant.

Conclusion: Our results suggest that bilirubin as an endogenous antioxidant can relieve neuroinflammation course. So we can conclude that in addition to immunomodulator therapy, we should pay more attention to antioxidant roles in neuroinflammatory diseases treatment in future.

P-26 Proteomic Analysis of Cerebrospinal Fluid for Relapsing-Remitting Multiple Sclerosis and Clinically Isolated Syndrome

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Background: The aim of this study was to identify changes in the proteome of cerebrospinal fluid of patients with the relapsing-remitting multiple sclerosis and clinically isolated syndrome compared to the healthy population.
Objectives: The aim of this study was to identify changes in the proteome of cerebrospinal fluid (CSF) and find out what proteins and in what quantities are found in CSF of patients with the relapsing-remitting (RR) MS and clinically isolated syndrome (CIS) at high risk of developing MS compared to the healthy population (control).

Materials and Methods: CSF from patients with MS (n=11) and controls (n=15) were analyzed.

Results: We found 26 protein groups significantly (P < 0.002) dysregulated in case samples compared to controls. Three of these proteins have been previously linked to RR MS - Ig gamma-chain C region, Ig Heavy chain V-III region BRO and Ig kappa chain C region.

Conclusion: This study demonstrated three proteins occurred only in patients with RR MS compared to CIS. These proteins should be prognostic biomarkers in identifying patients with high risk of developing MS.

Poster Session 6
MS Immunology

P-27
Th1, Th2 and Th17 Cytokine Profile in Patients with Multiple Sclerosis Following Treatment with Rapamycin
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Background: Management of Multiple Sclerosis is based on the usage of immunosuppressive and immune-modulating medications. Cytokines play an important role in the pathogenesis of Multiple Sclerosis, thus, this study aimed to evaluate the effects of rapamycin on the concentrations of Th1/Th2/Th17 serum cytokines in patients with MS.

Method: Six patients with relapsing remitting MS as a case and 6 normals as a control group were enrolled. The patients have been received 2 mg rapamycin daily for 6 months and the control group received nothing during 6 months of the experiment. Enzyme linked immunosorbent assay (Multi-AnalyteELISArray) technique was used for determination of serum concentrations of IL-2, IL-4, IL-5, IL-6, IL-10, IL-12, IL-13, IL-17, IFNγ, TNFα, GCSF and TGF-β before and after therapy with rapamycin.

Results: The mean absorbance of 10 (83.33%) out of the 12 studied cytokines showed reduction after the therapy with rapamycin including interleukins (IL), IFNγ and TNFα. The only statistically significant reduction was observed in the absorbance of IFNγ (P=0.028). Two cytokines illustrated increase in the patients' serum after the therapy, including GCSF and TGF-β (P=0.046).

None of the studied cytokines in the control group varied significantly after 6 months.

Conclusion: Based on the findings of the present study, rapamycin has some immunosuppressive effects, such as decreasing INFγ, which can improve the quality of life of the patients with MS. The increased level of TGF-β may also have benefits on the disease, but needs further clinical studies.

P-28
Heparin Binding Growth Factor Level in Association with Inflammatory and Anti-Inflammatory Cytokines in “Multiple Sclerosis“ Patients
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Objective: Midkine (MK) is a heparin-binding growth factor has various effects in induction of neurodegenerative diseases and promotes inflammatory responses by enhancing the migration of inflammatory leukocytes. No clinical or biological markers are available to have adequate sensitivity and exclusiveness for multiple sclerosis (MS).

Methods: To evaluate the MK levels and its relationship with inflammatory cytokines (IL-17 and IL-23) and anti-inflammatory ones (IL-10 and TGF-β) in multiple sclerosis (MS) patients, the serum concentration of these proteins was assessed by ELISA in 32 MS patients in comparison with 32 healthy subjects.

Results: Our data showed that the MK concentration in MS patients is lower than healthy controls. Also we observed a significant decrease in IL-10, IL-23, and TGF-β cytokine levels in MS patients. There was a significant correlation between MK and IL23 concentrations in our study cohort.

Conclusion: The MK level in sera from MS patients was variable. These results confirm a role for MK in inflammatory reactions in MS and advance studies are needed to assess the exact level of MK among different types of MS.

P-29
Investigation of Serum Interleukin 10 Levels in Patients with Multiple Sclerosis
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Background: Multiple sclerosis (MS) is a T-cell-mediated autoimmune disease characterized by demyelination, multifocal inflammation, reactive gliosis, and axonal loss in many regions of central nervous system (CNS). Interleukin 10 (IL-10) is an anti-inflammatory molecule and cytokine. IL-10 levels have been shown to be low in patients with MS in the literature.

Objective: To investigate serum levels of IL-10 in 203 MS patients with different clinical types of MS, different stages of the disease and the usage of different immunomodulating drugs.

Methods: We aimed to investigate serum levels of IL-10 in patients with MS.
Results: In patients with MS serum levels of IL-10 lower than the control group. However these results were not statistically significant.

Conclusions: Although the low serum levels of anti-inflammatory cytokine IL-10 in patients with MS is not statistically significant, further studies will clarify this issue in this regard.

P-30 Investigation of Serum Chemerin Levels in Patients with Multiple Sclerosis
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Background: Multiple sclerosis (MS) is a T-cell-mediated autoimmune disease characterized by demyelination, multifocal inflammation, reactive gliosis, and axonal loss in many regions of central nervous system (CNS). Chemerin was isolated as a natural ligand of the G protein–coupled receptor ChemR23. It plays a chemotactic role for the leukocyte populations that express ChemR23, particularly including immature plasmacytoid dendritic cells, immature myeloid dendritic cells, macrophages, and natural killer cells. In several studies, large numbers of dendritic cells have been found in inflamed lesions of the CNS and cerebrospinal fluids in patients with MS.

Objective: To investigate serum levels of chemerin in 182 patients with different clinical types of MS, different stages of the disease and the usage of different immunomodulating drugs.

Methods: We aimed to investigate the relationship between chemerin and dendritic cells in patients with MS.

Results: Patients newly diagnosed with MS, particularly those who do not use immunomodulating drugs or methylprednisolone, have high levels of chemerin. Conversely, we observed that patients who use methylprednisolone and immunomodulating drugs have low levels of chemerin. These data can give an indication of the course of the disease and suggest a response to treatment.

Conclusions: Our study supports the possibility that chemerin has pro-inflammatory properties and once again shows that dendritic cells play an important role in the pathogenesis of MS.

P-31 The Association between Plasma Chitotriosidase Concentration and the Disease Activity in Patients with MS
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Introduction: Multiple sclerosis is the most common autoimmune demyelinating disorder of central nervous system. The role of macrophage in myelin destruction in this disabling disease is undeniable. Chitotriosidase (Chit) is one of the mammalian enzymes synthesized and secreted by specifically activated macrophages. Recent studies indicate that Chit may have a role in the pathogenesis of MS disease.

Methods: We analyzed serum obtained from 40 relapsing remitting multiple sclerosis patients and 23 healthy individuals in Iranian population. Case and control group were sex and age matched, mean age were 31.92 and 33.54, respectively. In case group, sampling was done during attack before receiving steroid pulse or immunomodulatory drugs. ESS of patients was 1.6 (± 0.86). The concentration of Chit was measured by Enzyme linked Immunosorbent Assay (ELISA).

Results: Our results showed that there is no correlation between Chit concentration and MS disease (p= 0.87). Also, we did not find any association between Chit concentration and the disease activity in patients with MS. In addition no differences have been detected between relapsing and progressive clinical forms.

Conclusion: It seems Chit does not play a key role in the pathogenesis of MS and other inflammatory mediators might be involved in this scenario. However, it should be considered that chit expression is dependent to ethnic background. In our study, negative correlation between multiple sclerosis activity and chit activity compared to control group, may be due to high expression of chit even in normal Iranian population.

Poster Session 7
MS IFN beta

P-32 A Matching-adjusted Indirect Comparison of Clinical Effectiveness of Subcutaneous Peginterferon Beta-1a and Intramuscular Interferon Beta-1a for the Treatment of Relapsing Multiple Sclerosis
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Background: Subcutaneous (SC) peginterferon beta-1a (PEG-IFN) and intramuscular (IM) interferon (IFN) beta-1a have not been compared in head-to-head trials in relapsing-remitting multiple sclerosis (RRMS).

Objective: Indirect comparative effectiveness was determined by comparing annualised relapse rate (ARR), proportion of patients with confirmed relapses and 24-week confirmed disability progression (CDP) at 2 years with SC PEG-IFN 125 mcg every 2 weeks and IM IFN beta-1a 30 mcg once weekly in randomised Phase 3 trials.

Methods: Individual patient data from a trial of SC PEG-IFN (ADVANCE) and published aggregate data from a trial of IM IFN beta-1a (DECIDE) were utilised. A matching-adjusted indirect comparison was conducted by weighting individual PEG-IFN-treated patients using estimated propensity of enrolling in each treatment arm to match key aggregate baseline characteristics for IM IFN beta-1a-treated patients.

Results: To match a DECIDE criterion, patients from ADVANCE ≥55 years of age were excluded. Before matching, PEG-IFN-treated patients (n=499) had fewer gadolinium-enhancing lesions at baseline compared to IFN-beta-1a-treated patients (n=922). After matching (PEG-IFN effective n = 301), key baseline characteristics were balanced. At 2 years, matched patients with RRMS treated with SC PEG-IFN vs IM IFN beta-1a experienced numerically lower...
ARR (0.18 [0.082, 0.388] vs 0.39 [95% confidence interval not available in published data]), lower proportion with confirmed relapse (29% vs. 41%; \( P=0.0002 \)), and lower proportion with 24-week CDP (8% vs. 12%; \( P=0.047 \)).

**Conclusion:** In this propensity-matched indirect comparison, SC PEG-IFN 125 mcg every 2 weeks demonstrated better clinical outcomes, compared with IM IFN beta-1a 30 mcg once weekly.

**P-33**

**A Matching-adjusted Indirect Comparison of Clinical Effectiveness of Subcutaneous Peginterferon Beta-1a and Subcutaneous Interferon Beta-1a for the Treatment of Relapsing Multiple Sclerosis**

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**Background:** Subcutaneous (SC) peginterferon beta-1a (PEG-IFN) and SC IFN beta-1a are disease-modifying treatments for relapsing-remitting multiple sclerosis (RRMS) which have never been compared head-to-head. Matching-adjusted indirect comparison compares weighted individual patient data for one agent with aggregate data for another agent.

**Objective:** Indirect comparative effectiveness was determined for annualised relapse rate (ARR), proportion with confirmed relapses and 24-week confirmed disability (CD) at 2 years for patients with RRMS treated with PEG-IFN or SC IFN beta-1a in Phase 3 studies.

**Methods:** Individual patient data from a study of PEG-IFN 125 mcg every two weeks (ADVANCE), and published aggregate data from a study of SC IFN beta-1a 44mcg three-times per week (TIW) (CARE-MS II) with similar populations were utilised. A matching-adjusted individual patient data from a study of PEG-IFN 125 mcg every two weeks (ADVANCE), and published aggregate data from a study of SC IFN beta-1a 44mcg three-times per week (TIW) (CARE-MS II) with similar populations were utilised. A matching-adjusted indirect comparison was conducted by weighting individual PEG-IFN-treated patients, using estimated propensity of enrolling in each treatment arm to match multiple key aggregate baseline characteristics in SC IFN-beta-1a-treated patients. After matching, weighted efficacy outcomes for PEG-IFN were compared with summary efficacy outcomes for SC IFN beta-1a.

**Results:** After matching, baseline characteristics were balanced across treatment groups. At 2 years PEG-IFN (effective n=193) vs SC IFN beta-1a (n=187) treated patients experienced numerically lower: ARR (0.15 [95% CI: 0.12, 0.21] vs 0.39 [95% CI: 0.29,0.53]), proportion with confirmed relapse (23% vs 40%; \( P=0.0003 \)), and proportion with 24-week CD (5% vs 11%; \( P=0.032 \)).

**Conclusion:** In this matching-adjusted indirect comparison, SC PEG-IFN 125 mcg treatment every 2 weeks resulted in significantly fewer patients with relapse and confirmed disability, compared to SC IFN beta-1a 44mcg TIW for patients with RRMS.

**P-34**

**Effectiveness of Intramuscular Interferon Beta-1a in Four Recent Phase 3 Trials Compared with Its Registration Trial: A Literature Update**

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**Background:** Approximately 20 years ago, intramuscular (IM) interferon (IFN) beta-1a was one of the first disease-modifying therapies (DMTs) approved for treatment of relapsing-remitting multiple sclerosis (RRMS). Since then, however, the knowledge and management of multiple sclerosis (MS) have evolved, and IM IFN beta-1a is now being evaluated as a reference/comparator in trials evaluating new DMTs.

**Objective:** To examine the apparently consistent and/or increased effectiveness of IM IFN beta-1a in recent clinical trials compared with its registration trial.

**Methods:** MEDLINE and congress abstracts (1/2010-5/2015) were searched using MeSH terms that included “multiple sclerosis relapsing-remitting,” “interferon-beta,” “phase 3,” and “randomized controlled trial.” Four trials comparing IM IFN beta-1a with other DMTs (BRAVO, CombiRx, DECIDE, and TRANSFORMS) were identified. Key outcomes from each study (annualized relapse rate and 3- or 6-month confirmed Expanded Disability Status Scale (EDSS) progression) were compared with those from the IM IFN beta-1a RRMS registration trial (MSCRG).

**Results:** Across all 5 studies, baseline characteristics were generally similar (age, 36-39 years; relapses in previous year, 1.0-1.7; EDSS score, 2.0-2.5). Fewer relapses per patient-year were observed with IM IFN beta-1a in all 4 recent studies (BRAVO, 0.26; CombiRx, 0.16; DECIDE, 0.39; TRANSFORMS, 0.33) than in MSCRG (0.61). Percentages of patients with confirmed EDSS progression were as follows: BRAVO, 8%-11%; CombiRx, 22%; DECIDE, 18%-20%; TRANSFORMS, 8%; MSCRG, 21%.

**Conclusions:** The apparently increased effectiveness of IM IFN beta-1a in recent studies may stem from improvements in MS management relative to 2 decades ago. These observations may reset expectations for treatment outcomes going forward.

**P-35**

**Real-World Effectiveness and Utilization of Intramuscular Interferon Beta-1a vs Other Approved First Line Injectable DMTs in Patients with Multiple Sclerosis in the United States**

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**Background:** First-line injectable disease modifying therapies (DMTs) for relapsing-remitting multiple sclerosis have been approved for use in the United States for nearly 20 years. Recently, there has been a lack of real-world analyses to measure the effectiveness and treatment patterns of these therapies.

**Objective:** To measure the real-world annualised relapse rate of patients on first-line injectable DMTs, and the real-world utilisation of patients treated with intramuscular (IM) interferon (IFN) beta-1a.

**Methods:** A retrospective, observational, cohort study was conducted to examine relapse rates for patients with multiple sclerosis (MS) who were prescribed any first-line injectable DMT (IM IFN beta-1a, subcutaneous (SC) IFN beta-1a, SC IFN beta-1b or glatiramer acetate) between January 1, 2009 and March 31, 2013. Eligible patients were identified in the MarketScan Commercial Claims and Encounters Database, who had a diagnosis of MS (ICD-9 code 340) and were ≥18 years of age. Results are weighted by person-year and adjusted by multivariate analysis, controlling for age, gender and disease duration.

**Results:** A total of 73,383 patients were included as meeting these criteria. The average adjusted annualised relapse rate (ARR) across all first-line injectable DMTs was 0.294. IM IFN beta-1a was associated with a statistically significant reduction in ARR compared to other DMTs combined (0.274 vs 0.303, or a 90.4%
adjusted relapse rate ratio, \( p<0.0001 \)). Average duration of therapy of all therapies was 1.968 years.

Conclusions: When compared to other first-line injectable DMTs in this analysis, IM IFN beta-1a was associated with a lower annualised relapse rate.

P-36
Relapse Rates among Multiple Sclerosis Patients Treated with Different Disease Modifying Therapies in Germany
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Background: First-line injectable disease modifying therapies (DMTs) can reduce the number of relapses among patients with relapsing-remitting multiple sclerosis (RRMS). However, comparative information on relapse among those using intramuscular (IM) and subcutaneous (SC) agents is lacking.

Objective: To examine relapse occurrence among multiple sclerosis (MS) patients initiating treatment with IM interferon (IFN) beta-1a compared to SC IFN beta-1a, IFN beta-1b, and glatiramer acetate.

Methods: A retrospective database analysis using the Health Risk Institute research database containing healthcare claims of approximately 80 of the 130 independent German health insurances was conducted. MS patients initiating treatment with the respective DMT (index date) were identified between January 2009 and December 2012 and continuously insured for 12 months pre- and post-index date. Relapse rates, risk of relapse, and time to relapse were analysed.

Results: The analysis included 357 IM IFN beta-1a, 330 SC IFN beta-1a, 281 SC IFN beta-1b (147 Betaferon, 107 Extavia) and 422 glatiramer acetate patients. There was a significant difference in the adjusted annualised risk of relapse between the IM IFN beta-1a and the Betaseron group (HR=0.695 [0.527; 0.922]; \( P<0.01 \)) as well as a significant difference in mean (SE) time to first relapse (276.4 (7.0) vs. 246.2 (10.4); \( P=0.01 \)). No other significant differences were observed.

Conclusion: MS patients in Germany treated with IM IFN beta-1a had a lower risk of relapse and longer time to first relapse compared with a subgroup of SC IFN beta-1b. Additional research is needed to explore differences in other RRMS-related outcomes.

P-37
Neutralising Antibodies to Interferon-beta Therapy in Chinese Patients with Relapsing and Remitting Multiple Sclerosis.
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5Department of Medicine, Queen Elizabeth Hospital, Hong Kong.

Background and Objective: Neutralising antibodies (NAbs) to interferon-beta (IFN-beta) are associated with reduced treatment efficacy, disease relapse and progression. There is no such data for NAbs in Chinese multiple sclerosis patients. We performed a pilot study to evaluate the prevalence of anti-IFN-beta binding antibodies (BAbs) and NAbs in Hong Kong Chinese patients with relapsing and remitting multiple sclerosis (RRMS).

Methods: Seventy-three RRMS subjects receiving IFN-beta therapy for more than one year and 15 normal subjects were recruited. Clinical information, sera and total RNA of peripheral blood mononuclear cells (PBMCs) or PAXgene blood of each subject were collected. For each subjects, myxovirus resistance protein 1 (MxA) gene expression in the blood was measured by real-time PCR; sera were tested for 1) IFN-beta BAbs by a commercial ELISA; and 2) NAbs by luciferase reporter gene assay, in-house developed PCR-based and ELISA-based MxA induction assays.

Results: Forty-three out of 49 (87.8%) tested patient samples (using a clinical cut-off at 30 BVI) were BAbs positive while only 11 out of 73 (15.1%) tested patient samples were NAbs positive. The MxA gene expression of NAbs positive patients was significantly reduced (mean=0.11; n=10; \( P<0.001 \)) when compared to NAbs negative patients (mean=0.48; n=60), indicating a lower response to IFN-beta treatment.

Conclusions: This was a cross-sectional study demonstrating a low frequency of NAbs (15%) in Chinese RRMS patients upon IFN-beta therapy. The presence of NAbs were associated with poorer clinical response, its clinical utility as a biomarker for treatment response should be further evaluated in prospective studies.

Poster Session 8
MS Glatiramer

P-38
Twenty Years of Continuous Treatment of Multiple Sclerosis with Glatiramer Acetate 20 mg/mL Daily: Long-Term Disability Outcomes in the US Open-Label Extension Study
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Background: Glatiramer acetate (GA) is the only multiple sclerosis (MS) treatment evaluated for more than a decade in a continuous, long-term study. We report the 20-year results from the open-label extension of the US pivotal trial.

Objectives: To assess the long-term clinical profile of GA 20 mg/mL daily and the disease course, in patients with relapsing-remitting MS.

Methods: Eligible patients from the 36-month, placebo-controlled US glatiramer acetate trial, electing to participate in the extension phase, either continued or switched to GA treatment. For each patient, the initiation date of GA therapy is regarded as baseline.

Results: Of the 232 patients who received ≥1 dose of GA during the pivotal trial, 74 are ongoing. These patients, with an average disease duration of 27.3 years, have been treated continuously with GA for a mean of 19.3 years (SD=1.3, range 18–21). Mean scores on the Expanded Disability Status Scale (EDSS) rose to 3.1
P-39 Efficacy and Safety of a Three-times Weekly Dosing Regimen of Glatiramer Acetate in Relapsing-Remitting Multiple Sclerosis Patients: 3-Year Results of the Glatiramer Acetate Low-Frequency Administration (GALA) Open-Label Extension Study

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Background: The placebo-controlled (PC) phase of the GALA study showed that GA40 had significant clinical benefit over placebo at Year 1 in patients with relapsing-remitting multiple sclerosis. Patients completing the PC phase were invited to participate in an open-label (OL) extension.

Methods: The majority (97.2%, 1253/1289) of patients consented to receive GA40 in the OL extension after completing the 1-year PC phase; patients were evaluated for relapse and MRI outcomes. Early-start (ES, n=943) patients received GA40 throughout, whereas delayed-start (DS, n=461) patients were randomized to placebo and switched to GA if they entered the OL phase.

Results: During Year 1, ES patients had significantly lower annualized relapse rate (ARR) and fewer gadolinium-enhancing (GdE) T1 and new/enlarging T2 lesions than DS patients. During the OL phase, both groups receiving GA40 showed comparable yearly ARRs (range: 0.20–0.22) and, after 2 years of OL, GA40 treatment, ES and DS patients demonstrated similar numbers of lesions. Time to first relapse was significantly longer for ES patients than for DS patients (hazard ratio 0.746; P<0.001). Adverse events were consistent with the well-established GA safety profile.

Conclusion: In the GALA study, OL treatment with GA40 in Years 2 and 3 was associated with low disease activity. During OL treatment, the efficacy effect of GA40 is maintained, and DS patients experienced treatment benefits comparable to those observed in ES patients.

P-40 Patient Experience with Glatiramer Acetate 40 mg/mL Three-Times Weekly Treatment for Relapsing-Remitting Multiple Sclerosis: Results from the GLACIER Extension Study

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Methods: In the extension phase, patients converting from GA20 to GA40 perceive a convenience advantage compared to those continuing GA40. In the core phase, patients converting from GA20 perceived a 50% lower rate of injection-related adverse events (IRAEs) than those randomized to continue GA20. Patients’ expectations that GA40 would be more convenient than GA20 were confirmed after conversion. All core phase completers were eligible to receive GA40 during the extension phase.

Results: Almost all patients completing the core study continued to the extension phase. Converters and non-converters had the same mean duration of drug exposure (126 days) and similarly low annualized IRAE rates on GA40 during the extension phase (23.1 vs 28.0 events/year). Converters demonstrated an improvement in mean convenience score, from 78.0 following GA20 treatment to 82.2 following conversion to GA40. Those continuing on GA40 maintained convenience scores of 85.1 at the beginning of the extension phase and 84.9 at last observation.

Conclusion: The GLACIER study extension demonstrates that patients converting from GA20 to GA40 perceive a convenience benefit and report fewer IRAEs.

P-41 A Cost Analysis of Drug-related Monitoring Requirements for Glatiramer Acetate and Other Multiple Sclerosis Disease-modifying Therapies

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Background: Disease-modifying therapies (DMTs) available for multiple sclerosis differ in their monitoring requirements. To assess the cost implications resulting from differences in the monitoring requirements for DMTs in Australia (AU), New Zealand (NZ), South Korea (SK), and Taiwan (TW).

Objective: To evaluate the cost implications resulting from differences in the monitoring requirements for DMTs in Australia (AU), New Zealand (NZ), South Korea (SK), and Taiwan (TW).
P-42 Efficacy and Treatment Persistence of First-line Natalizumab vs. Interferon β or Glatiramer Acetate in relapsing MS

H Butzkueven,1 T Spelman,1 T Kalincik,1 V Jokubaitis,1 A Zhang,1 F vs. Interferon β or Glatiramer Acetate in relapsing MS
Efficacy and Treatment Persistence of First-line Natalizumab
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Background: We report findings from an observational, large-scale, head-to-head comparison study of efficacy and treatment persistence in patients who initiated either natalizumab or interferon (IFN)β/glatiramer acetate (GA) as first-line therapy.

Objective: To compare relapse occurrence, treatment persistence, and disability outcomes in treatment-naïve RRMS patients initiating natalizumab compared with IFNβ or GA first line, using propensity score-matched cohorts from observational MS registries.

Methods: Patients were enrolled in the MSBase Registry and treated first line with IFNβ or GA, or enrolled in the TYSABRI Observational Program (TOP) and treated first line with natalizumab. Patients had ≥3 months of on-treatment follow-up and active disease (≥1 gadolinium-enhancing lesion on cerebral MRI at baseline and/or ≥1 relapse within the 12 months prior to baseline). Propensity score matching was used to balance between-group baseline and disease characteristics. Endpoints included annualised relapse rate (ARR), time to first relapse, treatment persistence, and disability outcomes.

Results: A total of 366 patients receiving first-line natalizumab were matched to those receiving first-line IFNβ/GA. Compared with first-line IFNβ/GA, natalizumab was associated with a relative reduction in ARR of 68% (P<0.0001), 64% reduction in rate of first relapse (P<0.0001), and 27% reduction in discontinuation rate (P=0.01). There were no significant differences in confirmed disability progression and area under the EDSS-time curve.

Conclusion: Compared with initiating IFNβ/GA, natalizumab used as first-line therapy for RRMS improved relapse rates and treatment persistence. This needs to be balanced against the risk of Progressive Multifocal Leuкоencephalopathy in patients treated with natalizumab.

P-43 Long-Term Natalizumab Therapy: Progression of Disability and EDSS Milestones

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Background: The TYSABRI Observational Program (TOP) is on ongoing, open-label, prospective study of patients initiating natalizumab.

Objectives: To evaluate the risk of confirmed disability accumulation and the attainment of specific EDSS milestones at 288 weeks in TOP.

Methods: Data from patients with ≥24 months treatment were used to analyse cumulative probability of 24- and 48-week confirmed disability progression (increase in EDSS of ≥1.0 sustained for 24 or 48 weeks). In addition, transition to milestone EDSS scores ≥3.0, ≥4.0, and ≥6.0 according to baseline EDSS
subgroup was evaluated. Analyses were performed overall and in patients with and without on-treatment relapses.

**Results:** As of May 1 2014, 3253 patients completing ≥24 months in TOP had mean baseline EDSS of 3.4. 18.5% and 13.5% patients had 24- and 48-week confirmed EDSS progression, respectively. Cumulative probabilities of 24- and 48-week confirmed progression were higher in patients with on-treatment relapses compared with patients without relapses (23.6% vs 15.0% for 24-week, 17.7% vs 10.8% for 48-week progression; P<0.0001). In primary and sensitivity analyses, respectively, probability of 48-week confirmed EDSS transition was 11.1%, and 9.9% for scores of 0.0-2.0 to ≥3.0, 11.8% and 9.6% for 2.0-3.0 to ≥4.0, and 9.5% and 9.1% for 4.0-5.0 to ≥6. In lower EDSS ranges, risk of transition was significantly higher (P<0.0171).

**Conclusions:** After ~5.5 years, probability of 48-week confirmed disability progression measured by EDSS remained low with natalizumab but was significantly increased by presence of residual relapses. Sensitivity analyses suggest that progression at 48 weeks may reflect mostly irreversible disability worsening.

**P-44**

**Efficacy and Safety of Natalizumab in Multiple Sclerosis: Interim Observational Program Results from an Australian Cohort**

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**Background:** In this ongoing, open-label, multinational, prospective, observational study, patients receive natalizumab 300 mg intravenously every 4 weeks. Primary endpoint: incidence/type of serious adverse events (SAEs). Secondary endpoints include incidence of relapses and change in EDSS score.

**Results:** Data from 5770 patients (179 from the Australian cohort) that enrolled between July 2007 and May 2015 were analysed. Mean baseline EDSS was 3.5 (SD 1.62) and 3.8 (SD 1.86), in the global and Australian cohorts, respectively, and 12.1% and 19.6% patients had baseline EDSS ≥6. In the global and Australian cohorts, respectively, 10.8% and 20.1% patients experienced ≥1 SAE; the incidence of treatment-related SAEs was 3.8% and 4.5%. After 6 years of therapy, mean change from baseline in EDSS score was +0.5 in the Australian group and 0.0 in the global cohort. Annualised relapse rate (ARR) for the global group was 1.99 pre-treatment and 0.23 post-treatment; ARR pre- and post-treatment in Australian patients was 1.70 and 0.21. At 6 years, probability of confirmed EDSS progression was 23.9% and 31.85%, and confirmed EDSS improvement 33.08% and 40.47% in the Global and Australian cohorts respectively.

**Conclusions:** In the Australian cohort of patients treated with natalizumab, we observed a low incidence of treatment-related AEs, low relapse probability, and sustained clinical efficacy, comparable to the global cohort.

**P-45**

**Disease Course in Multiple Sclerosis (MS) Patients Switching from Fingolimod to Natalizumab**

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**Background:** To assess clinical course in MS patients who switched from fingolimod to natalizumab.

**Methods:** The TYSABRI® Observational Program (TOP) enrolls patients receiving natalizumab for the first time. Patients switching from fingolimod at enrollment (baseline) were analysed. Annualised relapse rates (ARRs) in the 12 months before and after baseline were recorded. Expanded Disability Status Scale (EDSS) score changes from baseline were evaluated. Cumulative probabilities of first relapse and 6-month confirmed ≥1-point EDSS worsening or improvement occurring within 12 months from baseline were estimated.

**Results:** As of May 1, 2014, 127 patients had switched from fingolimod; 95.3% received ≥2 DMTs prior to natalizumab. At baseline, median EDSS score was 4.0 and median disease duration 8.1 years. During the 12 months prior to the first natalizumab infusion, mean ARR was 2.09; it decreased to 0.43 during the first 12 months of natalizumab treatment (P<0.0001). Median and mean (standard deviation) EDSS score changes at month 12 were 0.0 and −0.4 (1.04), respectively (P=0.0044). Probabilities of confirmed EDSS worsening and improvement were 2% and 12%, respectively. Seven patients (5.5%) experienced ≥1 serious adverse event (SAE); no cases of progressive multifocal leukoencephalopathy were reported.

**Conclusions:** 1 year after switching to natalizumab from fingolimod, ARR was reduced and EDSS scores were stable. Incidence of SAEs in this subgroup is consistent with natalizumab’s known safety profile. Natalizumab may be a useful treatment option for patients switching from fingolimod.
P-46
MS Alemzutmab

Same as O-14

P-47
Same as O-15

P-48
Durable Effect of Alemtuzumab on Clinical Outcomes Over 5 Years in Patients with Active Relapsing-Remitting Multiple Sclerosis and an Inadequate Response to Prior Therapy Despite Most Patients Not Receiving Treatment for 4 Years: CARE-MS II Extension Study

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Background: In CARE-MS II (NCT00548405), alemtuzumab had superior efficacy versus SC IFNB-1a in active RRMS patients with inadequate response to prior therapy (≥1 relapse) over 2 years. Objective: Examine 5-year clinical efficacy/safety in CARE-MS II alemtuzumab-treated patients.

Methods: Alemtuzumab-treated patients received 2 annual courses (12 mg) and, in the extension (NCT00930553), as-needed alemtuzumab retreatment or other disease-modifying therapy (DMT). Endpoints: annualised relapse rate (ARR), sustained accumulation of disability (SAD; ≥1-point EDSS increase over 6 months), sustained reduction in preexisting disability (SRD; ≥1-point EDSS decrease over 6 months), no evidence of disease activity (NDA; no relapse, SAD, new/enlarging T2; or gadolinium-enhancing lesions).

Results: Extension enrolled 393 (93%) alemtuzumab-treated patients; 93% remained on study; 60% received no alemtuzumab since Month 12; 8% received another DMT. Low ARR was maintained from Years 3 (0.22) through 5 (0.18). Through Year 5, 75% were SAD-free and 43% achieved SAD. In Year 5, 58% of patients achieved NDA. In patients only receiving 2 initial courses, 46% achieved sustained NDA during the extension (3 years). Infusion-associated reaction and infection incidences decreased over time. Thyroid adverse events (AEs) peaked at Year 3, declining thereafter. Serious AE incidence was low.

Conclusions: Alemtuzumab’s efficacy was maintained over 5 years, despite most patients not receiving retreatment over the previous 4 years. Most patients who only received the initial 2 treatment courses were disease activity-free in absence of any additional treatment. This durable effect of the initial 2 courses may result from immunomodulatory effects of the distinct lymphocyte repopulation pattern following treatment.

P-49
Pregnancy Outcomes in Alemtuzumab-Treated Female Patients with Active RRMS in the Clinical Development Program

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Background: There are no clinical studies of alemtuzumab in pregnant women with multiple sclerosis (MS), but it is important to assess its effects on pregnancy. Alemtuzumab is low or undetectable in serum within 30 days, but women of childbearing potential should use contraception for 4 months after receiving alemtuzumab.

Objective: To report pregnancy outcomes in alemtuzumab-treated female patients.

Methods: In phase 2 (CAMMS223 [NCT00050778]) and 3 (CARE-MS I and II [NCT00530348, NCT00548405]) studies, patients received annual courses of alemtuzumab 12 or 24 mg. Patients could enter an extension (NCT00930553) for follow-up, with retreatment based on disease activity. Patients were not eligible for treatment while pregnant/lactating but remained on study.

Results: As of 01 July 2015, 1486 patients were exposed to alemtuzumab; 193 pregnancies occurred in 136 patients (n=167 completed with known outcome; n=16 ongoing; n=10 unknown outcome). Of completed pregnancies with known outcomes, 110 (66%) were live births with no congenital abnormalities. 37 (22%) spontaneous abortions occurred, which is not increased over spontaneous abortion rates in treatment-naive MS (up to 26%). 19 (11%) patients had elective abortions; 1 (0.6%) was stillbirth. Elective abortions were due to anembryonic gestation (n=2), extrauterine pregnancy (n=3), foetal defects (n=1; cystic hygroma and hypoplastic heart), or personal choice (n=6); 7 had no information available.

Conclusions: The most common pregnancy outcome in the alemtuzumab clinical programme was full-term live birth. There have been no teratogenic events or congenital anomalies reported in delivered infants. The rate of spontaneous abortion is similar to rates in treatment-naive MS patients.

Poster Session 11
MS other DMDs and Immunotherapy

P-50
Same as O-10

P-51
Accelerated Elimination Procedures are Well Tolerated and Highly Effective at Rapidly Reducing Teriflunomide Plasma Concentrations in Healthy Volunteers

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**Background:** Teriflunomide, a once-daily oral immunomodulator approved for relapsing-remitting MS, is rapidly absorbed and undergoes enterohepatic recycling, resulting in a long plasma half-life. Accelerated elimination is available to rapidly reduce plasma concentrations to <0.02μg/mL (the level expected to confer minimal teratogenic risk) when medically desirable (e.g. in pregnancy).

**Objective:** To assess the accelerated elimination of teriflunomide with cholestyramine or activated charcoal in healthy volunteers.

**Methods:** In 3 clinical pharmacology studies, healthy adult volunteers (N=85) received a loading dose of teriflunomide 70mg/day for 4 days followed by 14mg/day for 8 days. Accelerated elimination procedures (AEPs) with cholestyramine (8g or 4g, 3 times daily) or activated charcoal (50g 2 times daily) for 11 days were then initiated. Teriflunomide plasma concentrations were measured by liquid chromatography coupled with tandem mass spectrometry, with a lower limit of quantification of 0.01μg/mL, from blood samples obtained at baseline and specific timepoints throughout the studies, including before, during and/or after the AEP. Adverse events were evaluated at each study visit.

**Results:** All AEPs reduced plasma teriflunomide concentrations by ≥97% at Day 1 and 91% after Day 3. Overall, cholestyramine and activated charcoal were well tolerated in participants, with mild to moderate gastrointestinal events accounting for the majority of adverse events.

**Conclusions:** The AEPs investigated were all well tolerated and highly effective at rapidly reducing the plasma concentration of teriflunomide in healthy volunteers.

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**P-52**

**T and B Cell Driven Dimethyl Fumarate-Induced Lymphopenia in Patients with Multiple Sclerosis**

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**Background:** Tecfidera, an oral treatment option for multiple sclerosis (MS), is associated with lymphopenia as demonstrated in CONFIRM/DEFINE.

**Objective:** To evaluate the behavior of T cells in the lymphocyte subset who experience dimethyl fumarate (DMF)-induced lymphopenia.

**Methods:** A retrospective chart review was conducted of 13 patients with MS treated with DMF. Data was analyzed on patients with an absolute lymphocyte count that demonstrated at least a 30% drop from their baseline prior to starting DMF who underwent flow cytometry lymphocyte subset analysis after being on DMF treatment for at least 3 months.

**Results:** The population demographics included 11 female patients (85%) and 2 male patients (15%): with a mean age of 54.4 ± 0.7 years, disease duration of 9.2 ± 0.6 years. With the exception of one patient, all 12 patients demonstrated a drop in T cells. The CD8+ lymphocytes showed a greater reduction in % lower limit of normal (LLN) relative to CD4+ lymphocytes. CD19+ B cells were reduced in 5 patients. One patient discontinued DMF after 18 months due to a new relapse and gadolinium-enhancing lesions on magnetic resonance imaging. One patient discontinued DMF treatment after 24 months due to persistent Grade 3 lymphopenia.

**Conclusions:** Previous studies have been performed to understand whether primarily T cells or B cells drive lymphopenia. Performing routine flow cytometry may help manage patient response and safety to DMF treatment.

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**P-53**

**An Open-Label, Parallel-Group, Phase 1 Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of Delayed-Release Dimethyl Fumarate in Chinese, Japanese, and Caucasian Adult Healthy Volunteers**

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**Background:** Delayed-release dimethyl fumarate (DMF) has a favorable benefit-risk profile and is indicated for the treatment of patients with relapsing Multiple Sclerosis. The pharmacokinetics (PK) of DMF have not been assessed in Asian populations.

**Objectives:** To evaluate PK profile (primary objective) and safety/tolerability of DMF in healthy Chinese and Japanese volunteers, and a reference group of Caucasian volunteers.

**Methods:** 23 Chinese, 24 Japanese, and 24 Caucasian volunteers were enrolled in this Phase I study to receive two doses of open-label oral DMF 120 mg or 240 mg (1:1, nonrandomised, stratified by sex and ethnicity) over 24 hours. PK was assessed by measuring the metabolite monomethyl fumarate (MMF) in plasma samples. Safety assessments included vital signs, laboratory tests, and adverse events (4-day safety follow-up).

**Results:** Following DMF administration, mean concentration-time curves for MMF and individual PK parameters showed similar profiles across the 3 ethnic groups and were consistent with previous observations in mixed populations. Safety and tolerability were similar between ethnic groups, except for flushing, which was less common in Japanese participants (n=4, 17%) than in Chinese (n=17, 74%) or Caucasian (n=17, 71%) participants. Adverse events were reported by 23 (64%) participants who received 120 mg and 28 (80%) who received 240 mg; all were mild or moderate; none were serious. There were no clinically significant changes in vital signs or laboratory tests.

**Conclusions:** The PK and safety/tolerability profiles of DMF 120 mg or 240 mg twice-daily in Chinese and Japanese healthy volunteers are similar to those in Caucasians.

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**P-54**

**Safety and Efficacy Profile of Fingolimod in the Post-Marketing Setting in Japanese Patients with Multiple Sclerosis**

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**Background:** Following approval in 2011, a post-marketing surveillance (observation period, 2 years) began for all fingolimod-treated patients in Japan.

**Objective:** To evaluate initial 6-month safety and efficacy of fingolimod in real-world clinical settings in Japan.
Methods: 1018 patients initiating the medication before Sep 2014 were analysed. Demographics, reasons for discontinuation, serious adverse drug reactions (ADRs), ADRs of interest (cardiac events at initiation, hypertension, infections, macular oedema, hepatic enzyme elevations, lymphopenia/leukocytopenia), annual relapse rate (ARR) and physician's subjective efficacy assessment were evaluated. Cardiac and ophthalmological monitoring rates were collected.

Results: Mean age of the population was 39.9 years (females, 63.9%). Mean disease duration was 8.8 years; 63.2% had received prior interferon-beta therapy. During the 6-month period, ADRs were reported in 41.5% patients; most frequent were lymphopenia (16.5%) and abnormal hepatic function (12.9%). 7.1% patients reported cardiac ADRs predominantly during first dose observation. Incidence of infections and macular oedema was 3.7% and 0.7%, respectively. At the last observation point, ARR was 0.23 (0.97 at baseline), and physician’s subjective efficacy assessment indicated 71.8% as effective, 2.7% as ineffective, and 25.6% as unknown.

Conclusion: The safety and efficacy profile of fingolimod during initial 6-month follow-up in real-world clinical settings in Japan was comparable to that seen in other clinical trials in both Japan and other countries. A longer-term follow-up study is ongoing to further assess the safety and efficacy profile of fingolimod in Japanese MS patients.

P-55 CBP-307: A Second Generation S1P1 Modulator for the Treatment of Multiple Sclerosis
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Background: Modulation of the sphingosine-1-phosphate (S1P) receptor subtype 1 (S1P1) on T lymphocytes is highly efficacious in treating the relapsing-remitting form of multiple sclerosis (RRMS). Fingolimod (Gilenya), the first approved oral MS treatment, is a potent agonist of 4 of the 5 S1P receptor subtypes. Despite its high efficacy, fingolimod carries a number of side effects including bradycardia, liver enzyme elevation, reduced lung functions and increase blood pressure. In addition, it has a very long elimination half-life (144-216 h) and it takes at least 56 days for peripheral lymphocyte counts to return to baseline level after treatment discontinuation.

Objective: Our goal is to develop a second generation S1P1 modulator with (1) improved receptor selectivity particularly away from S1P3, (2) shortened drug half-life and time to full lymphocyte recovery after dosing discontinuation, and (3) reduced effect on heart rate at treatment initiation.

Methods: A randomized, double-blind, placebo-controlled Phase 1 clinical study has been conducted to assess the tolerability, pharmacokinetics and pharmacodynamics of CBP-307 in healthy volunteers in Australia.

Result: CBP-307 is highly selective with greater than 10,000 fold selectivity over S1P3. Full lymphocyte sequestration is achieved after 0.25 mg daily dosing. The elimination half-life is 25 hours, and the time to full lymphocyte counts recovery to baseline is 7 days after the last dose. Heart rate reduction is much more moderate compared to that reported for fingolimod at the approved dose of 0.5 mg.

Conclusion: CBP-307 is a promising second generation S1P1 modulator suitable for further clinical development as MS treatment.

P-56 A Review of Clinical Pharmacokinetics of Rituximab in Multiple Sclerosis
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Background: In patients with multiple sclerosis (MS) relapses support as important marks of disease activity. The United States expired patent in 2015, rituximab (MabThera, Zytux) may be considered as a B cell-depleting regimen in such condition.

Objective: Clinical data associated to pharmacotherapy consequence of rituximab are inadequate, therefore, reviewing articles and investigations could offer creative and satisfactory attention toward drug prescriptions.

Methods: Directory of Open Access Journals (DOAJ), Google Scholar, Pubmed (NLM), Library, Information Science and Technology Abstracts (LISTA, EBSCO publishing) and Web of Science with key words relevant to topic of this review were searched.

Results: Rituximab is considered as class C for pregnant woman. The molecular mass of drug is 1493859.7 gr/mol. With a half-life of 30 to 400 hours which is varied by dose and length of treatment, the drug has a bioavailability of 100 %. The route of administration is only by intra venous. Subcutaneous rituximab may become a useful option in patients with B-cell non-Hodgkin's lymphoma.

Conclusions: To complete benefit-risk assessment, direct thoughtful and well-adjusted rituximab data, attributed intervention in Iranian patients with multiple sclerosis should be based on clinical pharmacokinetics parameters in terms of dose, rout of administration, Cmax, C0 and half-life. Finally, despite the standard care for such patients all over of the world and Iran, there is still need for development of pharmacotherapy command in terms of research related to efficiency and adverse effects.

P-57 Mitoxantrone Treatment for Aggressive Multiple Sclerosis: 10 Years Follow Up Study
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Background: Mitoxantrone (MX), has been approved by US Food and Drug Administration (FDA) for the treatment of patients with aggressive or refractory multiple sclerosis (MS) in 2000. In most cases MX was used for relapsing –remitting MS (RRMS) with frequent and disabling relapses and for rapid secondary progressive MS (SPMS).

Objective: To evaluate the clinical and radiological outcome in patients with aggressive MS 10 years after treatment with MX.
Methods: Patients (n=21) diagnosed with worsening RRMS, SPMS, or primary progressive MS received intravenous (IV) MX infusion every 3 months at a dose of 12mg/m² body surface area per infusion plus 1g IV methylprednisolone. Patients were evaluated before treatment initiation, including cardiac dysfunction and an assessment of Expanded Disability Status Scale.

Results: Twenty-one MX-treated MS patients (14 females, 7 males) with mean age 43.5 years (range, 25-61 years), 4 had RRMS, 2 had PPMS, and 15 had SPMS. Mean disease duration to MX initiation was 11.7 years. Ten years following MX treatment 3 of our patients had died, 3 developed cancer, 5 were clinically improved, 4 had little change, and 12 continued deterioration. Four out of 5 patients with improvement had RRMS with gadolinium positive MRI lesions. One patient had transient atrial fibrillation.

Conclusions: Mitoxantrone was an effective and safe treatment in selected cases of rapidly progressive RRMS with active MRI lesions. Evidence for benefit in progressive forms of MS without MRI activity was lacking.

P-58
Comparing the Efficacy of Monthly Cyclophosphamide Infusions as Monotherapy in Relapsing Remitting and Secondary Progressive Multiple Sclerosis versus Daily Oral Fingolimod
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Background: Treating aggressive forms of RRMS and progressive disease forms of MS still presents a great challenge to neurologists. Patients with MS face not only physical disability but also neuropsychiatric problems such as anxiety and depression due to unpredictable relapse. Some of studies showed that cyclophosphamide (1000 mg per dose) as monotherapy in relapsing remitting (RR) and secondary progressive (SP) multiple sclerosis versus daily Fingolimod (0.5 mg per day). Since, the aim of this study was to compare these two treatment strategies in aggressive type MS including RR and SP ones.

Material and Methods: In a clinical trial study 15 RRMS patients were treated by cyclophosphamide and 15 patients were treated by Fingolimod for six months. EDSS score and relapse rate was compared between the two groups.

Results: The mean differences of EDSS in the cyclophosphamide and Fingolimod groups was -0.03±0.17 and 0.33±0.18 respectively and according to repeated measures ANOVA test, the decrease of EDSS in Fingolimod group was higher than the cyclophosphamide group (P<0.001). The relapse number was not different during 6 months before intervention (P=0.098) but it is different in the 6 months after treatment (p=0.023).

Conclusion: According to this study, using of daily oral Fingolimod is seems to be better than the monthly infusion of cyclophosphamide for prevention of relapses and improvement of EDSS in aggressive type of RRMS and SPMS patients and it can be considered as one of treatment options in such cases.

P-59
Same as O-16

Poster Session 12
MS Fampridine and other Therapies

P-60
Fampridine Improves Gait Parameters, Balance Test and Functional Independence Measurement (FIM) in Multiple Sclerosis
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Objective: Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS) that is prevalent among young adults and usually leads to chronic disability. Ambulation is important to patients with MS, and they perceive it as a major issue for their health. Clinical trials have demonstrated that dalfampridine improves walking ability among patients with MS. We aimed to evaluate this drug's efficacy on gait parameters, balance test, functional independence measurement retrospectively.

Methods: Data collected from 20 patients who have MS (15 women, 5 men; aged, 32-61 years) diagnosis and have been following by Kocaeli university department of neurology and also had been assessed about gait difficulties by department of physical medicine and rehabilitation before and after one month treatment of 4-aminopyridine (AP) between 2011-2012. In this retrospective pretest-posttest (one group) designed study, disease activity, temporal-spatial gait parameters (which were collected with computerized gait analysis), Berg-Balance test and functional independence measurement (FIM) data analyzed by using Wilcoxon test.

Results: We found significant difference at temporal-spatial gait parameters regarding cadence, stride length, double support and walking speed (P < 0.05). Berg-Balance test results was also significantly better after treatment with 4-AP (P < 0.05). Beside there was no significant change with FIM results (P > 0.05).

Conclusion: Although we could not confirm about an improvement at functional independency, Dalfampridine seems as an effective treatment for gait and balance imperfections for MS patients.

P-61
Prolonged-Release Fampridine Treatment and Walking Speed in Japanese Patients with MS: Design of the Multicentre, Double-Blind, Randomised, Placebo-Controlled MOTION-JAPAN Study
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Background: Walking impairment is common in patients with multiple sclerosis (MS). Prolonged-release (PR) fampridine (dalfampridine extended-release in the US) improved walking speed in two placebo-controlled studies in predominantly Caucasian MS patients.

Objective: The objective of the ongoing MOTION-JAPAN study is to evaluate the effect of PR-fampridine treatment on walking speed in Japanese patients with MS.
Methods: The MOTION-JAPAN is a 3-part study: Part A consists of a 2-week run-in, 14-week, placebo-controlled, randomized period followed by a 2-week off-treatment period designed to evaluate the effect of PR-fampridine 10-mg tablet twice daily on walking speed using the Timed 25-Foot Walk (T25FW). Part B is a 52-week, open-label PR-fampridine treatment extension period to provide long-term safety and tolerability data. Part C is an additional open-label extension to provide patients with continued access to PR-fampridine until marketed drug becomes available. Patients with progressive or relapsing MS who are able to complete 2 trials of the T25FW within 5 minutes during enrollment are eligible.

Results: As of May 2015, 101 patients were randomized and dosed. A total of 87 patients have completed Part A; 3 patients discontinued treatment; 2 due to adverse events and 1 due to consent withdrawal. At baseline, mean age was 43.6 years, 51% were female and the median EDSS score was 6.00. Part A is estimated to complete in October 2015.

Conclusions: Results of the MOTION-JAPAN study will establish whether PR-fampridine has an impact on walking in Japanese MS patients.

P-62 Patient-Reported Impact of Multiple Sclerosis in Patients Treated with Prolonged-Release Fampridine: Item-Level Analysis of the MSIS-29

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Background: Walking impairment is common among patients with multiple sclerosis (MS) and negatively impacts quality of life.

Objective: To evaluate the effect of prolonged-release (PR) fampridine (dalfampridine extended-release in the US) versus placebo on patient-reported physical and psychological health impact of MS.

Methods: Patients were randomised to PR-fampridine 10mg tablets (n=68) or placebo (n=64) in the 24-week, double-blind MOBILE study. Patient-perceived impact of MS was assessed at baseline and each study visit using the 29-item MS Impact Scale (MSIS-29) psychological (PSYCH) and physical (PHYS) impact subscales. Mean changes from baseline for each of the individual (MSIS-29) psychological (PSYCH) and physical (PHYS) impact subscales. Mean changes from baseline for each of the individual PHYS and 9 PSYCH items were calculated using all post-baseline visits up to 24 weeks. Treatment differences were assessed post-hoc using logistic regression adjusting for mean baseline item score.

Results: A higher proportion of patients treated with PR-fampridine reported a mean improvement in 16 of the 20 PHYS and 6 of the 9 PSYCH items versus placebo over 24 weeks. Improvements were statistically significant in four PHYS items: difficulties moving around indoors (62% vs 41%; P=0.013), difficulty doing things spontaneously (56% vs 38%; P=0.012), having to depend on others to do things (57% vs 39%; P=0.017), and taking longer to do things (62% vs 45%; P=0.040) and one PSYCH item: worries related to your MS (63% vs 41%; P=0.006).

Conclusions: Patients treated with PR-fampridine showed improvement in several psychological and physical health domains versus placebo. These results support that the mobility benefits associated with PR-fampridine translate into physical and psychological gains for MS patients.

P-63 High Dose Vitamin D on Interleukin-10 in Multiple Sclerosis: A Randomised, Double-Blind, Placebo-Controlled Clinical Trial

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Abstract: Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system. Vitamin D has been related to prevention of MS development and modulating its course. This study compared the effects of high dose vitamin D on interleukin-10 levels on MS patients in a double blind randomized clinical trial.

Methods: 94 patients with relapsing remitting multiple sclerosis (RRMS) were randomized to treatment vs placebo groups. Both groups received conventional MS treatments. The intervention group received 50,000 IU vitamin D every five days for 3 months. Demographic characteristics, EDSS score, disease duration, number of attacks and medications were recorded. Serum levels of Vitamin D and interleukin 10 (IL-10) were measured and compared at baseline and after 3 months.

Results: serum levels of IL-10 were 41.66±85.16pg/ml and 21.08±35.62 in the intervention and placebo group at baseline, respectively (p=0.161). After 3 months, IL-10 levels were 71.07±16.65 and 32.23±38.49 in the intervention and placebo group, respectively (p=0.0158). In linear regression model, interleukin levels showed significant difference in intervention and placebo groups (p=0.022, β=0.032)

Conclusions: IL-10 levels are reduced significantly in RRMS patients after taking high dose vitamin D for 3 months. High dose vitamin D might be useful in reducing inflammatory state in RRMS patients.

P-64 Therapeutic Effect of Rapamycin on the Clinical and Radiological Aspects in Patients with Multiple Sclerosis

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Background: Multiple sclerosis (MS) is an autoimmune disease characterized by demyelinating plaque in the central nervous system. The disease has no cure and no recognized definite cause yet. The available therapies are mostly disease modifying. The aim of the present clinical trial was to evaluate the therapeutic effects of rapamycin on the clinical, life quality and radiological aspects of the patients with MS.

Methods: In this phase I clinical trial, eight patients with relapsing remitting MS were chosen to be included in the trial. Patients have been received rapamycin (Rapacan, Biocen, India) for six months. The safety of drug on the participants was monitored by checking the hematological and blood biochemical parameters of the
patients in days 0, 30, 60, 90, 120, 150 and 180 after initiation of study. Magnetic resonance imaging (MRI) of the brain of the patients has been taken before and after therapy. Patients’ expanded disability status scale (EDSS) was also recorded.

Results: After the therapy was finished, all patients had some degrees of significant reduction in mean plaques area volume (P=0.012, Z=-2.520), and minimum and maximum volume (P=0.012, Z=-2.521) of the plaques. EDSS of 4 (50%) out of 8 patients was decreased after treatment with rapamycin, but was not significantly (P=0.059, Z=-1.89).

Conclusions: This study was the first clinical trial on the effect of rapamycin on multiple sclerosis, which showed promising results for treatment management of the disease. According to the findings, rapamycin is beneficially effective on multiple sclerosis and suggested for therapy of this disease.

P-65
Walking Impairment and Healthcare Resource Utilisation in Patients with Multiple Sclerosis: An Updated Analysis from 2015
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Background: Walking impairment affects up to 90% of patients with multiple sclerosis (MS) and often manifests as reduced walking speed (WS).

Objective: This analysis investigated the association between WS, measured by timed 25 foot walk test (T25FW), and direct healthcare resource utilization (HCRU) and support resources (such as walking aids and home/workplace modifications) at home and work using a cross-sectional study from 2015.

Methods: 490 neurologists from France, Germany, Italy, Spain, UK and US completed 10-15 prospective records for consulting MS patients. Of 5,397 MS patients, 162 patients had T25FW score and completed utilization of support services questionnaire and were included in this analysis. Logistic, ordered logistic, negative binomial and probit (with sample selection) regressions assessed the relationship between walking speed and physician-reported data on direct patient HCRU and patient-reported data on walking aids and home and workplace modifications. Covariates were age, sex, body mass index, time since MS diagnosis and relevant concomitant conditions.

Results: The mean age of patients was 44.0 years and mean time since diagnosis was 5.63 years. Reduced WS was associated with an increased number of visits to ER in the last 12 months (p=0.009), increased level of non-professional and professional caregiver need (p=0.001), and increased need for walking aids (p=0.001) and home modification (p=0.003).

Conclusions: This analysis demonstrated that reduced WS is associated with increased HCRU and additional support requirements, and confirmed results from a similar analysis using 2014 data. Therapies that improve WS may be beneficial to reduce economic burden associated with walking impairment.
Objective: We aimed to evaluate fatigue, sleep quality and their associations in patients with NMO.

Methods: We prospectively studied patients with NMO, who were in remission and seropositive for aquaporin-4 antibody. Fatigue, sleep quality and health-related quality of life were evaluated using the functional assessment of chronic illness therapy (FACTIT)-fatigue score, the Pittsburgh Sleep Quality Index (PSQI) and the short form 36 health survey questionnaire version 2 (SF-36v2), respectively. Patients with NMO were divided into the two groups based on the FACTIT-fatigue score as patients with fatigue, ≥43 vs. patients without fatigue, >43.

Results: A total of 31 patients were enrolled (26 females, age, 46.0 ± 14.2 years). The median EDSS score was 2.0 (IQR 1.0 to 3.5). 71% of all patients had fatigue; NMO patients with fatigue had significantly worse sleep quality than those without fatigue (P=0.023), and 70% of them were "poor sleepers" compared to 12.5% of those without fatigue (P=0.011). The physical and mental components scores of SF-36v2 were lower in patients with fatigue. Multiple linear regression analyses showed that the sleep quality was associated with the degree of fatigue (B=−2.447; 95%CI −4.220 to −0.675; P=0.009).

Conclusion: Fatigue is common in patients with NMO, and there is a significant correlation between fatigue and sleep quality.

P-69
A Natural History Study of the Effect of Pregnancy on Aquaporin 4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder
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Background: As in many autoimmune diseases, pregnancy may have an impact on neuromyelitis optica spectrum disorder (NMOSD), a Th2-mediated disease.

Objective: We studied the "natural history" of the effect of pregnancy on aquaporin 4 antibody-positive (AQP4+) NMOSD, in a patient series not exposed to immunosuppressants and/or disease modifying therapies during pregnancy and in preceding year.

Methods: Nineteen female patients diagnosed with AQP4+ NMOSD at Penang General Hospital, Penang, Malaysia were included. Their pregnancy history, number of relapses before pregnancy, during pregnancy and 1-year postpartum were reviewed.

Results: Four patients had never been pregnant. Seven patients had NMOSD onset many years (range: 7–44) after last pregnancy. Of the remaining 8 patients, there were 12 NMOSD-related pregnancies. NMOSD onset occurred in 5 patients during pregnancy or within 6 months postpartum. For the other 7 pregnancies (in 5 patients) that occurred after NMOSD onset, there were 8 relapses – 2 during pregnancy, and 6 at 0–3 months postpartum. Of note, after disease onset, all subsequent pregnancies were associated with relapses. 90% postpartum relapses/onset occurred during 0–3 months postpartum. Mean annualized relapse rate (ARR) was 0.43 before pregnancy, and it rose significantly to 3.43 at 0–3 months postpartum. Also, unlike multiple sclerosis, ARR was not reduced during pregnancy.

Conclusions: Pregnancy adversely affects the disease course of AQP4+ NMOSD, with 0–3 months postpartum posing high risk for relapse/onset attack. Without appropriate treatment, relapse rate is high. An international NMOSD pregnancy registry is useful to identify the suitable preventive therapies during pregnancy and postpartum period.

Poster Session 14
NMO Autoantibody and Immunology

P-70
Relation between Dietary Intakes of Antioxidants and IgG-NMO Titration in Patients with Neuromyelitis Optica
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Background: Neuromyelitis optica (NMO) is a severe relapsing inflammatory CNS demyelinating disease that predominantly affects the optic nerves and spinal cord. The discovery of specific immunoglobulin G (IgG) antibodies binding to CNS astrocytic membranes identified the target as the water channel aquaporin-4 (AQP4) and Studies have demonstrated the pathogenic potential of these autoantibodies. Immune-mediated inflammation and oxidative stress are involved in the pathogenesis of autoimmune disease, and dietary antioxidants have the potential to alleviate autoimmune disease symptoms by targeting inflammation and immune modulation.

Objective: To investigate the relation between dietary intakes of antioxidants and IgG-NMO titration in serum.

Method: Dietary intake of antioxidant components (vitamin E, Vitamin C, zinc, selenium, beta-carotene and alpha-tocopherol) were assessed with food frequency questionnaire (FFQ) with 168 items and investigated with IgG-NMO titration in 29 patients with NMO.

Results: IgG-NMO titration in 9 patients was positive and in others was negative. Dietary intakes in all components of antioxidants, in patients with negative IgG-NMO was more than in patients with positive IgG-NMO but only dietary intakes of vitamin C was significant between patients with positive and negative IgG-NMO (P= 0.033) and in others components does not significant different between two groups. Age and gender were not confounder variables.

Conclusion: Physiological variation in dietary intakes of antioxidants may exert a major impact on IgG-NMO synthesis and inflammation in patients with NMO and antioxidants may dose play role in prognosis of NMO.
P-71 Low Prevalence Of Anti Aquaporin 4 Antibody in Multiple Sclerosis and Neuromyelitis Optica Cases In Western Australian Cohort

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Background: Neuromyelitis optica (NMO) or Devic’s disease is relatively rare in Western countries among the CNS inflammatory disorders. In Japan and other Asian nations however, NMO comprises a larger proportion of CNS inflammatory disorders. The major advance in distinguishing NMO from MS was the discovery that many patients with NMO have detectable serum antibodies that target the water channel aquaporin-4 (AQP4-immunoglobulin G [IgG]).

Objective: To investigate the prevalence of anti-AQP4 antibody in MS and NMO patients from the Western Australian cohort using a new highly sensitive test.

Methods: We used a cell-based assay with cells transfected with 2 isoforms of AQP4 (M1 and M23) and primate cerebellum tissue (Euroimmun, Luebeck, Germany) to detect AQP4 antibody in 420 sera of patients with NMO, MS and diagnostic requests from patients with demyelinating disease presentation suspicious for NMO. The anti-AQP4 antibody test was performed at PathWest Laboratory Medicine, QEII Medical Centre.

Results: From 420 patients only six 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 NMO, although isolated longitudinally extensive myelitis and other cases with features suspicious for NMO were usually negative. 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.

P-72

Same as O-3

P-73

Same as O-2

P-74 Recurrence of NMOSD with Anti MOG Antibody was Suppressed by Immunosuppressant

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Background: Neuromyelitis optica spectrum disorder (NMOSD) with anti myelin oligodendrocyte glycoprotein (MOG) antibody (NMOSD-MOG) have treated with steroid pulse therapy in active stage, and steroid pulse therapy is effective treatment. NMOSD-MOG is often showed recurrence like the NMOSD with anti AQP4 antibody. However, preventing a recurrence of NMOSD-MOG has not been reported.

Objective: We evaluate the preventive effect of recurrence by steroid and/or immunosuppressant in patients with NMOSD-MOG.

Methods: Ten patients with NMOSD-MOG were examined in this study. 6 patients with NMOSD-MOG were treated with steroid and/or immunosuppressant (tacrolimus). 4 patients with NMOSD-MOG were not treated. We examined the annual relapse rate (ARR) of NMOSD-MOG before and after treatment.

Results: Mean ARR (n=6) of before treatment is 1.06 [0.38-1.5] and that of after treatment is 0.06 [0-0.17]. Mean ARR (n=4) without treatment is 0.65 [0.45-1.0]. Mean ARR of after treatment was significantly lower than that of before treatment (p=0.03) and without treatment (p=0.01).

Conclusion: Our observation suggested that steroid and/or immunosuppressant showed the preventive effect of recurrence of NMOSD-MOG.

P-75 Clinical and Radiological Features in Patients with Neuromyelitis Optica and Anti-Phospholipid Antibody Syndrome - A Case-Series Study

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Background and Objective: There have been few reports of coexistence of neuromyelitis optica (NMO) and antiphospholipid antibody syndrome (APS). The aim of this study is to present the clinical and radiological features of NMO with APS.

Methods: We retrospectively collected data of anti-aquaporin-4 antibody, anti-cardiolipin antibody, lupus anticoagulant, and anti-beta-2 glycoprotein I antibody in 76 patients who was diagnosed as NMOSD based on the revised diagnostic criteria for NMO and NMOSD proposed by Wingerchuk et al. We also analyzed their clinical and radiologic features of brain and spine MRI.

Results: 6 patients (3 patients with NMO and 3 with NMOSD) were finally diagnosed as having APS, who fulfilled the...
P-76 Glycyrrhizic Acid Might Reduce The NMO-Igg Induced Cell Death by Inhibition of The Complement Activation

**Objective:** We aimed to investigate the biologic effects of GL for NMO in vitro.

**Methods:** In cell-line model (AQP4 overexpressing U87 cells, and primary culture of mice astrocyte), we treated NMO patient serum and GL at various dose, and checked change of multiple biologic parameters.

**Results:** Treatment of NMO patient sera (0.5, 1, 2.5, 5, and 10%) dose-dependently increased LDH release in both AQP4 overexpressed U87 cells and primary culture of mice astrocyte. Treatment of GL (0.1, 0.5, 1, 1.5, and 2 mM) reduced the complement mediated cytotoxicity of NMO IgG in a dose-dependent manner. Though GL did not block the binding of NMO IgG to AQP4 overexpressed U87 cells, it reduced binding of C1q to NMO-IgG.

**Conclusions:** Our result implies that GL might play a protective role in the pathogenesis of NMO, through the inhibition of the complement activation.

P-77 Same as O-4

**Poster Session 15**

**NMO Laboratory Test**

P-78 Expression of HLA-DP in Neuromyelitis Optica Patients

**Objective:** To investigate the relationship between serum 25-hydroxyvitamin D3 and Neuromyelitis Optica Spectrum Disorder (NMOSD).

**Methods:** 58 patients diagnosed as NMOSD and 116 age-, sex-, and season-matched healthy people were enrolled in this study. Patients and healthy controls were divided into four different groups: NMOSD patients, NMOSD patients in remission or in acute phase and healthy people. Clinical features of patients were collected which show that 43 patients were experiencing acute...
phase while the others stayed in remission. The serum samples of people included were collected and then to detect the concentration of serum 25(OH) D3 through enzyme-linked immunosorbent assay (ELISA). Clinical features and concentration of 25(OH) D3 were compared between different groups.

Results: Healthy people (n=116) had a higher serum 25(OH) D3 level than patients with NMOSD (n=58) (61.01±19.09 vs 46.25±22.38 nmol/L, P<0.01). Among the NMOSD patients, serum 25(OH) D3 of patients in remission (n=15) was higher than that of patients in acute phase (n=43) (63.17±24.72 vs 40.35±18.39 nmol/L, P<0.01). NMOSD patients in remission had a lower EDSS score than patients in acute phase (3.73±1.74 vs 4.81±1.59, P<0.05). And an inverse correlation was found between serum 25(OH) D3 and EDSS score of patients in acute phase (r=-0.394, P<0.01).

Conclusion: Low levels of serum 25(OH) D3 is a warning of attack in NMOSD patients. Vitamin D deficiency may lead to a more severe attack on NMOSD patients at acute phase which is attributed to the immunoregulation function of vitamin D.

P-80
Vitamin D Level may be Associated with The Relapse Free Time in Neuromyelitis Optica Spectrum Disorder
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Background and Objective: Low levels of 25-hydroxyvitamin D [25(OH) D3] was reported to correlate with disability or disease activity in autoimmune disorders. The aim of this study is to investigate whether low vitamin D levels are associated with the time to next relapse in NMOSD patients.

Method: We reviewed 63 anti-aquaporin-4 antibody (AQP-4 Ab) positive NMOSD patients between April, 2006 and August, 2014. Among them 10 patients were excluded due to short follow-up period. Aquaporin4-antibody (AQP4-ab) was measured using cell-based indirect immunofluorescence assay and serum 25(OH) D3 levels were measured using high-performance liquid chromatography. Regarding 25(OH) D3 levels, we divided 3 groups; vitamin D severe deficiency (<12 ng/ml), mild deficiency (12 to 20 ng/ml), and non-deficiency (≥20 nmol/L). The time to next relapse was compared between the three groups with the robust sandwich estimate of Lin and Wei for the covariance matrix including the recurrent events.

Result: Among 53 patients, 23 patients were considered as the severe deficiency group, 19 patients were in the mild deficiency group, and 11 patients were in the non-deficiency group. The time to the first relapse was not significantly different, between the three group (the deficiency group, 34 months; the insufficiency group, 26 month; the sufficiency group, 23 months, P=0.392). However, considering all recurrent relapses, the relapse free time was significantly shorter in the mild deficiency group, compared to the non-deficiency group (p=0.0466).

Conclusion: Our study suggests that vitamin D levels may be associated with relapse free time in NMOSD patients. However, further large prospective studies are needed.

P-81
Serum Levels of Vitamin D and IgG-NMO Titration in Patients with Neuromyelitis Optica (NMO & NMOSD); Is There Any Correlation?
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Background: Neuromyelitis optica (NMO, Devic’s syndrome and NMOSD) are inflammatory disorders of the central nervous system (CNS) that present typically with relapses of optic neuritis (ON) or myelitis which IgG auto antibodies against aquaporin 4 (AQP4) water channel protein probably play a pathogenic role. Vitamin D may modulate B-cell function and dampen the synthesis of IgG and may play a role in NMO as an important factor involved in immunological pathways.

Objective: To investigate the relation between vitamin D levels and IgG-NMO titration in serum.

Method: 25-hydroxyvitamin D (25(OH) D) and IgG-NMO were assessed in serum in 29 patients with NMO.

Results: IgG-NMO titration in 9 patients was positive and in others was negative. 25(OH) D level means in patients with negative IgG-NMO was 32.4mg/dl and in patients with positive IgG-NMO was 23.44 mg/dl. There was significant correlation between the IgG titration and 25(OH) D levels in serum. The levels of 25(OH) D in serum was different between patients with positive and negative IgG-NMO (P =0.036). Age, gender and latitudewere not confounder variables.

Conclusion: Physiological variation in vitamin D may exert a major impact on IgG-NMO synthesis in patients with NMO and vitamin D may dose play role in pathogenesis of NMO.

P-82
Association between Serum Lipid Levels and Disease Activity/Disability in Patients with Neuromyelitis Optica Spectrum Disorder
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Background and Objective: Neuromyelitis optica (NMO) is characterized by the involvement of optic nerve and spinal cord, with the positivity of the antibody against aquaporin-4 (AQP4), a CNS water channel consisting of the blood-brain-barrier (BBB).
The breakdown of vascular endothelium at BBB could activate CNS inflammation by the entry of immune cells into brain. We tried to investigate the associations of dyslipidemia with disability and activity in patients with NMO spectrum disorder.

Methods: Forty-one patients with NMOSD having anti-aquaporin-4 antibody (AQP4-ab) and 287 age- and sex-matched healthy controls were included. We measured triglycerides, high and low density lipoproteins (HDL, LDL) and total cholesterol.

Results: The prevalence of dyslipidemia was not different between patients with NMOSD and healthy controls (15.7%, and 16.5%) (p > 0.05), and NMOSD patients showed similar frequencies of dyslipidemia between during attack (16.0 %) and in remission (15.4%). EDSS scores both at the time of sampling (median [range], 4.5 [3.0-8.5] vs. 3.1 [0-8.0]; p < 0.05) and at the last visit (4.5 [2.5-9.5] vs. 2.75 [0-7.5]; p < 0.05) were significantly associated with baseline LDL levels.

Conclusions: Our study suggests that the prevalence of dyslipidemia is not different between patients with NMOSD and healthy controls. However, dyslipidemia, particularly high LDL levels may be associated with disease disability in NMOSD, which implies that lifestyle changes may be beneficial for NMOSD to improve neurological disability.

P-83 Comparison of Heparin Binding Growth Factor Level in Multiple Sclerosis against Neuromyelitis Optica Patients

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Objective: A heparin-binding growth factor known as Midkine (MK) possess various effects in different tissues of the body, including an important role in induction of oncogenesis, inflammation and restoration of tissues. MK with promoting effects in inflammatory responses through enhancing the leukocytes migration in neurological diseases. The present study aimed to assess the concentration of this growth factor among multiple sclerosis (MS) patients with first attack and neuromyelitis optica or NMO also called Devic disease.

Methods: The MK level was assessed in 100 new case of MS, 80 Devic patients and 40 healthy samples. Sera were isolated from blood samples and stored at −20°C for a maximum of 48 h before being stored at −70°C prior to analysis using a MK sandwich ELISA kit. Data was analyzed by SPSS software.

Results: Our results showed that the MK concentration in MS patients with first attack was so higher than Devic subjects, significantly. The mean average of MK was 1191.39±356.78 in MS patients, 882.67±212.93 in Devic patients and 612.96±81.58 in healthy controls. However, dyslipidemia, particularly high LDL levels may be associated with disease disability in NMOSD, which implies that lifestyle changes may be beneficial for NMOSD to improve neurological disability.

Poster Session 16
NMO Neuroimaging and Neurophysiology

P-85 Neuromyelitis Optica with Magnetic Resonance Imaging Findings of Cerebral Lesions at Onset

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Neuromyelitis optica (NMO) is characterized by severe attacks of optic neuritis and myelitis. Although patients with NMO displaying cerebral lesions on magnetic resonance imaging (MRI) scans have been recently recognized, the clinical characteristics
and prognosis for these patients have not been defined. In this study, we retrospectively analyzed patients with NMO displaying cerebrospinal lesions at disease onset on MRI scans. We found that cerebral lesions were not uncommon (8/110) as presenting manifestations in NMO, and that these lesions predominantly occurred in pediatric through young adult populations (4–25 years old). Acute disseminated encephalomyelitis-like cerebral symptoms were most common (5/8) and often led to a misdiagnosis. The MRI findings showed that the cerebral lesions were heterogeneous and nonspecific for an NMO diagnosis. Although the relapse frequency after treatment was decreased in most cases, the residual disabilities were severe. Our study highlights that NMO patients with cerebral lesions, regardless of whether the patients are seropositive or seronegative for NMO-IgG, should receive immunosuppressant therapy to avoid significant residual cognitive, mental, and physical disabilities.

P-86
Same as O-6

P-87
Same as O-7

P-88
Linear Lesions: A Precursor to Longitudinally Extensive Spinal Cord Lesions
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Objective: To investigate the relationship between linear lesions (LL) and the development of longitudinally extensive spinal cord lesions (LESCL) in Chinese patients with neuromyelitis optica or longitudinally extensive transverse myelitis.

Method: The clinical records of 143 patients with these conditions were reviewed. Forty-one patients with LL were divided into three groups according to the order of appearance of LL and LESCL simultaneously (n = 10), LL first (n = 26), or LESCL first (n = 5). The remaining 102 patients without LL were used as a control group.

Results: Patients who developed LL first demonstrated a lower annualized relapse rate than those in the simultaneous group (1.00 [0.23–10.00] vs. 4.38 [0.60–6.67], p = 0.017) and the control group (1.00 [0.23–10.00] vs. 2.00 [0.24–10.00], p = 0.007). Among all patients with LL, there were significantly more who developed them before LESCL than those who developed them after LESCL (p < 0.001) or at the same time (p = 0.008). The mean time before the appearance of LESCL was 9.0 months (2–35 months) in the ‘LL-first’ group, which was shorter than that in the control group (12 months [1–60 months], p = 0.010). The rate of positivity for anti-aquaporin 4 IgG antibodies was higher in patients with LL compared with controls (90.24% vs. 64.71%, p = 0.002).

Conclusion: LL may be a precursor to LESCL and assist early diagnosis of neuromyelitis optica and longitudinally extensive transverse myelitis.

P-89
Metabolic Profiling Of Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder by Nuclear Magnetic Resonance
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Background: Multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) are inflammatory diseases of the central nervous system (CNS). Although several studies have characterized the metabolome in cerebrospinal fluid (CSF) from MS and NMOSD patients, comparative analyses between relapse and remission have not been performed.

Objectives: In the present study, we aimed to determine the disease-specific metabolites and to investigate the metabolites that characterize the disease activity.

Methods: We performed 1H-nuclear magnetic resonance (NMR) spectroscopy-based metabolomics on CSF samples from 23 patients with MS (9 relapse vs. 14 remission) and 43 patients with NMOSD (24 relapse vs. 19 remission) and 12 healthy controls (HCs).

Results: CSF acetate was decreased at both MS and NMOSD relapses, whereas CSF lactate was increased at NMOSD relapse. Acetone and glycerate were elevated in both MS and NMOSD-derived CSF samples irrespective of disease activity. Citrate and valine were decreased in MS-derived CSF irrespective of disease activity.

Conclusions: For the first time, we investigated the metabolic changes according to disease activity in patients with MS and NMOSD. This study shows that 1H-NMR spectroscopy can be a helpful tool to distinguish between MS and NMOSD and to investigate the metabolic changes occurring at relapse.

P-90
Optical Coherence Tomography after First-Ever Optic Neuritis Helps Discriminating Neuromyelitis Optica from Multiple Sclerosis
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Retinal nerve fiber layer thickness (RNFLT) measured by optical coherence tomography (OCT) has been
suggested to be useful in differentiation between neuromyelitis optica (NMO) and multiple sclerosis (MS). However, multiple episodes of optic neuritis (ON) result in cumulative severe reduction of RNFLT, making differentiation of these two diseases difficult.

Objectives: The aim of this study was to discriminate between NMO and MS in early phase, using OCT after first-ever optic neuritis.

Methods: In this cross-sectional study, OCT and visual function testing were performed in 73 patients with NMO spectrum disorders and 38 patients with MS

Results: NMO was associated with thinner RNFLT and worse visual acuity (VA) than MS after first-ever ON (p < 0.001 in both), whereas there was no difference in RNFLT and VA between first episode NMO-ON and multiple episodes MS-ON. After first-ever ON, RNFLT of 78.9 μm was 93.9% specific for NMO, and RNFLT of 78.9 μm with VA less than 0.4 decimal was 100% specific for NMO.

Conclusions: Evaluation of first-ever ON has an advantage on detecting differences between NMO and MS, avoiding the obscuration of disease specific changes by further attacks of ON. OCT after first-ever ON showed significantly more severe retinal damage in NMO than MS, which could establish cut-off value. Peripapillary RNFLT and VA after first-ever ON can help us to discriminate NMO from MS in early phase.

P-91 Visual Evoked Potentials in Neuromyelitis Optica Spectrum Disorder
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Background: Multiple sclerosis (MS) and Neuromyelitis optica spectrum disorder (NMOSD) have frequent involvement of the optic nerve. In NMO, optic neuritis (ON) and visual dysfunction tend to be more severe and are often bilateral. The abnormal visual evoked potential (VEP) patterns in MS have already well-defined and used as a diagnostic parameter in MS. However, few studies have been established in NMOSD and the VEP parameters described in MS have been used in the evaluation of NMOSD.

Methods: Patients with seropositive NMOSD participated in the study. After exclusion of other eye diseases, VEP using full-field pattern-reversal with measuring visual acuity and low contrast sensitivity of 4.0 were performed in 73 patients with NMO spectrum disorders and 38 patients with MS.

Results: Normal VEPs were seen in 14% of patients with NMO spectrum disorders. Normal latency of P100 wave with normal amplitude which was known as ‘MS pattern’ was identified in 10%. Both abnormal latency and amplitude was seen in 19%. Normal VEPs were seen in 14% of patients with MS. In 17% of patients with NMO, bilateral optic neuritis was observed.

Discussion: In NMOSD, ‘absent VEPs’ was most frequently seen with lowest frequency of MS pattern. The identification of VEP patterns in NMO may help to differentiate this condition from MS.

Poster Session 17
NMO Treatment

P-92 Clinical Efficacy of Plasmapheresis for Patients with Acute Severe Attack CNS Inflammatory Disease
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Objectives: To evaluate clinical efficacy of plasmapheresis in severe attack CNS inflammatory demyelinating disease

Methods: Seventeen patients were diagnosed of CNS inflammatory demyelinating disease (mainly Neuromyelitis optica spectrum disorder) 15 patients, idiopathic transverse myelitis one patient and bilateral simultaneous optic neuritis in one patient), with had severe acute attack and received plasmapheresis due to poor response to high-dose intravenous methylprednisolone (IVMP) therapy were include in this retrospective study. The outcomes of this study were functional outcome improvements at 6 months after plasmapheresis.

Results: Immediate effect of plasmapheresis following IVMP therapy led to significant improvement in 35% (6 patients) of 17 patients and increased to 59% (10 patients) after 6 months follow up. Plasmapheresis was generally well tolerated in all patients. However serious side effect can be occur due to insertion of central venous catheter. Younger patient or lower gait score before attack were associated with significant improvement (p=0.035 and p= 0.007 respectively). Lower baseline Expanded Disability Status Scale (EDSS) score and visual outcome score (VOS) before attack were also associated with significant improvement with p value trended to be significance (p=0.052).

Conclusion: Plasmapheresis following IVMP therapy is effective in treatment of patient with severe attack CNS inflammatory demyelinating disease. Lower baseline of pre-existing neurological damage may be associated with better prognosis.

P-93 Azathioprine for First-Line Treatment in Patients with Aquaporin-4 Antibody-Positive Neuromyelitis Optica and Neuromyelitis Optica Spectrum Disorder: 4-Year Long-Term Efficacy and Tolerability
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Background: Although several immunosuppressant drugs are available recently, azathioprine (AZA) is commonly used as a first-line treatment of neuromyelitis optica (NMO) and its spectrum disorders (NMOSD).

Objective: The purpose of this study is to assess efficacy and tolerability of AZA in NMO and NMOSD patients over 4 years.

Methods: We retrospectively reviewed medical records of 35 aquaporin-4 antibody-positive NMO and NMOSD patients treated with AZA.

Results: Patients were followed up for a mean 51.1±24.3 months. Mean age was 46.5±13.7 years. Mean AZA treatment duration was
36.0±18.4 months and received 94.3±34.3 mg/day. Annualized relapse rates (ARR) were higher in pretreatment than post-treatment periods (2.82 vs. 0.33, p<0.0001) and Expanded Disability Status Scale (EDSS) score was improved during AZA treatment (3.8 vs. 2.5, p<0.0001). Eight (23%) patients were relapsed during AZA treatment, prednisone was added in four patients and four patients were switched to other immunosuppressive drugs. Leukopenia was reported in 12 (34%) patients. In 5 patients who EDSS score was more than 7.5, 4 patients experienced aggravation or no change in EDSS score. In comparison, 4 patients of EDSS score 6 to 6.5 experienced improvements of their EDSS score to mean EDSS score 3.

Conclusions: AZA monotherapy and AZA with prednisone 10 mg was effective as a first-line treatment options for Korean NMO and NMOSD patients, and patients with leukopenia were almost well tolerable. AZA is more effective in patient with low EDSS score, and is not effective in patient who EDSS score was higher than 7.5.

P-94 Preliminary Exploration of Predictors on Azathioprine Safety Evaluation in Patients with NMOSD
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Objective: Searching for AZA-related safety-evaluated indicators in NMOSD patients

Methods: The members were diagnosed as NMOSD treated with AZA. TPMT allele (*3C) was tested by FISH. AZA metabolites were determined by HPLC. In the long run, situation of drug use, side effects and relapse were gained.

Results: 42 patients were engaged, and the average age of onset was 35.5 years. AZA was taken in 38, whose median duration of symptoms prior to initiation of AZA was 4.6 years. Median post-treatment follow-up was 8.1 months: 4 relapse with ON. 9 patients discontinued drug (side effects, 6; disease progression, 1; self-withdrawal, 2). Side effects were found in 52.6% including hepatotoxicity 14, myelosuppression 4, skin rash 2, pancreatitis 1. In patients suffering hepatotoxicity, 92.9% with hepatotoxicity were given liver protective drugs or dosage reduction. Patients who suffered myelosuppression, severe skin rash and pancreatitis, discontinued AZA. In two weeks all indicators returned to normal. TPMT*3C was tested in 42, and heterozygous TPMT*3C discovered in 1 and homozygous variants in 1. The median 6-TGNs concentration was 292.3±103.1 pmol/8*10^8 erythrocytes, and 6-MMPN 2100.5±814.4, 3802.0. 1 patient with heterozygous type, suffered slight-medium hepatotoxicity 2 month later, her 6-MMPN concentration was < 5700 pmol/8*10^8 erythrocytes. 1 patient with homozygous variants, no abnormal indicators were found and her 6-TGNs concentration was < pmol/8*10^8 erythrocytes. 1 patient with homozygous variants, no abnormal indicators were found and her 6-MMPN concentration was < 5700 pmol/8*10^8 erythrocytes.

Conclusions: Azathioprine is generally effective and well-tolerated. The analysis of TPMT*3C genotype, along with 6-TGNs and 6-MMPN concentration determined, could monitor the safety effectively on azathioprine treatment in patients with NMOSD.

P-95 Nursing Aspects in Management of Singaporean Children with Multiple Sclerosis (MS), Neuromyelitis Optica (NMO) and Anti-Myelin-Oligodendrocyte Glycoprotein (Anti-MOG) Demyelination
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Background: Paediatric patients diagnosed with multiple sclerosis (MS) or Neuromyelitis Optica (NMO) face chronic, recurrent and disabling disease. Recently, Anti-Myelin-Oligodendrocyte Glycoprotein (Anti-MOG) variants are described and prognosis is uncertain. Neurology nursing has an important management role.

Objective: To describe role of neurology resource nurse (NRN) in management of patients with MS, NMO and Anti-MOG at KKHH. To identify issues regarding living with chronic disease, accepting diagnosis, treatment and coping with challenging symptoms.

Methods: Diagnostic criteria for MS and NMO were according to the PMS2012 revisions. Anti-MOG was diagnosed if the patient had clinic-radiological CNS demyelination with anti-MOG antibody seropositive. A search was conducted on KKH paediatric neurology patient database, age up to 18 years.

Results: We identified 5 patients: 2 with MS, 1 with NMO and 2 with Anti-MOG. MS patients are a 15 year old boy and a 16 year old girl. They struggled with side effects and new symptoms. NRN advised, validated and reassured them and expedited specialist assessment. The NMO patient is a 7 year old girl with significant unilateral visual loss and leg weakness. The NRN acknowledged family’s concern with coping with child’s condition, long-term disability as well as future progression. Anti-MOG patients are two boys ages 7 and 9 years. They experienced lower limb weakness and loss of bladder control. NRN provided up-to-date information and supported patient and family with urine catheterisation and adapting to daily life.

Conclusions: NRN identified issues and challenges for these patients and assisted patient and family cope with disease.

P-96 A Pilot Study to Evaluate the Role of Integrative Medicine to Manage Fatigue in Chinese Patients with Multiple Sclerosis and Neuromyelitis Optica
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Background and Objective: Fatigue associated with multiple sclerosis (MS) and neuromyelitis optica (NMO) is common and difficult to manage. Integrative medicine may be beneficial. We investigated how Chinese Medicine (CM) evaluates fatigue of MS/NMO.

Methods: We analyzed the clinical features and CM syndromes in a cohort of Chinese patients with MS/NMO attending the Integrative Medical Center from August 2014 to June 2015. All subjects were assessed by a neurologist, a CM Practitioner and a
Poster Session 18 Disease Model

P-97
Chemokine Receptor Antagonists Ameliorate Experimental Autoimmune Encephalomyelitis
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Objective: Chemokine and chemokine receptors (CCRs) play important roles in the immune response by regulating leukocyte migration. We previously reported the pathogenetic role of CCR4 in experimental autoimmune encephalomyelitis (EAE) using CCR4 and CCR6 knockout mouse model. We examined whether CCR4 antagonism ameliorate EAE disease course.

Method: C57BL/6 female mice were injected subcutaneously with 0.2 ml of inoculums containing 400 microgram of MOG35-55 in complete Freund’s adjuvant. Mice were given 10mg/kg of Compound 22, small-molecule antagonist of CCR4 (n = 9), or dimethyl sulfoxide (DMSO) as a control (n = 10) intraperitoneally on day 0, day 7, day 14, day 21, day 28 postimmunization. Immunized mice were examined and scored daily.

Results: Compound 22 significantly ameliorates EAE disease severity. In max score, Compound 22 vs DMSO were 0.8 ± 1.1 vs 2.6 ± 1.5, mean ± standard division, P <0.05. In cumulative score, Compound 22 vs DMSO were 10.3 ± 10.6 vs 23.0 ± 12.3, mean ± standard division, P <0.05.

Conclusions: CCR4 antagonists might be therapeutic targets of multiple sclerosis.

P-99
Similar as O-17

P-100
Fingolimod Reduces the Extent of Demyelination and Inflammation with Increase in Oligodendrocyte Progenitors Following Local Administration of Lysolecithin in Mice
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Introduction: Multiple sclerosis (MS) characterized by infiltration of immune cells into the CNS which leads to demyelination, oligodendrocyte death and secondary axon degradation. Fingolimod (FTY720), a sphingosine 1-phosphate (S1P) receptor modulator, is a medicine to treat relapsing-remitting MS. Fingolimod act S1P receptors on astrocytes, microglia or oligodendrocytes. In this study, we evaluated the effect of FTY720 on the levels of myelination and inflammation and number of OPCs in an experimental model of demyelination induced by lyssolecithin (LPC).

Methods: Animals received Fingolimid (1mg/kg, PO) for nine or twelve days to address its effect on inflammation and demyelination, respectively. Demyelination was induced by direct injection of 1 µl lyssolecithin solution (1%, w/v) into corpus callosum of mice on day six. Mice were transcardially perfused with 4% paraformaldehyde. Luxol fast blue (LFB) and H&E staining were used to determine the extent of demyelination area and inflammation scores, respectively. Results were confirmed by Immunostaining against PLP, CD45 and Olig2 antibodies.
**P-101**

**Nano-Curcumin Effect on CNS Myelin and the Inflammation Process in Experimental Autoimmune Encephalomyelitis**

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**Background:** Multiple Sclerosis (MS) is an inflammatory demyelinating disorder of the central nervous system (CNS). Polyphenol curcumin, the main active compound of tumeric (Curcuma Lunga), has been used in traditional medicine as an effective drug for a variety of diseases. Different formulations of curcumin are made to increase its bioavailability and effectiveness. Polymerized Nano-Curcumin (PNC) is a nanoformulation of curcumin.

**Objective:** We demonstrate the beneficial effect of PNC in experimental autoimmune encephalomyelitis (EAE), as an animal model of MS.

**Methods:** EAE was induced in Lewis rats. PNC (12.5 mg/kg curcumin) was administered intraperitoneally for 18 days from the day of EAE symptoms onset. To assess the prophylactic effect of PNC some rats received PNC from the day of EAE induction. Clinical signs of EAE were monitored and histological studies were performed on lumbar spinal cord. Some inflammatory markers were evaluated by Real Time PCR and Immunohistoflorescence (IHC).

**Results:** PNC treatment resulted in a significant decrease in EAE scores and delay in relapse. As pretreatment it delayed and reduced the scores much more. Histological studies also confirmed a significant decrease in the demyelination. Gene expression results showed increased pro-inflammatory and decreased anti-inflammatory genes expression following EAE induction which was reversed by PNC. IHC data confirmed decreased inflammation in the spinal cord of PNC treated rats when compared to EAE animals.

**Conclusion:** Previous reports showed the beneficial effect of curcumin at doses 100-200 mg/kg. Taken together, our results demonstrated that PNC formulation can enhance the effect of curcumin in EAE model of MS.

**P-102**

Same as O-5

**Poster Session 19**

**Case Report MS**

**P-103**

**Tumefactive Multiple Sclerosis in Indonesian Patient**

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**Background:** Tumefactive multiple sclerosis (MS) is a rare variant of MS. It refers to demyelinating brain lesions more than 2 cm in white matter region with mass-like effect or vasogenic edema and post-gadolinium magnetic resonance imaging (MRI) typically showing an incomplete ring enhancement.

**Objective:** To report tumefactive MS case in Jakarta

**Methods:** Case report

**Results:** A 16-year-old man came to our hospital with chief complaint weakness on left extremities since 4 month. He also complained about visual disturbance. Expanded Disability Status Scale (EDSS) was 1.5. The brain Magnetic Resonance Spectroscopy (MRS) examination showed 4 lesions of varying sizes at bilateral frontal and parietal lobes, as well as the left lower brainstem. The largest lesion with peri-lesional edema is at the right parieto-frontal lobe showed elevated choline peak, reduced N-acetyl aspartate (NAA), and increased lactate on MRS, while other lesion showed mildly elevated choline peak and NAA isn’t significantly reduced. No significant increase in the perfusion of the lesions when compared to the rest of the brain. This can be seen in tumefactive demyelination. Visual Evoked Potential and laboratory results were within normal limits. After treatment with methylprednisolone 1000 mg the EDSS decrease to 1.0. Brain MRI evaluation showed lesion at the right side periventricular lateral of white matter region become smaller.

**Conclusions:** Diagnosing tumefactive MS is difficult but MRS can help distinguish it from malignancy.

**P-104**

**Tumefactive Demyelinating Lesion or Concurrent Neoplasm: A Diagnostic Challenge in a Multiple Sclerosis Patient**

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**Background:** Demyelinating lesions larger than 2 cm is defined as tumefactive demyelinating lesion (TDL). If the disease occurs in the form of a single large lesion diagnosis can be mostly with a biopsy or surgical resection. Magnetic resonance imaging (MRI) features are mimicking neoplasms like little mass effect and edema.

**Objective:** This case report discusses a multiple sclerosis (MS) patient with a new relapse, MRI revealed a new large single lesion suggested a neoplastic lesion.

**Methods:** Case report

**Results:** A 22 years old female patient admitted to our hospital because of double vision and clumsiness. She was under treatment of beta-interferon with a diagnosis of MS. It was considered a new relapse. Brain MRI revealed a large, round shape demyelinating lesion 23x18 mm in size in the left frontal lobe. It was large space occupying lesion, had little mass effect and edema and suggested a neoplasm like glioma or lymphoma. Magnetic Resonance Spectroscopy (MRS) findings did not
suggest neoplasia. After 7 days of high dose methylprednisolone therapy patient’s neurological complaints reduced. 3 months later in the follow up MRI showed reduction of the lesion size. The patient’s new relapse was considered to be due to a tumefactive demyelinating lesion.

Conclusions: Tumefactive demyelinating lesions rarely can appear as new lesions in MS patients. Follow up MRI and MRS tests may help us to make differential diagnosis.

P-105
Recurrence of Tumefactive Demyelinating Lesions in Two Cases: A Rare Entity
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Background: Tumefactive demyelinating lesions (TDLs) are defined as over 20 millimeters in size, frequently missed as tumor or abscess. Edema without relative mass effect, incomplete ring of gadolinium enhancement and high percentage (85.2%) of additional white matter lesions (aWMLs) are important radiological features of TDLs. Recurrence of TDLs is notably rare and lack of aWMLs is also atypical.

Objective: To show the recurrence of TDLs without association of additional white matter lesions in neuroimaging.

Methods: A forty-seven year-old female and a twenty-eight year-old male patient whom were followed with recurrent tumefactive lesions were included.

Results: A forty-seven year-old female was presented to another clinic with subacutely developed left-sided weakness 8 years ago. Magnetic resonance imaging (MRI) showed a large mass-like, contrast-enhanced lesion in the right frontoparietal lobe, initially diagnosed as tumor in which biopsy active demyelination. Eleven months later, she was hospitalized with subacute development of motor aphasia, confusion and right-sided weakness. MRI revealed a mass-like, open-ring contrast-enhanced, left temporal lobe-located lesion. A twenty-eight year-old male patient was presented to another clinic with subacutely developed right-sided weakness 8 years ago. Cranial CT showed a space-occupying lesion in right frontoparietal lobe. He had initial diagnosis of tumor. Seven years later, he was admitted with epileptic seizures and left-sided weakness. MRI revealed a mass-like, open-ring contrast-enhanced, right frontal lobe-located lesion.

Conclusions: Our two cases set unique examples of recurrent TDLs without any additional white matter lesions, showing atypical presentation of this certain entity, with no current evidence of tumor.

P-106
Rare Case Report of Two Multiple Sclerosis Patients from Indonesia
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Background: Multiple Sclerosis (MS) is a neurodegenerative disease, rarely found in the tropics region. Until today, Indonesia doesn't have any epidemiological data of MS. We reported two multiple sclerosis patients from Indonesia.

Case Report: Case I, A woman aged 55 years complained weakness of the four limbs followed by the numbness from two fingers below the collarbone downward, and blindness in both eyes. Physical examination revealed weakness of inferior extremity UMN type and the right superior extremity and also bilateral anopia. Funduscopic examination revealed primary optic disc atrophy. Brain and spine MRI revealed multiple lesions in lateral periventricular region and multiple lesions from C5 until T5. Patient was diagnosed with Multiple Sclerosis Primary Progressive types according to the revised McDonald criteria 2010. Case II, A woman aged 30 years complained weakness of both inferior extremity and visual impairment. The symptoms has been experienced since 4 years ago but improved after a few days later and the weakness of both inferior extremity improved after 8 months. Physical examination revealed weakness of inferior extremity UMN type. Spine and Brain MRI revealed multiple lesion from C3 until T2 and multiple lesion at periventricular region. Patient was diagnosed with relapsing remitting multiple sclerosis types according to the revised 2010 McDonald criteria.

Conclusions: Mc Donald revised 2010 criteria may provide early diagnosis of MS with high specificity and sensitivity. Although MS mostly affects Caucasian but also in fact experienced in tropical regions such as Indonesia.
P-108  
Coexistence of Autoimmune Diseases: Multiple Sclerosis, Hashimoto's Thyroiditis and Sjögren Syndrome  

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Background: The coexistence of Multiple Sclerosis (MS) with other autoimmune diseases have been reported. We report a case of untreated MS in a patient who has Hashimoto's thyroiditis along with Sjögren Syndrome.  

Case: A 50 year old woman presented with left hemiparesis, dysarthria, hyperactive deep tendon reflexes, positive hoffmann and Babinski's signs on the left side, dryness in the mouth. Anti-thyroid peroxidase antibodies (anti-TPO) was 873 (N <10) and anti-thyroglobulin antibodies (anti-TG) was 3660 (N: 5-100). SS-A was (++) . Bilateral optic atrophy was identified on optic coherence tomography (OCT). P100 was found to be prolonged in the right eye. Multiple pericapsal and brainstem plaques, contrast enhancement in one plaque, as well as cortical-subcortical and callosal atrophy were detected in cranial magnetic resonance imaging (MRI). There were multiple short segment plaques in the cervical spinal cord. Oligoclonal band was positive, IgG index was 0.85. Thyroid ultrasound (USG) and MR revealed tissue changes consistent with thyroiditis. There was chronic inflammation in the salivary gland biopsy. MS diagno sis was based on clinical and laboratory findings. The patient suffers from both Hashimoto thyroiditis and Sjögren Syndrome.  

Conclusion: To our knowledge, there have not been any reported cases of Hashimoto's thyroiditis and Sjögren Syndrome with MS occurring in the same patient. The presence of an autoimmune disease is associated with high risk for other autoimmune diseases in the same individual.

P-109  
A Klippel-Trenaunay Syndrome Patient Who Develops Multiple Sclerosis  

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Background: The Klippel-Trenaunay syndrome patients' clinical characteristics are port-wine stain, varicose veins, and bony and soft-tissue hypertrophy of an extremity.  

Objective: To discuss the case of a patient diagnosed with Klippel-Trenaunay Syndrome who develops Multiple Sclerosis.  

Case Report: A 25-year-old male patient was admitted to our hospital with complaints of numbness below the chest, blurred vision in his left eye and numbness in his hands and feet. 2 years ago he had similar complaints and resolves spontaneously. He is a Klippel-Trenaunay Syndrome Patient and uses 100 mg/day acetylsalicylic acid. His neurological examination revealed hypoesthesia below T4 level and right horizontal nystagmus. Magnetic resonance imagining (MRI) of the brain, cervical and thoracic showed demyelinating lesions suggesting multiple sclerosis. The patient's complaints declined after 5 days of corticosteroid-pulse treatment.

Conclusions: Klippel-Trenaunay Syndrome is a rare congenital disease. Association of Klippel-Trenaunay Syndrome and MS is the first case in the literature as we know it.

P-110  
Drug Choice of Long-Term Treatment of Patients with Multiple Sclerosis  

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Objective: To discuss drug choice of long-term treatment of patients with multiple sclerosis  

Methods: Report a case of MS patient in our hospital and with long-term follow-up.  

Results: Female 44, complained of "repeated attacks of numbness, weakness and decreased vision for 12 years". First treatment with glucocorticoids, completely relieve. 8 years ago another attack, glucocorticoids and interferon treatment, fully recovered, stop using interferon about 6 years ago. 2 years ago, the symptoms relaps ed again. Continued with interferon treatment, but her symptoms aggravated when the prednison reduced to 40-10 mg in many times. 4 months ago her symptoms aggravated during the glucocorticoids decrement, EDSS score of 7.5. Treatment with ivig, and used tacrolimus instead interferon. The symptoms gradually improve, EDSS score of 6.5. Now the patient in the further treatment.  

Conclusions: When the long-term using of interferon can’t continue to improve MS patient’s symptoms, Maybe the better way is to choose other drugs, but the effect still needs further research.

P-111  
Fingolimod Experience in Malaysia Tertiary Center  

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Background: Fingolimod (FYT) therapy for relapsing remitting multiple sclerosis (RRMS) is available in few Neurology Centers in Malaysia. A retrospective data of two patients were reviewed.  

Case 1: A 27-year old Malay lady presented with two episodes of right sided hemiparesis associated with right optic neuritis that occurred eight months apart. Two MRI were compared and demonstrated increased hyperintense T2 lesion in the periventricular, juxtacortical area and short segment spinal cord lesion in C2 with gadolinium enhancing lesion. She was started on FYT and her first dose was uneventful; however she developed transient maculopapular rashes on both thighs after second week of the initiation of the drugs. The FYT was withheld for five days and the rash slowly disappeared without specific treatment. No further recurrence of rash or clinical relapse observed in the last six months.  

Case 2: A 27-year old Malay lady with RRMS was referred to our center for second line therapy. She tolerated the first dose of FYT and no clinical relapse was observed in the last 21 months. Repeat MRI brain at 20 months showed burn out lesion in the white
matter lesion over the juxtacortical, periventricular in the frontal and parietal area, and spinal cord lesion at the cerebral and lumbar region with no evidence of new enhancing lesion. 

**Conclusions:** FYT therapy is well tolerated by our patients. More patients and longer duration of treatment are important information in order to evaluate the efficacy and safety of this novel therapy in multiethnic population.

**P-112**

**Case Report:** Transient Rash Following Fingolimod Initiation in Relapsing Remitting Multiple Sclerosis; To Stop or Continue?  
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**Background:** Rash following a Fingolimod (FYT) treatment in relapsing remitting multiple sclerosis (RRMS) is rare. In Malaysia, not all tertiary centers have access to prescribe this novel therapy for multiple sclerosis patients.

**Method:** We encountered a case of RRMS who developed transient rash following FYT treatment.

**Case presentation:** A 27-year old lady presented with two episodes of right sided hemiparesis associated with right optic neuritis that occurred eight months apart. Her two MR of the brain and spine were compared and demonstrated increasing numbers of T2/Flair hyperintense lesions in the periventricular region involving the corpus callosum, juxtacortical area with gadolinium enhancing lesion and short segment lesion in C2. Her evoked potential studies were abnormal. However she declined cerebrospinal fluid examination. She was diagnosed with highly active RRMS and started with oral FYT 0.5mg daily. Her first dose FYT initiation was uneventful. However she developed maculopapular rash on both thighs after two weeks of starting the medication. There were no vesicles or any mucosal involvement. There was no new medication or previous history of drug allergy reported in this patient. The FYT was stopped for five days and the rash slowly disappeared without specific treatment, hence FYT was reintroduced. She was reviewed at regular interval and no recurrence of the rash or clinical relapse were observed in the last six months.

**Conclusions:** Our findings indicate that a transient rash can be seen in patient treated with FYT. Patient should be informed and close follow up is warranted to avoid unnecessary treatment interruption.

**P-113**

**Idiopathic and unexplainable Thrombocytopenia after Fingolimod Usage**  
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Fingolimod is one of the outstanding medication in MS. Its usage is available for the last five years. It is a new oral drug called a sphingosine 1-phosphate receptor modulator. Its mode of action is thought to be by retaining certain white blood cells (lymphocytes) in the lymph nodes, thereby preventing those cells from crossing the blood-brain barrier into the central nervous system (CNS). Preventing the entry of these cells into the CNS reduces inflammatory damage to nerve cells in MS is main target of effectiveness.

**Discussion and Conclusion:** As natalizumab acts as a potent drug inducing modulation of immune system, occurrence of opportunistic infections should be awaited. We suggest three possible risk factors for opportunistic infection in our subject – use of immunosuppressive drugs prior to natalizumab treatment, active smoking and living in the endemic area for infection with MK. We consider lung disease of our subject caused by MK to be an opportunistic infection during long-term natalizumab treatment.

**P-114**

**Asymptomatic Non-Tuberculous Mycobacteriosis as an Opportunistic Infection in a Subject Treated with Natalizumab for Relapsing-Remitting Multiple Sclerosis - Case Report**  
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**Background and Objective:** Natalizumab is a recombinant humanised α4-integrin antibody to human α4β1-integrin approved for treatment of active relapsing-remitting multiple sclerosis (RRMS). Efficacy is high however serious side effects can occur. We bring a case report of asymptomatic mycobacteriosis kansasi (MK) during natalizumab treatment.

**Case Report:** A male of Caucasian race born in 1986 with RRMS was treated with natalizumab since May 2008. JC virus antibodies status was negative. Further disease course was favourable. In December 2011 during routine preoperative exam (planned surgery for inguinal hernia) pathological lesion on chest X-ray was found in the upper lobe of the left lung. The patient (active smoker 15 cig/day) did not experience any respiratory or other symptoms. Chest CT raised suspicion of granulomatous inflammation and bronchoscopy was performed. MK was found in sputum specimen repeatedly. Natalizumab was suspended and patient received the combination of antituberculous drugs until the negativity of the sputum specimen regarding mycobacteria. On follow up chest X-ray vast regression of cavitation in the upper lobe of the left lung was observed. MS course is still favourable.

**Discussion and Conclusion:** As natalizumab acts as a potent drug inducing modulation of immune system, occurrence of opportunistic infections should be awaited. We suggest three possible risk factors for opportunistic infection in our subject – use of immunosuppressive drugs prior to natalizumab treatment, active smoking and living in the endemic area for infection with MK. We consider lung disease of our subject caused by MK to be an opportunistic infection during long-term natalizumab treatment.
P-115
Reduction of Disease Activity in Patient with Relapsing-Remitting Multiple Sclerosis after Switch to Teriflunomide from Interferon Beta-1a: A Case Report
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Background: Many patients with multiple sclerosis (MS) have a suboptimal response to disease-modifying therapy (DMT). In patients with suboptimal response to an initial DMT, switching to another DMT with different mechanism of action may reduce the activity of the disease. We report a patient with relapsing-remitting MS (RRMS), who suffered from frequent minor relapses despite good compliance to interferon (INF) beta-1a therapy, dramatically responded to teriflunomide.

Case report: A 45-year-old female who was diagnosed RRMS was received INF beta-1a for 3 years. Before INF beta-1a treatment, there was four times of clinical relapse for 6 years without any DMT and three times of clinical relapse confirmed by MRI and two times of new asymptomatic lesions since she has received INF beta-1a. An increased disease activity with suboptimal response was considered. We switched INF beta-1a to teriflunomide since October 2014. Follow up brain MRI performed after 6 months revealed no new T2 lesion and no gadolinium enhanced lesion. And she had no clinical relapse and adverse effect except tolerable mild hair thinning during 12 months.

Conclusion: This report highlights the therapeutic efficacy of teriflunomide in RRMS with suboptimal response to the initial DMT. Also, because of teriflunomide has different mechanism of action (limits the proliferation of activated T and B cells), switching to teriflunomide may be considerable option when disease activity is increased.

Poster Session 20
Case Report NMO

P-116
Neuromyelitis Optica Spectrum Disorder Presenting with Psychiatric Symptoms: A Case
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Background: Neuromyelitis optica and neuromyelitis optica spectrum disorders (NMOSD) are affecting optic nerves, spinal cord and other structures of central nervous system including brain and brainstem. We report a case of NMOSD presented with psychiatric symptoms.

Case: A 45-year-old woman was transferred from a psychiatric hospital. Her initial symptoms were headache, refusal of food and staying in bed all day. In the psychiatric hospital, she showed mutism, immobility and negativism. She refused any kinds of foods and drugs. It was difficult to eye contact. On admission to the neurologic department 1 month after symptom onset, she showed confused and delirious mental status, light perception only in both eyes, and right arm weakness (MRC grade 3-4). Axial T2-weighted FLAIR MRI showed lesions involving periependymal cerebral and brainstem, bilateral internal capsules and cerebral peduncle. Spinal cord MRI was unremarkable. Serum ANA (1:320), anti-SSA (>200.0 u/mL) and SSB (36.1 u/mL) antibodies were positive. Serum AQP4-IgG antibody was negative (cell-based assay). In the cerebral spinal fluid, white blood cell count was 2/mm³ and protein level 108 mg/dL. Salivary scintigraphy showed abnormal findings. Steroid pulse therapy (methylprednisolone 1.0 g/day i.v.) was done for consecutive 5 days and then changed to oral prednisolone 60 mg. Her psychiatric symptoms and vision started to improve.

Conclusion: This is a rare case of NMOSD presenting with psychiatric symptoms at initial attack.

P-117
Nmo-Spectrum Disorder in The Elderly: Beware The Mimics
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Background: NMO-spectrum disorders may affect the elderly but their initial presentations may be confused by clinical mimics.

Objective: We present the clinical and radiologic features of two older patients with NMO-spectrum disorder, who presented with cervical-degenerative and stroke-like features.

Methods: Case series

Results: Patient 1: A 67-year-old woman presented with neck pain and right upper limb numbness and weakness. Neurologic examination revealed right hemiplegia, upper limb hyporeflexia, right extensor plantar reflex and T4 sensory level. MRI showed C6/7 disc herniation and a central canal stenosis. A longitudinally-extensive T2 hyperintensity at C6/7 level extending up to C2 prompted consideration of transverse myelitis. Cerebrospinal fluid examination showed mild inflammatory changes, and Aquaporin-4 antibody seropositivity confirmed a NMO-spectrum disorder. The patient recovered well after intravenous steroids and remained relapse-free on maintenance immunosuppression for one year.

Patient 2: A 65-year-old man presented with left cheek numbness, abducens neuropathy, dysmetria and intractable hiccups. MRI showed left pontomedullary junction T2 hyperintensity with DWI restricted diffusion, suggestive of acute ischaemic stroke. Two months later, he developed recurrent hiccups, SIAH and right-sided weakness that evolved to tetraparesis and respiratory failure. Repeat MRI showed T2 hyperintensity in the medulla, extending caudally to C4. He was treated with steroids and plasma exchange, with slow improvement of motor function. Aquaporin-4 antibody testing yielded a positive result.

Conclusion: New-onset NMO can occur in elderly patients, and should be considered when clinical features are suspicious. Aquaporin-4 antibody confirms diagnosis of NMO-spectrum disorders.
P-118
Intractable Hiccups in Patient with Neuromyelitis Optica Spectrum Disorder
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Background: It is widely, well known that Neuromyelitis optica spectrum disorder (NMOSD) presents with symptoms such as intractable vomiting and hiccups. However, to our knowledge, hyponatremia associated with cerebral salt wasting syndrome (CSW) has never been described in a patient with NMOSD. In this report, we describe a case of a young male patient with NMOSD and systemic lupus erythematosus (SLE) who presented with intractable vomiting and hiccups.

Case presentation: A 22-year-old man presented with intractable vomiting and hiccups. Five weeks after onset of these symptoms, he developed numbness in the right arm. Brain magnetic resonance imaging (MRI) showed hyperintense lesions around the third ventricle and hypothalamus, and MRI of the cervical cord revealed no abnormalities at first but, five weeks later, he began to show mild weakness in the right arm. Brain magnetic resonance imaging (MRI) showed hyperintense lesions around the third ventricle and hypothalamus, and MRI of the cervical cord showed lesions confined in the brainstem area and hypereflexia with bilateral extensor plantar response.

Conclusion: When the first symptom is only intractable vomiting and hiccup, it is difficult to make the diagnosis of NMOSD in a young male patient. The development of hyponatremia in NMOSD may be attributed to cerebral salt wasting syndrome.

P-119
Application of The 2015 Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorder in A Young Woman with Recurrent Brainstem Symptoms
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Backgrounds: Recently the International Panel for NMO Diagnosis has proposed 2015 revised diagnostic criteria of NMOSD. We applied this new diagnostic criteria to a young woman who had recurrent brainstem symptoms and NMO typical brain lesions.

Case: A 22-year-old woman presented with suddenly developed diplopia. Her brain MRI showed multiple lesions with cloud-like enhancement in right periventricular white matter, left posterior limb of internal capsule, cerebral peduncle, middle cerebellar peduncle and right lateral medulla. The symptom was gradually resolved with high dose corticosteroid pulse therapy. However, she suffered 3 more recurrent attacks after this first event. The second attack was paresthesia on left side limb with a new brainstem lesion in right lower pontine tegmentum. The third attack was presented with cerebellar ataxia, and MRI revealed new lesions in region adjacent to the fourth ventricle and central tegmental tract on midbrain level. The fourth attack was horizontal diplopia with MRI lesions in left superior cerebellar peduncle and area adjacent to the fourth ventricle. The multiple laboratory tests with CSF and serum through these attacks didn't show abnormal findings including AQP4-IgG by cell-based assay.

Conclusion: In our case, the patient was young woman and the brain MRI showed lesions confined in the brainstem area and corticospinal tract which are typically seen in NMOSD. But this case does not meet the 2015 revised diagnostic criteria for NMOSD. The effort to clarify the diagnosis of NMOSD has been made up to date, but still the diagnosis of patients with AQP4-IgG seronegative remains unclear.

P-120
Case Report of Newly Diagnosed Neuromyelitis Optica Spectrum Disorder in a Patient with Systemic Lupus Erythematosus Presenting with Acute Disseminated Encephalomyelitis
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Objective: To describe a case of neuromyelitis optica spectrum disorders (NMOSD) presented with acute disseminated encephalomyelitis (ADEM).

Methods: Patient description: A 17-year-old Thai woman was diagnosed with systemic lupus erythematosus (SLE) for 4 years with the criteria of malar rash, discoid rash, photosensitivity, renal involvement, leukopenia, antinuclear antibody (ANA) and anti-double strand deoxyribonucleic acid (anti-dsDNA) positive. Previous active disease occurred 3 years ago when she had mononeuropathy multiplex. Oral prednisolone was gradually decreased to 5 mg/day. She was well until 3 days before admission when she developed convolution of the right extremities and altered state of consciousness. Physical examination revealed a febrile woman, stuporous; normal optic discs; gaze preference to the right which could be corrected with vestibulo-ocular reflex, equally reactive pupils without relative afferent pupillary defect; spastic tone in all extremities, more on the left; motor strength grade III on the right and grade I on the left; generalized hypreflexia with bilateral extensor plantar response.

Results: Brain MRI revealed patchy hyperintense lesions on T2W images at bilateral subcortical white matter and contiguous intramedullary spinal lesion extending from T2 to T7. There was no other clinical evidence of active lupus. Diagnosis of ADEM was considered. And since AQP4-antibody was positive, NMOSD associated with SLE was given. Unresponsiveness to high dose steroids prompted further treatment with plasma exchange, 1.5 times plasma volume, for 7 cycles. She gradually improved until she could walk with gait aid in six months.

Conclusions: ADEM can be the first manifestation of seropositive NMOSD patients.
P-121
Relapsing Demyelinating Polyneuropathy Associated with Neuromyelitis Optica
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Background: Central nervous system (CNS) demyelinating disorder has been rarely reported in association with peripheral nervous system involvement. We present here a patient with demyelinating polyneuropathy who was also affected with neuromyelitis optica (NMO).

Case: A 27-year-old female experienced gait disturbance, both leg weakness and sensory symptoms. She was diagnosed with inflammatory polyneuropathy and started steroid treatment. Afterwards, she presented with facial palsy and both leg weakness with sensory change and buttock pain. Deep tendon reflexes were decreased in all extremities. Nerve conduction study was consistent with demyelinating polyneuropathy. After steroid therapy, her symptoms and electrodagnostic study parameters improved. She experienced mild relapses and steroid therapy was effective. At the age 36, decreased left visual acuity and dysarthria developed. Brain MRI revealed no remarkable findings, but left P100 latencies were prolonged on visual evoked potential. At the age 45, numbness and pain of left facial area developed. Brain MRI demonstrated newly developed T2 high signal lesion at left pons. Serum anti-Aquaporin4 antibody was positive. One year later, she felt heaviness of her left leg. This time, deep tendon reflexes were brisk. Spinal cord MRI showed T2 high signal lesion on cervical level. The findings satisfied the diagnostic criteria of NMO. High dose steroid treatments were done.

Conclusion: When patients with demyelinating polyneuropathy develop NMO, manifestations of central and peripheral disease involvement seem to respond to high dose steroid therapy. We suggest that there may be common antigenic targets in central and peripheral nervous system.

P-122
Acute Myopathy in Neuromyelitis Optica
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Backgrounds: Myopathy associated with neuromyelitis optica (NMO) was recently reported and characterized by reduced AQP4 immunoactivity at sarcolemmal membranes.

Objective: The present study focuses on a 49-year-old man with NMO who developed acute myopathy associated with recurrent high serum creatine kinase (CK) levels during NMO attack.

Methods: To investigate the cause of acute myopathy associated with high serum CK level, immunohistochemical stains, light and electron microscopic study of biopsied muscle were performed.

Results: Light microscopy showed accumulations in subsarcolemmal area and type II muscle atrophy. Electron microscopy revealed myofibril disruption commencing at the Z-disk and scattered electron-dense materials, which morphology suggested with myofibrillar myopathy (MFM). Immunohistochemistry stain for AQP4 showed preservation of immune reactivity at sarcolemma. Up-regulated human Ig G-Fc and major histocompatibility complex (MHC) class I antigen were found along with sarcolemma. After plasmapheresis with rituximab treatment, there was no further relapse and normal creatine kinetic level with neurological improvement were showed for 15 months.

Conclusions: This study implies that NMO patient with episodic hyperCKemia may have variable phenotypes on pathologic finding. Further accumulation cases and studies are needed to elucidate the relationship between myofibril destruction and AQP4 autoimmunity.

P-123
Dose Syphilis Cause Neuromyelitis Optica Spectrum Disorder? Case Study
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Background: Neuromyelitis optica spectrum disorder (NMOSD) is characterized by optic neuritis, longitudinally extensive transverse myelitis (LETM), or area postrema syndrome. Chronic infection such as HIV or syphilis is one of the red flags of NMOSD. We report a case presenting with LETM and area postrema lesion following treatment of latent syphilis.

Case report: A 72-year-old man presented with diplopia and dizziness in November 2012. Brain MRI showed left dorsolateral medulla lesion on T2 weighted image. He had a history of latent syphilis, and serologic test for syphilis was positive. He was treated with penicillin G intravenously, and his symptoms and MRI lesions were improved. In December 2014, he presented with altered mentality and dyspnea. Brain and spine MRI showed cervical LETM extending to dorsolateral medulla and thoracic myelitis. CSF study revealed pleocytosis (WBC 160, lymphocyte 70%) with elevated total protein (74 mg/dL). CSF test for syphilis was negative. IgG index and oligoclonal band were negative and serum anti-aquaporin-4 antibody was negative. He was treated with methylprednisolone pulse therapy in tentative diagnosis of NMOSD. His symptoms were improved nearly completely and mild gait instability was left 9 months later.

Discussion: This case is compatible to NMOSD without AQP4-IgG in terms of clinical symptoms and MRI findings. Symptoms were improved completely after methylprednisolone pulse therapy. Syphilis could lead to chronic CNS infection mimicking NMOSD however syphilis might be one of causes of post-infectious NMOSD like this study.
P-124
Rapid Exacerbation of Neuromyelitis Optica after Rituximab Treatment
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Background: Rituximab (RTX) is recommended as an off-label prescription to treat refractory NMO. We described two patients with suboptimal response or deterioration after RTX treatment.

Case 1: A 58-year-old male Australian patient of Maori ethnicity presented with recurrent disabled mobility and swallowing difficulties from June 2006. In July 2009, MRI revealed a spinal cord lesion in T3-6 segments. Serum NMO-IgG was negative. He was diagnosed with NMO and received one cycle of RTX in August 2009 after Six cycles of plasmapheresis, followed by oral prednisolone. On 14 December 2009, the patient was admitted with urinary retention in March 2010. NMO-IgG was negative, and she was diagnosed with NMO. She received 3 interferon-beta injection or azathioprine couldn’t modify the course. The patient suffered 5 subsequent relapses over the next 2 years. In December 2013, NMO-IgG was shown to be seropositive and she was diagnosed with NMO. She received 3 rounds of RTX, combined with oral methylprednisolone. Three additional episodes of limb weakness occurred after the first round. And just 10 hours after the first infusion of the third rounds, her lower limb weakness worsened. Repeated MRI revealed myelitis at the level of medulla oblongata and C1-T11 with patchy enhancement.

Conclusions: Our cautionary cases highlight that in a small proportion of refractory NMO, rituximab may either fail or induce rapid relapse of NMO.

Poster Session 21
Case Report ‘ADEM’ myelitis and Optic Neuritis

P-125
Acute Disseminated Encephalomyelitis Presented With Tremor as Initial Symptom
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Background: Acute disseminated encephalomyelitis (ADEM) is a post-infectious immune-mediated complication of the central nervous system. Multiple neurological deficits can occur but rarely movement disorders.

Case Report: A 24-year-old female patient was admitted because of an ongoing tremor in both her arms and hands after a common cold 2 weeks prior to her visit. After admission, her mental status declined going into a coma within 2 days. Brain magnetic resonance imaging (MRI) showed a mild enhancing bilateral multifocal white matter change compatible with ADEM. The cerebrospinal fluid (CSF) analysis showed an absence of pleocytosis and oligoclonal bands. Tests for viruses, bacteria, fungi and NMMA receptor antibodies were all negative. Antiepileptic agents were administered because of the electroencephalography (EEG) finding of the patient as status epilepticus. Immunosuppression therapies were tried, and the patient gradually improved and was transferred to rehabilitation.

Conclusion: Herein, we report a young adult female patient who presented with a tremor as the first neurological manifestation of ADEM.
P-127  
A Case of Antiphospholipid Syndrome with Transverse Myelitis Mimicking Guillain-Barré Syndrome

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Background: Antiphospholipid syndrome (APS) rarely manifests as myelopathy or peripheral neuropathy related to vasculitis. We present a case of APS with transverse myelitis (TM) concurrent with inflammatory multiple mononeuropathies.

Case: A 10-year-old girl presented with quadriaparesis with fever. Neurologic examinations revealed motor weakness of both lower extremities (Medical Research Council (MRC) grade I/I) and both upper extremities (MRC grade II/II). The deep tendon reflexes (DTR) were hyporeflexive in both upper and lower limbs, and Babinski sign was negative. On nerve conduction study (NCS) of the first day, F-waves were unobtainable on several nerves, but motor and sensory NCS were normal on tested nerves of upper and lower limbs. Intravenous immunoglobulin treatment for five days administered on suspicion of Guillain-Barré syndrome. After 1 week, NCS results were compatible with multiple motor axonal mononeuropathies. For two months, motor weakness of upper extremities improved gradually. Serial NCS also showed gradual recovery of F-waves and CMAP amplitudes. But, her DTR became hyperactive on left lower extremity. In spine MRI, T2-high signal intensity lesions in spinal cord from C5 to T2 level were seen, which suggest TM. On evaluation of myelitis, anti-phospholipid IgG, anti-cardiolipin IgM and IgG were positive. She is treated with prednisolone and aspirin for 6 months. Her motor weakness has been slightly improved, but she only could stand with help.

Conclusions: We experienced rare case of APS which showed intercurrent inflammatory peripheral neuropathies with transverse myelitis. In the patient with concurrent peripheral and central nervous system inflammation, APS should be investigated thoroughly.

P-128  
Absence of Late Response in A Case Of Longitudinally Extensive Transverse Myelitis

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Background: Absent or prolonged late response (F-wave and H-reflex) is the most sensitive abnormality in the early Guillain–Barré syndrome (GBS).

Objectives: To report a case of transverse myelitis with absent late response.

Methods: A 52-year-old woman presented with weakness of both legs and a thoracic sensory level.

Results: Neurologic examination showed paraplegia (MRC 0), areflexia, and sensory level to all modalities at T12. Initial MRI of the cervical and thoracic spine was normal. Cerebrospinal fluid was also unremarkable. Electrodagnostic study showed absent late response but other conduction studies were normal. These findings were more consistent with GBS than transverse myelitis. Follow-up spine MRI showed extensive high signal intensities in the spinal cord. She was diagnosed as acute transverse myelitis and treated with plasma exchange.

Conclusions: In patients with acute onset tetra- or paraplegia, absent late response dose not distinguish between GBS and transverse myelitis.

P-129  
Atopic Myelitis in Pregnancy, First Report from Indonesia

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Background: Atopic Myelitis (AM) is a myelitis of unknown cause with either hyperIgEamei and mite antigen-specific IgE positivity or coexistent atopic disease. This is the first report of AM from Indonesia.

Objective: To report an Atopic Myelitis case

Methods: Case Report

Result: A 39 year old female with astma bronchial history since childhood came to our hospital with numbness in her arms and legs. It followed by weakness and difficulty in urinating. She was at 22 week pregnant. Neurological examination revealed hypoesthesia below the Cervical 3 level. Motor power decreased in fourth extremities with exaggerated deep tendon reflex in arms and legs. MRI examinations revealed intramedullary lesion from brainstem to C3 and Th1 and 2 which were hypointens in T1-weighted image and hyperintens in T2-weighted image and no gadolinium enhancing. Cerebrospinal fluid examination showed pleocytosis with normal protein and glucose level. Total IgE level was increased 6365 U/mL. We conclude the case as Atopic Myelitis and treated with methylprednisolone.

Conclusions: This is the first report of myelitis case associated with hyperIgEEmia and atopic disease from Indonesia.

P-130  
A Case of Myelitis Associated With Varicella-Zoster Virus in an Immunocompetent Adult

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Background, Objective, Method: Myelitis is rarely associated with varicella-zoster virus (VZV) infection in immunocompetent patients. The pathogenesis of neurological complications associated with VZV infection is largely unclear. Direct viral invasion or allergic mechanisms after VZV infection has been supposed in the pathogenesis of VZV myelitis. We describe a myelitis caused by VZV in an immunocompetent adult.

Results: A 50 years-old man present with paresthesia of right lower limbs and Lhermitte’s sign without weakness nor voiding difficulty during 1 weeks with starting symptom of pain and skin rash in left T4 dermatome. His serum routine lab was normal range. However, serum IgM for VZV was positive. A spine MRI revealed a T2-high signal lesion with focal enhancement in the thoracic spinal cord. The cerebrospinal fluid was clear and the pressure was normal. Serum fluorescent antinuclear antibodies and double stranded DNA antibodies titer was normal. He was diagnosed with myelitis associated with VZV infection. He was treated with intravenous acyclovir and methylprednisolone. Within 2 months, his symptoms were improved.

Conclusions: It is suggested that VZV should be considered as a possible cause of a myelitis even in immunocompetent adult.
P-131
Cytomegalovirus Associated Transverse Myelitis in Immunocompetent Patient: Case Report
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Background: Acute transverse myelitis (TM) is a focal inflammatory disorder of the spinal cord with sensory, motor and autonomic dysfunction. Cytomegalovirus (CMV)-associated transverse myelitis is rare in the immunocompetent host. We describe an immunocompetent patient with atypical transverse myelitis and anecephalitis associated with CMV infection.

Case report: A twenty year old previously healthy female presented with acute onset bilateral leg and arm weakness and numbness. She had never received immunosuppressive or irradiation treatment. MRI showed hyperintensity of central and posterior portion of all spinal cord in T2 weighted and FLAIR images. Spinal cord and brain MRI were no enhancement with contrast. Serologic tests ruled out an acute infection with HIV, herpes simplex viruses’ varicella-zoster virus, Epstein-Barr virus, measles and mumps viruses, toxoplasma gondii, and Treponema pallidum. Both anti-CMV IgM and IgG were elevated in the serum. However, a more sensitive assay resulted in low IgG avidity, suggesting primary CMV infection.

Conclusion: Our patient had evidence of spinal cord inflammation evidenced by CSF pleocytosis and MRI appearance. Infectious, parainfectious or post-vaccinal states, multiple sclerosis, or autoimmune disorders are the possible causes of TM. Cytomegalovirus (CMV) can cause severe disease in immunocompromised patients, either via reactivation of latent CMV infection or via acquisition of primary CMV infection. CMV-associated transverse myelitis is rare in the immunocompetent host.

P-132
Coexisting Optic Neuritis with Sjögren’s Syndrome: Case Report
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Background: Optic neuritis is known as a neurologic manifestation of systemic autoimmune diseases, particularly Sjögren’s syndrome.

Objective: To report a case of optic neuritis with Sjögren’s syndrome in Indonesian patient

Methods: Case report

Result: A 32-year-old woman came to the hospital because of intermittent blurred and dark vision on both eyes since nine years ago. There were improvement in the right eye but not in the left. Visual evoked potentials showed demyelinating type pariall block of visual tract of left eye. She also complained intermittent weakness and pain of both extremities since ten years before admission. Neurological examination revealed motor weakness on her extremities with exaggerated physiological reflex. Magnetic Resonance Imaging of the brain and spinal cord and somatosensory evoked potential showed no abnormalities. Cerebrospinal fluid analysis were in normal limit, aquaporin-4 antibody has not been tested. One year before admission, patient also complained sensation of sand and dry on her eyes, and dry on her mouth. Schirmer test were decreased on both eyes. Unstimulated saliva flow rate were decreased and revealed xerostamia and hiposalivation. Result of SS-A antibody examination were above normal limit. The patient received analgaetics and steroid as therapy.

Conclusion: Optic neuritis has been associated with Sjögren’s syndrome. The patient were suspected neuromyelitis optica spectrum disorder (NMOSD). Serology examination of aquaporin-4 antibody should be done to confirm the diagnosis of NMOSD.

P-133
An Ethmoid Sinus Mucocele Simulating as Retrobulbar Optic Neuritis
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Background: Optic neuritis (ON) typically presents with sudden loss of vision and eyeball pain in young adults, often associated with multiple sclerosis or neuromyelitis optica. However, inflammation of the optic nerve can be due to infection or spread of inflammation from the meninges, sinususes or orbit. Retrobulbar ON also could be mimicked by compressive lesions of the brain or optic nerve.

Case: A 60-year-old woman with history of hypertension and hyperlipidemia presented with diminution of vision and pain in the right eye aggravating for two days, associated with headache on the right frontal area. She had no symptoms of upper respiratory infection or sinusitis. On examination, she had a decreased visual acuity of the right eye, permitting only light perception. Pupils were round and isocoric, however, the light reflex was sluggish on the right side with a relative afferent pupillary defect. Eye movements were full in all directions. Fundus examination revealed normal disc in either eye. No other systemic or neurological deficit was present. Retrobulbar ON was suspected, however, the MRI showed a 2.7 × 1.7 × 2 cm – sized lesion at the right posterior ethmoid sinus with encasement of right optic canal, suggesting mucocele. Under a dignosis of compressive optic neuropathy associated with the ethmoid sinus mucocele, an endoscopic ethmoidectomy was performed, and the patient’s visual acuity was completely recovered after two weeks.

Conclusions: Our case suggests that a neuroimaging study should be considered essential in cases of retrobulbar ON even in the presence of a single atypical feature.

P-134
Ischemic Strokes in a Young Woman With Manifestations of Multiple Sclerosis: Can Ischemic Stroke Mimic Multiple Sclerosis?
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P-134
Ischemic Strokes in a Young Woman With Manifestations of Multiple Sclerosis: Can Ischemic Stroke Mimic Multiple Sclerosis?
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Objective: The aim of this case report was to describe the clinical, radiological and immunological findings of a case of ischemic stroke due to acute thrombosis of the left internal carotid artery and multiple watershed infarctions mimicking multiple sclerosis (MS).

Clinical Presentation and Intervention: A 24-year-old right-handed Iranian woman was initially diagnosed with MS. She presented with weakness in right lower limb. The cerebral fluid attenuation inversion (FLAIR) magnetic resonance imaging (MRI) showed few small and round lesions in deep white matter, semi-oval centraums, paraventricular region and subcortical region on left hemisphere. MS was suspected. The patient's neurological status worsened, after four days she presented hemiparesis, dysarthria, hemifacial paresis. The cerebral diffusion-weighted magnetic resonance imaging (DW-MRI), apparent diffusion coefficient (ADC), Duplex scan (DS), complete blood count (CBC), coagulation, blood chemistry, blood lipids, and autoimmune and immunodiagnostics pathology were done. Mild inflammatory syndrome, test for anti-double stain DNA, IgG anti-cardiolipin antibodies, and lupus anticoagulant were positive. DNA bound lactoferin, anti-Sm antibodies, Anti-Sjogren's-syndrome-related antigen-A auto-antibodies, and IgM anti-cardiolipin antibodies, IgG and IgM fosfatildil serin and anti-beta 2 glycoprotein were negative. The patient proved to have an ischemic stroke due to acute thrombosis of the left internal carotid artery and multiple watershed infarctions. Heparin and after that Warfarin therapy was started. She was currently treated with warfarin, Hydroxychloroquine (200 mg/d) anti vitamin K, and symptomatic. The outcome was favorable.

Conclusion: Our case presented with clinically susceptible symptoms of MS but found to have stroke after neurological assessment with overlap systemic lupus erythematosus.

P-136
Balo's Concentric Sclerosis or Primary Angiitis of The CNS? A Diagnostic Dilemma
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Backgrounds: Differential diagnosis of space occupying lesions may not be straightforward. Here we present a case with typical MRI features of Balo's concentric sclerosis (BCS), but with contrasting final histologic findings.

Case: A 18-year-old woman presented with acute onset of right leg weakness that started an hour ago. She was treated with TPA with presumptive diagnosis of a hyper-acute ischemic stroke. However, brain diffusion weighted images showed pattern of vasogenic edema, and routine brain MRI showed a mass like lesion in left posterior periventricular white matter with low signal intensity on T1 and high signal intensity on T2 weighed images. The lesion showed concentric onion-like partial enhancement. According to history and imaging findings, tumefactive demyelinating lesion, lymphoma, and brain abscess was our differential diagnosis; however, BCS was the most possible diagnosis based on MRI findings. She underwent biopsy to differentiate probable abscess or tumor from demyelinating lesion. Surprisingly biopsy revealed lymphocytic vasculitis, a subtype of primary angiits of the CNS (PACNS). She had an unremarkable collagen vascular workup and CSF study. She underwent high dose steroid pulse therapy of 2 cycles for 2 weeks, and there was only minimal improvement of her condition. Two months later, her symptoms were almost improved without any immune modulating treatment.

Conclusion: Although histologic finding is more suggestive of PACNS, clinical findings such as clinical course and MRI feature were more compatible with BCS rather than PACNS. This case highlights the diagnostic dilemma in a patient with a solitary brain lesion.

P-137
Longitudinally Extensive Spinal Cord Lesions and Cerebral White Matter Abnormalities by Chlorfenapyr Ingestion
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Background: Chlorfenapyr is a novel insecticide commercially used for crop protection, which is known to lead to lethal clinical outcome in most reported cases with chlorfenapyr ingestion.

Objective: The aim of this case report was to describe the clinical, radiological and immunological findings of a case of ischemic stroke due to acute thrombosis of the left internal carotid artery and multiple watershed infarctions mimicking multiple sclerosis (MS).

Clinical Presentation and Intervention: A 24-year-old right-handed Iranian woman was initially diagnosed with MS. She presented with weakness in right lower limb. The cerebral fluid attenuation inversion (FLAIR) magnetic resonance imaging (MRI) showed few small and round lesions in deep white matter, semi-oval centraums, paraventricular region and subcortical region on left hemisphere. MS was suspected. The patient’s neurological status worsened, after four days she presented hemiparesis, dysarthria, hemifacial paresis. The cerebral diffusion-weighted magnetic resonance imaging (DW-MRI), apparent diffusion coefficient (ADC), Duplex scan (DS), complete blood count (CBC), coagulation, blood chemistry, blood lipids, and autoimmune and immunodiagnostics pathology were done. Mild inflammatory syndrome, test for anti-double stain DNA, IgG anti-cardiolipin antibodies, and lupus anticoagulant were positive. DNA bound lactoferin, anti-Sm antibodies, Anti-Sjogren's-syndrome-related antigen-A auto-antibodies, and IgM anti-cardiolipin antibodies, IgG and IgM fosfatildil serin and anti-beta 2 glycoprotein were negative. The patient proved to have an ischemic stroke due to acute thrombosis of the left internal carotid artery and multiple watershed infarctions. Heparin and after that Warfarin therapy was started. She was currently treated with warfarin, Hydroxychloroquine (200 mg/d) anti vitamin K, and symptomatic. The outcome was favorable.

Conclusion: Our case presented with clinically susceptible symptoms of MS but found to have stroke after neurological assessment with overlap systemic lupus erythematosus.

P-136
Balo's Concentric Sclerosis or Primary Angiitis of The CNS? A Diagnostic Dilemma
Byung-Jo Kim, Yeon-Sun Woo, Yoo-Hwan Kim, Hung Youl Seok, Chan-Nyung Lee
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Backgrounds: Differential diagnosis of space occupying lesions may not be straightforward. Here we present a case with typical MRI features of Balo's concentric sclerosis (BCS), but with contrasting final histologic findings.

Case: A 18-year-old woman presented with acute onset of right leg weakness that started an hour ago. She was treated with TPA with presumptive diagnosis of a hyper-acute ischemic stroke. However, brain diffusion weighted images showed pattern of vasogenic edema, and routine brain MRI showed a mass like lesion in left posterior periventricular white matter with low signal intensity on T1 and high signal intensity on T2 weighed images. The lesion showed concentric onion-like partial enhancement. According to history and imaging findings, tumefactive demyelinating lesion, lymphoma, and brain abscess was our differential diagnosis; however, BCS was the most possible diagnosis based on MRI findings. She underwent biopsy to differentiate probable abscess or tumor from demyelinating lesion. Surprisingly biopsy revealed lymphocytic vasculitis, a subtype of primary angiits of the CNS (PACNS). She had an unremarkable collagen vascular workup and CSF study. She underwent high dose steroid pulse therapy of 2 cycles for 2 weeks, and there was only minimal improvement of her condition. Two months later, her symptoms were almost improved without any immune modulating treatment.

Conclusion: Although histologic finding is more suggestive of PACNS, clinical findings such as clinical course and MRI feature were more compatible with BCS rather than PACNS. This case highlights the diagnostic dilemma in a patient with a solitary brain lesion.

P-137
Longitudinally Extensive Spinal Cord Lesions and Cerebral White Matter Abnormalities by Chlorfenapyr Ingestion
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Background: Chlorfenapyr is a novel insecticide commercially used for crop protection, which is known to lead to lethal clinical outcome in most reported cases with chlorfenapyr ingestion.
**Objective:** To report a case with acute onset of chlorfenapyrid-induced leukoencephalopathy, who initially misdiagnosed as having an inflammatory demyelinating disease.

**Case:** A 54-year-old man was brought to our emergency room with a sudden onset of quadriplegia. He had been diagnosed as Henoch-Schönlein nephritis 3 months ago, and taking 60mg of oral prednisolone with hypertension and diabetes drug. Neurologic examination revealed weakness in bilateral upper and lower extremities of MRC grade 2–3. Pain sense was decreased below T2 dermatome and vibration sense was decreased below T10 level with hyper-reflexia and bowel & bladder dysfunction. T2-weighted spinal MRI showed high signal intensity from medulla below T2 dermatome and cerebral peduncle regions, in T2 and fluid-attenuated inversion recovery (FLAIR) sequences. There was a lesion in the left parietal lobe that exhibited linear gadolinium enhancement. The results of neurological examination showed a daily decline. On the 3rd day of admission, he had a high fever and a follow-up CSF examination showed increased ICP (350mmH2O) and protein, leukocytosis. Considering the bacterial meningitis at the age over 50, vancomycin, ceftriaxone and ampicillin was added. On the 9th week after being ingested. Detailed history taking was mightily important to identify the exact etiologies, especially in toxic leukoencephalopathies-suspected patients.

**Conclusions or Comments:** Chlorfenapyrid-induced leukoencephalopathy may be often non-fatal, which developed neuronal toxicities several weeks after being ingested. Detailed history taking is mightily important to identify the exact etiologies, especially in toxic leukoencephalopathies-suspected patients.

**P-139**

**Primary Central Nervous System High Grade B-cell Lymphoma Mimicking Relapsing Remitting Inflammatory Demyelinating Disease**

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**Background:** Primary central nervous system (CNS) lymphoma (PCNSL) is a very rare intracranial neoplasm occurring in elderly patients without immunodeficiency. PCNSL has a similar clinical course and radiological findings to inflammatory demyelinating disease.

**Objective:** To discuss the case of a patient prediagnosed with multiple sclerosis and then diagnosed as high-grade B-cell non-Hodgkin's lymphoma after brain biopsy.

**Case Report:** A 64-year-old female patient was admitted to our hospital with complaints of headache, difficulty speaking, and gait instability. Magnetic resonance imaging (MRI) of the brain showed multiple white matter lesions, especially periventricular and cerebral peduncle regions, in T2 fluid-attenuated inversion recovery (FLAIR) sequences. There was a lesion in the left parietal lobe that exhibited linear gadolinium enhancement. The patient's complaints declined after 7 days of corticosteroid-pulse treatment. Two months later, she developed right hemiparesis. She had another 7 days of corticosteroid-pulse treatment but did not benefit properly. Follow-up brain MRI revealed new lesions and remaining gadolinium enhancement in the left parietal lobe. The results of neurological examination showed a daily decline. Neoplasm could not be ruled out through brain MRI or positron emission tomography (PET) scans; thus, a stereotactic-guided biopsy of the brain lesions was performed. The pathological findings suggested high-grade B-cell non-Hodgkin's lymphoma.

**Conclusions:** PCNSL is a rare form of extranodal non-Hodgkin's lymphoma, its diagnosis is supported by MRI but is ultimately confirmed by stereotactic biopsy. Clinicians should be alert to the possibility of PCNSL, especially when a patient whose brain MRI showed inflammatory demyelinating white matter lesions is unresponsive to corticosteroids.

**P-140**

**A Case of Immunoglobulin G4 Related Pachymeningitis**

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**Background:** Immunoglobulin G4 (IgG4) related disease is an immune-mediated fibroinflammatory condition that can affect multiple organs: the pancreas, biliary tree, salivary glands, periorbital tissues, kidneys, lungs, lymph nodes, meninges, aorta, breast, prostate, thyroid, pericardium, and skin. Rare cases of dural involvement by IgG4-related disease have been reported. I describe a case of IgG4-related pachymeningitis.

**Case:** A 51-year-old woman was admitted to our hospital because of generalized seizure and headache. Brain magnetic resonance imaging (MRI) showed dural thickening and enhancement in the
bilateral frontal and parietal areas. CSF examination revealed 1 cells/μL with normal protein and glucose levels and cytology was negative. To investigate the cause of the pachymeningitis, a meningeal biopsy was performed. Hematoxylin and eosin stain showed acute and chronic inflammation with fibrosis. IgG4 immunohistochemistry showed prominent IgG4 plasma cells within the inflammatory infiltrate. Serum IgG level was normal but IgG IV subclass level (3000.0 mg/L) was significantly elevated. She was treated with intravenous dexamethasone (20 mg/day) followed by oral prednisolone. After 1 year of treatment, brain MRI showed marked decrease of dural thickening and enhancement.

**Conclusion.** I report a case of IgG4 related pachymeningitis improved with corticosteroid. IgG4-related disease should be included in the differential diagnosis in patients with hypertrophic pachymeningitis.
Clinical Inertia in MS Management

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Recent data indicate that the fundamental features of multiple sclerosis (MS) in Asian populations do not differ from those in white populations, if neuromyelitis optica spectrum disorders have been properly excluded. This suggests that the 2010 McDonald diagnostic criteria and the new treatment paradigm to attain ‘no evidence of disease activity (NEDA; no relapses, no sustained disability progression, and no new lesions on MRI)’ is also applicable to the diagnosis and management of MS patients in Asia. There is increasing evidence that patients with MS benefit most from early treatment and uncontrolled disease activity in the early phase of disease dictates poor prognosis. Therefore, treatment response must be carefully monitored and continually re-evaluated. Implementation of the new therapeutic aim of NEDA is crucial to protect MS patients from irreversible disability and to prevent the development of a secondary progressive course, for which no effective therapy is yet available. While clear definition of treatment failure and standardized follow-up method for detecting disease activity in daily practice needs to be established, switching into a more potent drug is recommended to patients who exhibit continued disease activity despite the treatment. Clinical inertia, i.e., failure to intensify treatment despite a suboptimal response to first-line treatment, is a major contributor to inadequate disease care and disability progression in patients with MS. The main causes of clinical inertia include uncertainty regarding treatment failure and a lack of organization or training in how to follow patients with MS to detect clinical worsening and disease activity in daily practice. In Asia, lack of attention to the burden of disease and lack of reimbursement for novel effective drugs for MS (probably due to its low prevalence in Asia) influence clinical inertia. Recent data suggest that the window of opportunity to influence disease progression with therapy might be not as long as previously thought. Therefore, it is very important to detect disease activity early in the disease course to achieve the best possible NEDA outcome. Trials to establish new standard and practical therapeutic goals for MS management are ongoing. In order to reduce clinical inertia, physicians should keep up-to-date and be encouraged to promote a more active approach to MS care.

Functional and Long Term Outcomes in MS – Where’s the Evidence?

Helmut Butzkueven (Australia)
MBBS, FRACP, PhD, Director of the MS service at Box Hill Hospital, Professor of Department of Medicine, University of Melbourne and Deputy Director of the Melbourne Brain Centre at the Royal Melbourne Hospital, Melbourne, Australia

Increased availability and choice of treatments for Multiple Sclerosis are leading to a “treat to target” approach for MS. The concept of proactive monitoring using scheduled MRI and systematic collection of a minimum clinical dataset will be briefly discussed. The term “real-world evidence” in Multiple Sclerosis encompasses a wide variety of different data collection methodologies distinct from Phase II or III clinical trials. Registries can provide structured, prospectively collected real-word evidence for analysis of treatment efficacy, treatment sequencing outcomes and serious adverse event identity and frequency if an appropriate minimum dataset and minimum data quality expectations are fulfilled. As an example of a Phase IV outcomes registry, evidence for natalizumab treatment efficacy and safety gathered from the 5000 patient+ Tysabri Observational Program will be discussed. Results from the globally operative MSBase Registry, which has attracted over 35,900 patient records at more than 200 MS centres over the last 11 years will be highlighted. A matching methodology known as “propensity matching” used extensively in MSBase to compare treatment outcomes, will be illustrated. Approaches to long-term outcome prediction modeling using the MSBase registry dataset will also be briefly introduced.

Measuring and Managing Disease Activity – How and When?

Jeannette Lechner-Scott (Australia)
FRACP, PhD, Hunter Medical Research Institute University Of Newcastle, Australia John Hunter Hospital New Lambton Heights, NSW, Australia

There has been a quiet revolution in MS over the last two decades. Since the introduction of the first disease modifying treatment of MS, beta-interferon, in 1993 our knowledge about disease pathomechanisms has exponentially increased. With the development of new therapeutic options the goal post of treatment has shifted from reducing relapses to reducing disability progression to disease freedom and lately disability improvement. We have learned an important factor in achieving these goals is to start therapy as early as possible. The expansion of treatment options now available in many regions (in Australia 11 medications are allowed to be given as first line therapy) challenges the neurologist to individualise therapy based on prognostic factors and to adjust therapy to ongoing disease activity. This requires ongoing review of clinical parameters as well as imaging. Monitoring is also required as increasing efficacy of our therapies have come with a price. Side effects can occur even years after administration of therapy. This presentation will address these factors with examples of practical application.
Seoul, Republic of Korea 2015

Teva

The Story of Copaxone: An Approach to the Treatment of Multiple Sclerosis
Friday 20 November 2015, 8:30-10:00

Two Decades of Subcutaneous Glatiramer Acetate Injection: The History of Copaxone Treatment
Corey Ford (USA)
Information not available at time of printing.

Three Times Weekly Glatiramer Acetate in Relapsing-Remitting Multiple Sclerosis; The GALA Study MRI and 36 Month Update
Robert Zivadinov (USA)
Information not available at time of printing.

Genzyme

Reshaping MS with Alemtuzumab
Chairperson: Ho Jin Kim (Republic of Korea)
Friday 20 November 2015, 17:00-18:30

Immune Pathogenesis of MS and Role of High Efficacy Therapies
Scott Zamvil (USA)
Donnie Smith Chair in Multiple Sclerosis Research; Professor of Neurology; Faculty, Program in Immunology; Faculty, Biomedical Sciences Graduate Program; University of California, San Francisco (UCSF)
Information not available at time of printing.

Clinical Experience with Alemtuzumab in MS
Pamela McCombe (Australia)
Associate Professor of School of Medicine, University of Queensland; Senior Research Fellow in the Neuroimmunology Research Unit, Department of Medicine, at the University of Queensland
Information not available at time of printing.
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