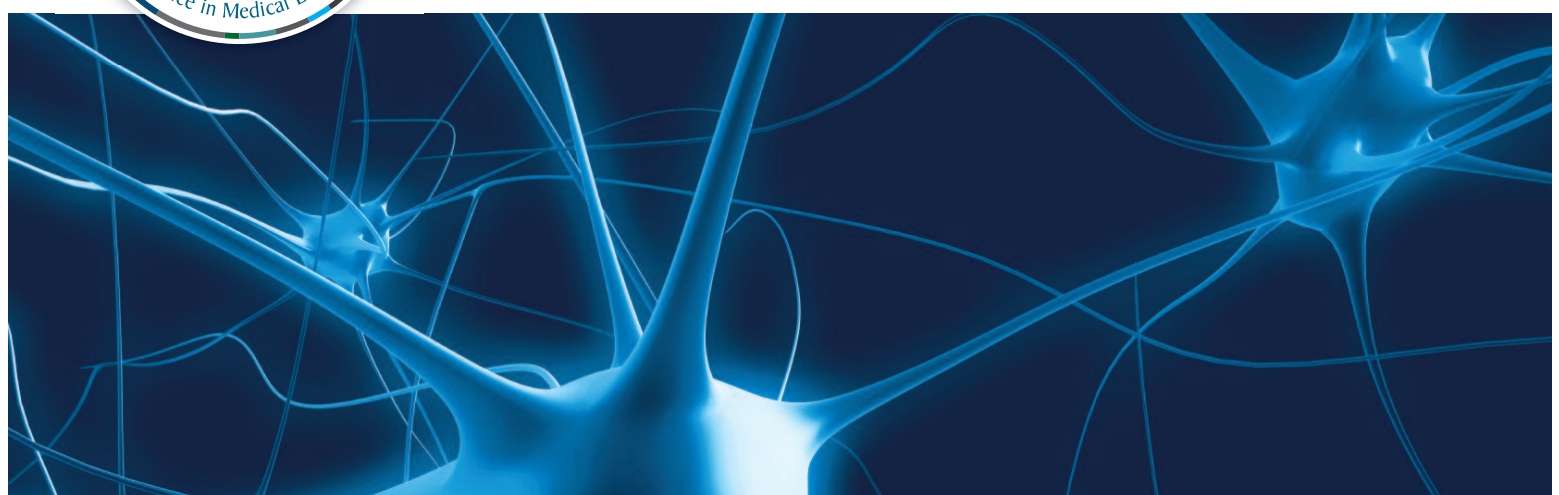




ECTRIMS
EUROPEAN COMMITTEE FOR TREATMENT
AND RESEARCH IN MULTIPLE SCLEROSIS



MS Academia
Multiple sclerosis advanced course
13 September 2016 - London, UK



MS Academia: Multiple sclerosis advanced course

Overview

Multiple sclerosis (MS) is a multifaceted neurological disorder whose management requires a multidisciplinary team of highly specialised health professionals. The availability of new and sophisticated diagnostic tools and the discovery of new treatments has made daily clinical practice even more challenging for physicians involved in MS patient management. Tailoring the treatment to individual patient needs and establishing the right time to start therapy or to switch from traditional first-line disease-modifying therapies to other first- or second-line therapies are the biggest issues. The goal of this learning activity is to update participants about MS pathogenesis and diagnostic criteria and to provide a comprehensive overview of past and future disease-modifying therapies. In addition, the participant will be taught about strategies for symptomatic and rehabilitative care which have proven to be a necessity in overall MS management. Session II will be composed by a case based series of lectures offering a practical approach to the hottest topics related to diagnosis. The initial case discussion will stimulate the a discussion between the participants and the presenters and will set the ground for the diagnosis key aspects knowledge sharing.

Learning objectives

By attending this live educational course, participants will be able to:

- Illustrate the immunological factors involved in the pathogenesis of multiple sclerosis
- Integrate clinical, neurophysiological, and MRI findings into the accurate diagnosis of multiple sclerosis and the exclusion of MS mimickers
- Incorporate information regarding the risks and benefits of currently available drugs for multiple sclerosis into treatment decisions
- Include symptomatic management of multiple sclerosis into the treatment paradigm of comprehensive management throughout the spectrum of the disease

Target audience

This programme is appropriate for neurologists who specialize in MS as well as other clinicians with a special interest or focus on this disease.

Chairs

Giancarlo Comi

Department of Neurology
Institute of Experimental Neurology
Vita-Salute San Raffaele University
Milan, Italy

Hans-Peter Hartung

Department of Neurology
Heinrich-Heine-University
Düsseldorf, Germany

Fred D. Lublin

Corinne Goldsmith Dickinson Center
for Multiple Sclerosis
Mount Sinai School of Medicine
New York, NY, USA

This live educational course is endorsed by ECTRIMS
(European Committee for Treatment and Research In Multiple Sclerosis).

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AND RESEARCH IN MULTIPLE SCLEROSIS

CME Provider

EXCEMED is a non profit foundation dedicated, since the last four decades, to the development of high-quality medical education programmes all over the world.

EXCEMED adheres to the guidelines and standards of the European Accreditation Council for Continuing Medical Education (EACCME®) which states that continuing medical education must be balanced, independent, objective, and scientifically rigorous.



Continuing medical education

The EXCEMED **“MS Academia: Multiple sclerosis advanced course”** is accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) to provide the following CME activity for medical specialists. The EACCME® is an institution of the European Union of Medical Specialists (UEMS), www.uems.net

The CME **“MS Academia: Multiple sclerosis advanced course”** held on 13 September 2016 in London, UK, is designated for a maximum of **6 (six) hours** of European external CME credits (ECMEC). Each medical specialist should claim only those credits that he/she actually spent in the educational activity.

Through an agreement between the European Union of Medical Specialists and the American Medical Association, physicians may convert EACCME® credits to an equivalent number of AMA PRA Category 1 Credits™. Information on the process to convert EACCME® credit to AMA credit can be found at www.ama-assn.org/go/internationalcme.

Live educational activities, occurring outside of Canada, recognized by the UEMS-EACCME for ECMEC credits are deemed to be Accredited Group Learning Activities (Section 1) as defined by the Maintenance of Certification Program of The Royal College of Physicians and Surgeons of Canada.



EXCEMED adheres to the principles of the Good CME Practice group (gCMEp).



General information

This live educational course takes place at:

ExCeL Exhibition Centre

Royal Victoria Dock, 1 - Western Gateway
South Gallery
London, UK

Language

The official language of this live educational course is English.

CME Provider

EXCEMED - Excellence in Medical Education

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Programme

Programme

Tuesday, 13 September 2016

8.15 Opening and introduction
G. Comi (Italy) - H.P. Hartung (Germany) - F.D. Lublin (USA)

Session I Etiology and pathogenesis

Chairs: H.P. Hartung (Germany) - F.D. Lublin (USA)

- 8.30 L1: Genes**
J. Hillert (Sweden)
- 9.00 L2: Environmental factors and microbiota**
A. Ascherio (USA)
- 9.30 L3: Pathology**
W. Brück (Germany)
- 10.00 L4: Immunopathogenesis: the crosstalk between B and T cells**
A. Bar-Or (Canada)
- 10.30  Session discussion**
- 10.40 Coffee break**

Session II Diagnosis. Case based story session

Chairs: G. Comi (Italy) - F. D. Lublin (USA)

This session will propose a practice-based approach to the key elements of MS diagnosis. Presenters will offer actual examples from their own clinical experiences to effectively illuminate the most important diagnostic elements of MS.

- 11.00 CBS1: Diagnosis and differential diagnosis**
M. Tintoré (Spain)
- 11.30 CBS2: MRI in diagnosis and monitoring of MS and treatments**
M.A. Rocca (Italy)
- 12.00 CBS3: Neurophysiology in diagnosis and monitoring of MS**
L. Leocani (Italy)
- 12.30 L5: Assessment of treatment response**
R. Fox (USA)
- 13.00  Session discussion**
- 13.10 Lunch**

Session III Treatment

Chairs: H.P. Hartung (Germany) - G. Comi (Italy)

- 14.20 L6: Efficacy and safety of immunomodulators in RR MS**
M.S. Freedman (Canada)
- 14.50 L7: Efficacy and safety of immunosuppressants in RR MS**
G. Giovannoni (UK)
- 15.20 Coffee break**
- 15.40 L8: Treatment individualization and new treatment algorithms**
G. Comi (Italy)
- 16.10 L9: Pharmacological and non pharmacological approach to progressive MS**
A.J. Thompson (UK)
- 16.40 L10: Future therapies**
H.P. Hartung (Germany)
- 17.10  Session discussion**
- 17.20 PD: Treatment in Practice – Panel discussion**
G. Comi (Italy)
M. Freedman (Canada)
G. Giovannoni (UK)
F. Lublin (USA)
- 17.50 Concluding remarks**
- End of the course**

Legend: L : Lecture  : Discussion PD : Panel discussion CBS : Case based story

Disclosure of faculty relationships

EXCEMED adheres to guidelines of the European Accreditation Council for Continuing Medical Education (EACCME®) and all other professional organizations, as applicable, which state that programmes awarding continuing education credits must be balanced, independent, objective and scientifically rigorous. Investigative and other uses for pharmaceutical agents, medical devices and other products (other than those uses indicated in approved product labeling/package insert for the product) may be presented in the programme (which may reflect clinical experience, the professional literature or other clinical sources known to the presenter). We ask all presenters to provide participants with information about relationships with pharmaceutical or medical equipment companies that may have relevance to their lectures. This policy is not intended to exclude faculty who have relationships with such companies; it is only intended to inform participants of any potential conflicts so that participants may form their own judgements, based on full disclosure of the facts. Further, all opinions and recommendations presented during the programme and all programme-related materials neither imply an endorsement nor a recommendation on the part of EXCEMED. All presentations represent solely the independent views of the presenters/authors.

The following faculty provided information regarding significant commercial relationships and/or discussions of investigational or non-EMEA/FDA approved (off-label) uses of drugs:

Alberto Ascherio	Declared no potential conflict of interest.
Amit Bar-Or	Dr Bar-Or has participated as a speaker at meetings sponsored by, received consulting fees and/or received grant support from: Amplimmune, Bayhill Therapeutics, Berlex/Bayer, Biogen Idec, Diogenix, Eli-Lilly, Genentech, GlaxoSmithKline, Guthy-Jackson/GGF, Merck/EMD Serono, Medimmune, Mitsubishi Pharma, Novartis, Ono Pharma, Receptos, Roche, Sanofi-Genzyme, Teva Neuroscience, Wyeth.
Wolfgang Brück	Declared the receipt of grants and contracts from: Teva, Biogen, Genzyme, Novartis. He declared receipt of honoraria or consultation fees: Teva, Biogen, Genzyme, Novartis, Bayer, Merck. He declared to be member of a company advisory board, board of directors or other similar group: Teva, Biogen, Novartis
Giancarlo Comi	Declared the receipt of honoraria or consultation fees from: Excemed, Merck, Novartis, Teva, Sanofi, Genzyme, Biogen, Roche, Almirall, Chugai, Receptos, Forward Pharma.
Robert Fox	Declared the receipt of grants and contracts from: Biogen, Novartis. He declared receipt of honoraria or consultation fees from: Actelion, Mallinckrodt, Genentech, Biogen, Novartis, Teva, Xenoport.
Mark S. Freedman	Declared the receipt of honoraria or consultation fees from: Actelion, BayerHealthcare, BiogenIdec, Chugai, EMD Canada, Genzyme, Merck Serono, Novartis, Hoffman La-Roche, Sanofi-Aventis, Teva Canada Innovation. He declared to be member of a company advisory board, board of directors or other similar group: Actelion, BayerHealthcare, BiogenIdec, Hoffman La-Roche, Merck Serono, Novartis, Opexa, Sanofi-Aventis and the participation in a company sponsored speaker's bureau: Genzyme.
Gavin Giovannoni	Over the last 15 years Por. Giovannoni has received personal compensation for participating in Advisory Boards in relation to clinical trial design, trial steering committees and data and safety monitoring committees from: Abbvie, Bayer-Schering Healthcare, Biogen-Idec, Canbex, Eisai, Elan, Fiveprime, Genzyme, Genentech, Gsk, GW Pharma, Ironwood, Merck, Merck-Serono, Novartis, Pfizer, Roche, Sanofi-Aventis, Synthon BV, Teva, UCB Pharma and Vertex Pharmaceuticals.
Hans-Peter Hartung	Declared the receipt of honoraria or consultation fees from: Biogen, Novartis Opexa, Genzyme, Roche, Teva, Receptos, GeNeuro.
Jan Hillert	Declared the receipt of grants and contracts from: Biogen, Novartis, Genzyme. He also declared receipt of honoraria or consultation fees from: Biogen, Novartis, Teva, Genzyme and to be member of a company advisory board, board of directors or other similar group: Biogen, Genzyme.
Letizia Leocani	Declared the receipt of grants and contracts from: Research support - Merck Serono, Novartis. She declared to be member of a company advisory board, board of directors or other similar group: Biogen. She declared also benefit from a relationship with a commercial enterprise: travel support - Biogen, Almirall.

Fred D. Lublin	Declared the receipt of grants and contracts from: Biogen Idec, Novartis Pharmaceuticals Corp, Teva Neuroscience Inc., Genzyme, Sanofi, Celgene, Transparency Life Sciences, NIH, NMSS. He declared receipt of honoraria or consultation fees from: Bayer HealthCare Pharmaceuticals, Biogen Idec, EMD Serono Inc., Novartis, Teva Neuroscience, Actelion, Sanofi/Genzyme, Acorda, Questcor/Malincrodt, Roche/Genentech, MedImmune, Osmotica, Xenoport Receptos, Forward Pharma, Akros, TG Therapeutics, Abbvie, Toyama, Amgen, Medday, Atara Biotherapeutics. He declared to be member of a company advisory board, board of directors or other similar group: Multiple Sclerosis and Related Disorders. He declared takeholder in a company: Cognition Pharmaceuticals Inc.
Maria Assunta Rocca	Declared participation in a company sponsored speaker's bureau: Biogen-Idec, Novartis, Teva Neuro Sciences, Genzyme.
Alan J. Thompson	Declared the receipt of grants and contracts from: MS Society of GB&NI, Wellcome Trust, Eisai, Wolfson. He declared receipt of honoraria or consultation fees from: Biogen, Eisai, MedDay. He declared benefit from a relationship with a commercial enterprise: SAGE Publication-honorarium as Editor-in-Chief of Multiple Sclerosis Journal.
Mar Tintorè	Declared the receipt of grants and contracts from: Biogen and Novartis. She declared receipt of honoraria or consultation fees from: Almirall, Bayer, Biogen-Idec, Genzyme, Merck, Novartis, Sanofi Aventis, Roche, Teva. She declared to be member of a company advisory board, board of directors or other similar group: Biogen Idec, Genzyme, Novartis, Roche, Teva.

Biographies



Alberto Ascherio

Department of Epidemiology and Nutrition
Harvard School of Public Health
Harvard Medical School
Boston, MA, USA

Alberto Ascherio, MD, DrPH, is a Professor of Epidemiology and Nutrition at the Harvard T. H. Chan School of Public Health and a Professor of Medicine at the Harvard Medical School. Dr. Ascherio trained in internal medicine at the University of Milan, and subsequently practiced medicine and public health in Latin America and Africa. He completed his doctoral degree in epidemiology at the Harvard T. H. Chan School of Public Health. Dr. Ascherio's research is primarily devoted to finding the causes of multiple sclerosis (MS), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS). Since 1997, he has directed the investigation of neurodegenerative diseases in several large cohorts. Among the most notable discoveries to which he has contributed are the key roles of infection with the Epstein-Barr virus, vitamin D insufficiency, and cigarette smoking as risk factors for MS, the importance of vitamin D status as a determinant of MS progression, the role of caffeine consumption and urate as negative risk factors for PD and of urate elevation as a promising therapeutic strategy, and the identification of positive and negative environmental risk factors for ALS.



Amit Bar-Or

Neuroimmunology Unit
Montreal Neurology Institute
Montreal, Canada

Amit Bar-Or is a neurologist and Professor, Department of Neurology and Neurosurgery, McGill University and Associate Director of the Montreal Neurological Institute and Hospital (Translational), where he also serves as Director of the Experimental Therapeutics Program and Scientific Director of the Clinical Research Unit. His clinical focus is Multiple sclerosis and related conditions, in both adults and children, and he presently serves as President of the Canadian Network of MS Clinics (CNMSC). Dr. Bar-Or's Neuroimmunology lab examines mechanisms of immune regulation with particular focus on defining functionally distinct immune cell subsets and their roles in autoimmune diseases, as well as immune-glial and immune-neural interactions, and how such interactions contribute to injury and repair in the central nervous system (CNS). An overall emphasis is on translational and biomarker development work in humans, including deep immune-monitoring of well-characterized patient cohorts participating in experimental therapeutic trials. This combination allows for translation of basic lab discoveries to understanding and development of novel experimental therapies for patients with autoimmune and neurological diseases.

Dr. Bar-Or has received multiple accolades for his research, is a lecturer in great demand. He coordinates several multi-center national and international translational research initiatives and serves on the scientific boards of the Guthy-Jackson Greater-Good Foundation for NMO research and the Accelerated Cure Project, (ACP), and on the Boards and/or Scientific Advisories of the American Committee for Treatment in MS (ACTRIMS); The International Society for Neuroimmunology (ISNI) and the German National Kompetenz Network in Neuroimmunology. He is on the Steering Committee of the Immune Tolerance Network, serves as Chair of CME and member of the Education Committee of the Federation of Clinical Immunology Societies (FOCIS), and as member of several editorial boards including Neurology, and Clinical and Experimental Neuroimmunology.

Biographies



Wolfgang Brück

Institute of Neuropathology
University Medical Centre Göttingen
Georg-August-Universität
Göttingen, Germany

Wolfgang Brück has been Professor of Neuropathology and Director of the Department of Neuropathology at the University Medical Centre Göttingen, Germany, since 2002. In recent years he has also served as Dean of Research and Infrastructure in the Faculty of Medicine at Georg-August-University Göttingen. He received his medical degree from Johannes Gutenberg University Mainz, Germany, and attained his habilitation and *venia legendi* for neuropathology from Georg-August University Göttingen. Wolfgang Brück's research focuses on the immunopathology of multiple sclerosis (MS), in particular on mechanisms of degeneration (myelin, oligodendrocytes, axons neurons) and remyelination in MS lesions. One of the major results of his studies is the definition of different immunopathological subtypes of multiple sclerosis. In recent years, pediatric MS became a focus of his work. The studies in human tissue are paralleled by experimental studies in animal models of MS including autoimmune models in rodents and non-human primates as well as models of toxic demyelination/remyelination. Throughout his career, Professor Brück has been actively involved with numerous neurological and neuropathological societies and committees. He is also on the Scientific Advisory Board of the Cambridge Centre for Myelin Repair, University of Cambridge, UK, the Edinburgh Centre for Translational Research, UK, and The Myelin Project. Professor Brück has received various awards for his contributions to research in MS, including the Langheinrich Award for Multiple Sclerosis Research (2000), the Hans Heinrich Georg Queckenstedt Award for Multiple Sclerosis Research (2002), the HG Mertens Prize for Innovative Research in Neurology (2008), and the Kohn Memorial Lecture Prize from the British Society of Toxicological Pathology (2011). He has also authored numerous papers published in peer-reviewed journals, and is an editorial board member and regular reviewer for several scientific journals.



Giancarlo Comi

Department of Neurology
Institute of Experimental Neurology
Vita-Salute San Raffaele University
Milan, Italy

Giancarlo Comi is Professor of Neurology, Chairman of the Department of Neurology and Director of the Institute of Experimental Neurology at Vita-Salute San Raffaele University, Milan, Italy. He is also President of the European Charcot Foundation (ECF), a member of the Board of Administration of the Italian Multiple Sclerosis Foundation and of the Scientific Committee of Associazione Italiana Sclerosi Multipla, Co-Chair of the Scientific Steering Committee of the Progressive MS Alliance and a fellow of the European Academy of Neurology (EAN). He has served as a past president of the European Neurology Society, the Italian Society of Clinical Neurophysiology, and the Italian Society of Neurology. In recent years, Professor Comi has received the "Gh. Marinescu" honorary award from the Romanian Society of Neurology and has been awarded honorary memberships of the Russian Neurological Academic Society, the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), the European Neurological Society (ENS) and the Sociedad Espanola de Neurologia. He also received the Charcot Award for MS Research from the MS International Federation (MSIF) in 2015. Most recently, Professor Comi was awarded the Gold Medal of "Benemeranza Civica" from the City of Milan. Prof. Comi has authored and co-authored more than 1000 articles in peer-reviewed journals, and edited several books. He has been the invited speaker for more than 450 conferences, both nationally and internationally. He sits on the executive boards of various scientific associations and on the editorial boards of *Clinical Investigation*, *European Journal of Neurology* and *Multiple Sclerosis*. He is also the Associate Editor of the *Neurological Sciences*.



Robert Fox

Mellen Center for Multiple Sclerosis
Cleveland Clinic
Cleveland, OH, USA

Robert Fox is Staff Neurologist at the Mellen Center for Multiple Sclerosis and Vice-Chair for Research of the Neurological Institute, Cleveland Clinic. He received his medical degree from Johns Hopkins University, neurology training at the University of Pennsylvania, a master's degree in Clinical Research from Case Western Reserve University, and multiple sclerosis fellowship training at Cleveland Clinic. Dr. Fox's current research interests focus clinical trials in multiple sclerosis, innovative MRI techniques to evaluate tissue recovery after injury and the effects of MS treatments, as well as MS patient decision-making and tolerance to risk. He serves as an advisor for many clinical trials, including the principal investigator of the NIH-funded SPRINT-MS phase II trial of ibudilast in progressive MS. In addition, he serves as the Managing Director of the NARCOMS MS Patient Registry, which currently follows over 12,000 people with MS. Dr. Fox serves as a member of various advisory and review committees for the National MS Society (USA) and National Institutes of Health (USA), the General Advisory Council for the Cleveland Clinic Clinical Research Unit, the Editorial Board of *Neurology and Multiple Sclerosis Journal*, and as a consultant to the pharmaceutical industry.



Mark S. Freedman

Multiple Sclerosis Research Unit
The Ottawa Hospital
Ottawa, Canada

Mark Freedman is Professor of Medicine (Neurology) at the University of Ottawa, Senior Scientist at the Ottawa Hospital Research Institute and Director of the Multiple Sclerosis Research Unit at the Ottawa Hospital-General Campus. His extensive research includes molecular neurochemistry, cellular immunology, and clinical studies in MS. His basic science interest concerns immune mechanisms of damage in MS, with a particular interest in the role of the innate immune system such as gamma-delta T-cells. His main clinical interests are cell-based therapies for MS. He was the lead investigator of the Canadian Bone Marrow Transplant Study in MS and he co-heads an international study of mesenchymal stem cells for the treatment of MS. He is the current Treasurer of ACTRIMS.

Biographies



Gavin Giovannoni

Department of Neurology, Institute of Cell and Molecular Science
Queen Mary University London & Barts and The London NHS Trust
London, UK

Gavin Giovannoni was appointed to the Chair of Neurology, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London and the Department of Neurology, Barts and The London NHS Trust in November 2006. In September 2008 he took over as the Neuroscience and Trauma Centre Lead in the Blizard Institute. Gavin did his undergraduate medical training at the University of the Witwatersrand, South Africa, where he graduated cum laude in 1987. He moved to the Institute of Neurology, University College, Queen Square, London in 1993 after completing his specialist training in neurology in South Africa. After three years as a clinical research fellow, under Professor Ed Thompson, and then two years as the Scarfe Lecturer, working for Professor W. Ian McDonald, he was awarded a PhD in immunology from the University of London in 1998. He was appointed as a Clinical Senior Lecturer, Royal Free and University College Medical School, in 1998 and moved back to Institute of Neurology, Queen Square in 1999. He was promoted to Reader in Neuroimmunology in 2004. His clinical interests are multiple sclerosis and other inflammatory disorders of the central nervous system. He is particularly interested in clinical issues related to optimising MS disease modifying therapies. His current research is focused on Epstein Barr virus as a possible cause of multiple sclerosis, defining the "multiple sclerosis endophenotype", multiple sclerosis related neurodegeneration, multiple sclerosis biomarker discovery, multiple sclerosis clinical outcomes and immune tolerance strategies. His team focus on translational research and therefore have an active clinical trial programme.



Hans-Peter Hartung

Department of Neurology
Heinrich-Heine-University
Düsseldorf, Germany

Hans-Peter Hartung is currently chair of the Department of Neurology at Heinrich Heine University Düsseldorf, a position he has held since 2001, and since 2013 director of the Center for Neuropsychiatry. He is in charge of two busy inpatient departments with a total of 100 beds including supraregional comprehensive stroke unit. Professor Hartung's clinical and translational research interests are in the field of basic and clinical neuroimmunology and in particular multiple sclerosis and immune neuropathies. He has authored or co-authored more than 900 articles in peer-reviewed journals, one hundred book chapters and edited nine books. He oversees the various research activities (clinical and preclinical) in his department that relate to Parkinson's and movement disorders incl deep brain stimulation, stroke, neuromuscular disorders, neuro-HIV and infectious diseases, spinal cord injury, repair strategies in CNS and PNS. He has been involved as member of the Steering Committee in numerous international multi-centre therapeutic phase 2 and 3 trials in multiple sclerosis, Guillain-Barré Syndrome and CIDP. He was President of ECTRIMS and serves amongst others on the executive boards of the European Charcot Foundation (treasurer), the International Society of Neuroimmunology, European School of Neuroimmunology, Peripheral Nerve Society, WHO Working Group on Multiple Sclerosis, GBS Foundation International, the Medical Advisory Board of the International (MSIF) and the German MS Society, and the US NMS Society and ECTRIMS clinical trials committee, and member of the management groups of the EAN panels on general neurology and multiple sclerosis. He was member of the executive committee of the European Neurological Society and member of the teaching course committee of the European Federation of Neurological Societies. He is/ was also member of the Editorial Board of a number of international journals including *Annals of Neurology*, *Nature Reviews Neurology*, *Current Opinion in Neurology*, *European Neurology*, *Journal of Neuroimmunology*, *Journal of Neuroinflammation* (Associate Editor), *Journal of Neurology*, *Journal of Neurology Neurosurgery Psychiatry*, *Neurorehabilitation and Neural Repair* (Associate Editor), *Open Access Neurology*, *Frontiers Immunology*, *Frontiers Neurology* (Chief Specialty Editor), *Muscle Nerve* and others.



Jan Hillert

Department of Clinical Neuroscience
Karolinska Institutet
Stockholm, Sweden

Jan Hillert has been Professor of Neurology at the Karolinska Institute, Stockholm, Sweden, since 2001, and in 2010 was appointed Chairman of the Department of Clinical Neuroscience. Professor Hillert has led a multiple sclerosis (MS) clinic for over 10 years and is founding chair of the Swedish Multiple Sclerosis Registry, which contains information on 15,000 MS patients. He is actively engaged in several MS clinical trials and has published 240 peer-reviewed papers. Professor Hillert's research primarily focuses on the genetic aspects of MS and has contributed to the discovery of several MS genes. Additional research interests include immunology and treatment aspects of MS, including treatment-induced antibodies. Current research efforts focus on translational epidemiology, integrating clinical, genetic, environmental, and public registry data both nationally and internationally.



Letizia Leocani

Institute of Experimental Neurology
University Vita-Salute IRCCS
San Raffaele Hospital
Milan, Italy

Letizia Leocani is Associate Professor of Neurology at San Raffaele University and Supervisor of the Experimental Neurophysiology Unit and of Magnetic IntraCerebral Stimulation center. She had a PhD in Human Physiology and she has been Research Fellow at the Human Motor Control Section of the National Institutes of Health in Bethesda-USA. She is Co-Chair of the Clinical Neurophysiology scientific panel of the European Academy of Neurology. Her fields of interest involve translational validation of electrophysiological and OCT markers of neurological diseases and of treatment using non invasive brain stimulation.

Biographies



Fred D. Lublin

Corinne Goldsmith Dickinson Center for Multiple Sclerosis
Icahn School of Medicine at Mount Sinai
New York, NY, USA

Fred D. Lublin, M.D. is the Saunders Family Professor of Neurology at The Icahn School of Medicine at Mount Sinai and Director of the Corinne Goldsmith Dickinson Center for Multiple Sclerosis at that institution. As a neuroimmunologist, Dr. Lublin has a special interest in immune functions and abnormalities affecting the nervous system. He has been involved in both basic science and clinical research. He and his colleagues were among the first in the country involved with studies of Interferon beta-1b, which was approved by the Food & Drug Administration in 1993 to treat the relapsing-remitting form of Multiple Sclerosis. He is currently involved with several new clinical research protocols on promising agents for treating various aspects of MS. He was chairman of the National MS Society (USA) advisory committee on clinical trials of new drugs in Multiple Sclerosis and the National Multiple Sclerosis Society's Research Programs Advisory Committee. He was a member of the National MS Society National Board of Directors. He is immediate past Chair of the New York City/Southern New York Chapter of NMSS Clinical Advisory Committee. He is a member of the International Medical & Scientific Board of the Multiple Sclerosis International Federation. Dr. Lublin and his colleagues at the National MS Society have re-defined the clinical course definitions of MS, updated in 2014. He has chaired a task force on the ethics of placebo-controlled trials in MS. Dr. Lublin is a member of the international panel that periodically redefines the diagnostic criteria for MS. Dr. Lublin is co-chair of the National Institute of Neurological Diseases and Stroke MS Common Data Element committee and a member of their steering committee. He is a member of the WHO Advisory Group for the Revision of ICD-10 Diseases of the Nervous System working group on demyelinating diseases of the central nervous system. He is a Co-Chief Editor of the journal *Multiple Sclerosis and Related Disorders*. Dr. Lublin has published numerous scientific articles and belongs to many professional societies and advisory boards. Dr. Lublin has served as a consultant to the National Institutes of Health and to many pharmaceutical/biotech companies in all phases of new drug development and in preparation for presentation to the FDA and their advisory panels. He was the Principal Investigator of the NIH-sponsored multicenter Combination Therapy study in Multiple Sclerosis.



Maria Assunta Rocca

Neuroimaging Research Unit, Institute of Experimental Neurology
Division of Neuroscience, San Raffaele Scientific Institute
Vita-Salute San Raffaele University
Milan, Italy

Maria A. Rocca took her Graduation in Medicine in 1996 and her Post-Degree Graduation in Neurology in 2002. Dr. Rocca is currently Head of the "Neuroimaging of CNS White Matter Unit", Department of Neurology, Institute of Experimental Neurology, Scientific Institute Ospedale San Raffaele, Milan, Italy. Her activity is mainly focused on the application of structural and functional MR-based techniques to improve the understanding of central nervous system function and dysfunction in healthy individuals and diseased people, particularly patients with multiple sclerosis (MS) and other white matter disorders. Dr. Rocca is currently conducting and coordinating several national and international projects in adult and paediatric populations. She is also extensively applying advanced methods of analysis in an attempt to improve the understanding of the role of the brain's functional and structural plasticity in the different phases of MS, and the influence of pharmacological and rehabilitative interventions on brain reorganization. She is a member of various national and international scientific societies and, in some of them, covers or is covering institutional roles (MAGNIMS, EAN, Neuroimaging Study Group of the Italian Neurological Society, AMPC of the ISMRM). She has also coordinated the MRI acquisition and analysis of several large-scale international MRI-monitored trials of MS. Dr. Rocca is author or co-author of more than 350 papers published in peer-reviewed journals and of 40 book chapters. She is also a reviewer of several international scientific journals and for many governmental organisations and private foundations. She is the recipient of several national and international awards for her scientific work and her roles as a speaker and/or chairperson at more than 300 international congresses. Dr. Rocca is a Non-Tenured Professor at Università Vita-Salute San Raffaele, Milan, Italy.



Alan J. Thompson

Department of Brain Repair and Rehabilitation
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London, UK

Alan J. Thompson is Dean of the Faculty of Brain Sciences at University College London, Garfield Weston Professor of Clinical Neurology and Neurorehabilitation at the UCL Institute of Neurology, a consultant neurologist at the National Hospital for Neurology and Neurosurgery, Queen Square, and Chair of the Neuroscience Academic Medical Centre, UCLP Academic Health Sciences Centre. His main area of expertise is in the diagnosis, evaluation, and management of the progressive forms of multiple sclerosis, and focusing on the pathological mechanisms that underpin neurological disability and recovery. He has published extensively in high-impact journals. A further focus is neurorehabilitation. As Dean of UCL Faculty of Brain Sciences, he leads the strategic development of comprehensive programmes of research in dementia and mental health. Professor Thompson is Chair of the Scientific Committee of the International Progressive MS Alliance, an Emeritus Senior Investigator for the National Institute for Health Research, Editor-in-Chief for *Multiple Sclerosis Journal*, and a Guarantor of Brain. He received his undergraduate and postgraduate degrees from Trinity College Dublin, and an honorary doctorate from Hasselt University, Belgium.



Mar Tintoré

Multiple Sclerosis Centre of Catalonia (Cemcat)
Neurology-Neuroimmunology Department
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Abstracts



L1. Genes

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The success within the past few years to identify genes of importance for complex diseases such as multiple sclerosis (MS) is remarkable. This is essentially explained by methodological advances in combining large clinical materials with high thru-put genotyping techniques. As a consequence, we now have a list of over 200 genes or chromosomal loci for which very strong evidence indicates an influence in determining the risk of an individual in developing MS. The prime objective with risk gene identification has since long been increased understanding of the early triggering events in MS pathogenesis. As such clues for disease mechanisms, the new list of MS genes may eventually prove to be immensely important. In brief, most of the new genes are of clear importance for inflammation, thus supporting the hypothesis that MS is primarily a disease with autoimmune features. This presentation will briefly address which some of these genes are and how we came to identify them.

The presentation will also cover the current level of understanding and potential usefulness of genetic markers in diagnosis, prognosis and treatment decisions, i.e. the extent to which these or similar markers are associated with characteristics other than onset of disease. In brief, we have a considerable way to go before genetics may add substantially to the diagnostic accuracy in the MS clinic. Likewise, genetic markers have so far not enabled us to predict the course of our patients, but may be of some use if analysed in concert with other factors. Finally, there are already some examples of genetic factors influencing the response to treatment in autoimmune disorders, including MS.

In summary, the genomics mission in MS, expected to be completed within 5-10 years, has already proven to be a success. Hopefully, this will eventually be turned into practical consequences for patients and neurologists.



L2. Environmental factors and microbiota

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While genetic susceptibility explains the clustering of MS cases within families, the changes in MS risk that occur with migration can only be explained by changes in the environment. The strongest known risk factor is infection with the Epstein-Barr virus (EBV). MS is extremely rare in individuals who are not infected with EBV, but it has been shown in a longitudinal study that their MS risk increases sharply following EBV infection. As compared with uninfected individuals, the hazard of developing MS is at least 10 folds higher among individuals infected with EBV in childhood and over 20 folds higher among individuals infected in adolescence or later in life. Further, the antibody titer to the EBV nuclear antigen 1 is a strong marker of MS risk. Although the mechanisms underlying this association remain unclear, these data provide strong evidence of a causal relation between EBV infection and MS risk. Some aspects of the epidemiology of MS, however, are not explained by EBV, suggesting that either there are different EBV strains, with different propensity to cause MS, or other factors are also involved. In particular, there is increasing interest in the role of the gut microbiome. The possibility that variations in gut microbiome may contribute to MS risk is indirectly supported by the results of a recent longitudinal study in children at risk of type 1 diabetes, an autoimmune disease that shares some epidemiological features with MS, and by the results a few case-control investigations comparing the microbiome of individuals with MS with that of matched healthy controls, but results are still preliminary. Among other environmental risk factors, the most prominent is vitamin D insufficiency. An increased risk of MS in individuals with vitamin D insufficiency has been consistently observed in all longitudinal investigations, including studies examining vitamin D levels in utero or at birth with subsequent MS risk. Further, the causality of the relation between low vitamin D levels and MS risk is supported by the results of Mendelian randomization studies, and there is strong evidence that vitamin D insufficiency is a risk factor for conversion from CIS to MS and for MS progression. Ideally, the benefit of vitamin D supplementation for MS prevention should be supported by large randomized trials, but the ethical and logistic obstacles for preventive trials are formidable. Other preventable risk factors for MS include cigarette smoking and childhood obesity.



L3. Pathology

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Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system which leads to focal destruction of myelin, acute axonal damage/loss of axons and reactive astrogliosis in the white and grey matter. MS involves the entire central nervous system (CNS), including focal lesions in the white and grey matter as well as diffuse pathological changes the normal-appearing white and grey matter. White matter lesions differ in different disease stages and show variable involvement of the adaptive and innate immune system. In the cortical grey matter, three different lesion types are defined with subpial demyelination being the most frequent lesion type. Pathological changes occur also in the normal appearing white and grey matter including microglial activation as well as neuroaxonal damage.

The presentation discusses the pathological events occurring in the above mentioned three compartments including:

1. White matter lesion type in relapsing and progressive MS
2. Gray matter involvement (lesion types, neuronal pathology, meningeal inflammation)
3. Normal appearing brain tissue involvement (microglia activation, axonal and neuronal changes)

The major pathological differences between relapsing-remitting and progressive multiple sclerosis are described in detail as well as the main differential diagnoses of inflammatory demyelinating diseases.



L4. Immunopathogenesis: the crosstalk between B and T cells

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While MS has traditionally been thought of as principally a T cell-mediated disease, the substantial impact of selective B cell targeting on disease activity underscores key roles for B cells at least in the relapsing biology of MS. Of note, this contribution of B cells invokes important antibody-independent functions of B cells including their potential to act as either pro-inflammatory or anti-inflammatory mediators, thereby influencing disease-relevant T cell responses. Contrasting results of different treatments targeting B cells in patients (in spite of predictions of therapeutic benefits from animal models) call for a better understanding of the multiple roles that distinct human B cell responses likely play in MS. Most recently, the implication of a GM-CSF expressing subset of B cells in patients with MS points to a role of B cells in the activation of myeloid cells which, in turn, can induce pro-inflammatory T cell responses. The implications of such cascades of cellular immune interactions (B cell:Myeloid:T cell) in MS relapses are coming to the fore with growing interest also in their potential relevance to the CNS-compartmentalized processes influencing progressive (non-relapsing) disease.



CBS1. Diagnosis and differential diagnosis

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Diagnostic criteria for MS rely on the demonstration of CNS disease in space and time and in reasonable exclusion of other causes. Since McDonald 2001, in patients with a first attack, evidence for dissemination in space and time may be provided by MRI. The 2010 McDonald criteria selected the Magnims criteria for dissemination in space (DIS). DIS is defined as the presence of ≥ 1 asymptomatic T2 lesion(s) in at least two of four locations considered characteristic for MS in previous MRI criteria: juxtacortical, periventricular, infratentorial and spinal cord. These criteria highlighted the importance of lesion location for MS diagnosis. Controversies regarding the need to exclude the symptomatic lesion will be discussed. The presence of at least one asymptomatic gadolinium enhancing lesion or the presence of a new T2 irrespective of the timing of the new scan, qualifies for dissemination in time (DIT). In this setting, one single MRI performed at any time, demonstrating DIS and showing at least one or more asymptomatic gadolinium enhancing would be sufficient to diagnose MS. Although many studies have already shown the importance of CSF study in the diagnosis and differential diagnosis of MS, the presence of oligoclonal bands has not been included in the diagnosis algorithm. These criteria have been adapted to other populations such as patients with primary progressive MS or patients with paediatric MS. An overview of new directions for the future will be considered. Clinical cases to illustrate differential diagnoses will be presented.



CBS2. MRI in diagnosis and monitoring of MS and treatments

Maria Assunta Rocca

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Measures derived from conventional magnetic resonance imaging (MRI), including the number of active lesions, as well as the overall burden of T2-hyperintense and T1-hypointense lesions, and brain volume, have clear advantages over clinical assessment, including that they are more objective and have an increased sensitivity to multiple sclerosis (MS) related changes. For these reasons, conventional MRI has been incorporated into the diagnostic workup of patients with clinically isolated syndromes who are at risk of developing MS, and it is always recommended in patients with definite MS to monitor the course of the disease. Even though no standardised guidelines exist, follow-up brain MRI is advised whenever new diagnostic questions arise or new neurological symptoms develop, especially if suggestive of comorbid conditions. Patients about to start a new treatment or to change treatment should undergo a brain MRI scan. This MRI scan should then be repeated after 6 and 12 months to assess the effectiveness of the treatment regimen. In addition, conventional MRI-derived end-points have been used as primary and secondary outcome measures for monitoring MS clinical trials. The rationale for using conventional MRI scans as surrogates for clinical outcomes is that the efficacy of a treatment in reducing relapses can be predicted at a trial level by its capacity to reduce active MRI lesions. In this context, the most widely used conventional MRI measures are those reflecting disease activity (new or enlarged T2 lesion counts, enhancing and new gadolinium-enhancing lesion counts, enhancing lesion volume measurement) and accumulated disease burden (T2 lesion load assessment). In the near future, it is likely that novel MR markers of MS evolution will be offered by non-conventional techniques and ultra-high field scanners.

References:

1. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, Fujihara K, Havrdova E, Hutchinson M, Kappos L, Lublin FD, Montalban X, O'Connor P, Sandberg-Wollheim M, Thompson AJ, Waubant E, Weinshenker B, Wolinsky JS. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol* 2011;**69**:292-302.
2. Barkhof F, Simon JH, Fazekas F, Rovaris M, Kappos L, de Stefano N, Polman CH, Petkau J, Radue EW, Sormani MP, Li DK, O'Connor P, Montalban X, Miller DH, Filippi M. MRI monitoring of immunomodulation in relapse-onset multiple sclerosis trials. *Nat Rev Neurol* 2011;**8**:13-21.
3. Enzinger C, Barkhof F, Ciccarelli O, Filippi M, Kappos L, Rocca MA, Ropele S, Rovira A, Schneider T, de Stefano N, Vrenken H, Wheeler-Kingshott C, Wuerfel J, Fazekas F; MAGNIMS study group. Nonconventional MRI and microstructural cerebral changes in multiple sclerosis. *Nat Rev Neurol* 2015;**11**:676-86.
4. Wattjes MP, Rovira A, Miller D, Yousry TA, Sormani MP, de Stefano MP, Tintoré M, Auger C, Tur C, Filippi M, Rocca MA, Fazekas F, Kappos L, Polman C, Frederik Barkhof, Xavier Montalban; MAGNIMS study group. Evidence-based guidelines: MAGNIMS consensus guidelines on the use of MRI in multiple sclerosis--establishing disease prognosis and monitoring patients. *Nat Rev Neurol* 2015;**11**:597-606.



CBS3. Neurophysiology in diagnosis and monitoring of MS

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In Multiple Sclerosis (MS), the underlying pathology may precede by years the clinical presentation. Demyelination and neurodegeneration lead to accumulation or progression of disability, although may be countered by functional reorganization, together with some level of remyelination and neuroregeneration. Indeed, early MS disease course is dependent on the balance between demyelination and remyelination, with the clinical manifestation determined by the degree of plasticity offsetting the effect of damage. Although the pathogenesis of demyelination has been well described, the cellular and molecular mechanisms of neurodegeneration are not fully understood. Among the major factors, ion channel expression and redistribution, together with neuroprotective pathways counteracting oxidative stress and mitochondrial dysfunction have been identified¹ Neurophysiological methods, mainly evoked potentials, are currently used for the assessment of functional consequences of demyelination, remyelination and axonal loss occurring in the course of the disease, as well as in pre-clinical testing. The functional information provided by evoked potentials accounts for their correlation with disease severity and point to their possible role as paraclinical measure for monitoring disease progression. In particular, they can help assessing the functional impact of the disease on central sensorimotor and cognitive networks affected by MS, and may reveal subclinical lesions^{2,3}. Furthermore, they also provide some prediction on the future evolution of disability, consistently with the hypothesis that early demyelination may prompt future neuronal loss, as shown in longitudinal studies³. If further validated, neurophysiological methods may have a role in the early identification of patients who are more likely to develop future disability and for whom a closer clinical monitoring of treatment response is necessary. Finally, the possibility to demonstrate improved conduction through evoked potentials can represent a key feature in the assessment of efficacy of novel therapeutic approaches targeting remyelination.

References:

1. Friesse MA, Schattling B, Fugger L. Mechanisms of neurodegeneration and axonal dysfunction in multiple sclerosis. *Nat Rev Neurol* 2014;**10**:225–38.
2. Leocani L, Comi G. Neurophysiological markers. *Neurol Sci.* 2008;**29** Suppl 2:S218–21.
3. Leocani L, Comi G. Clinical neurophysiology of multiple sclerosis. *Handb Clin Neurol.* 2014;**122**:671–9.



L5. Assessment of treatment response

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After starting a disease modifying therapy, it is important to consider the goals of treatment so that efficacy can be appropriately assessed. Since there are many available DMTs, identifying a therapy with sub-optimal response is important so that patients can move on to an alternative therapy. Since current therapies are anti-inflammatory, assessment of subsequent clinical relapses and new or active lesions on MRI are both helpful outcomes for assessing the anti-inflammatory effect of MS disease modifying therapies (DMT). Most therapies take 3-6 months to become effective, so active inflammation before six months often does not lead to change in treatment. New lesions on MRI during DMT treatment have been associated with progressive disability in the long-term, which illustrates the utility of follow-up MRIs to assess efficacy. Progressive disability can be seen from either active inflammation (for example, residual injury from a clinical relapse) or from transition into progressive MS. The current DMTs have much less efficacy in slowing the gradual progression of disability that is seen in progressive MS. "No Evidence of Disease Activity" (NEDA) has been proposed as a useful outcome metric to assess efficacy of DMTs. The inclusion of gradually progressive disability in many definitions of NEDA may confuse the assessment of the anti-inflammatory activity of a DMT. Nonetheless, assessing for inflammation (clinical relapse or new/active MRI lesions) is an important component of the long-term care of MS patients.



L6. Efficacy and safety of immunomodulators in RR MS

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Immunomodulators were the first proven therapies shown to alter the natural history of relapsing MS. They have a proven safety record that is unmatched compared with more contemporary therapies, that spans nearly three decades. Some of the studies designed to show their efficacy when they were approved for treatment would today be considered to be inferior. In fact, the very first agent to be approved only added MRI as an afterthought and another agent focused only on relapses, showing no clear effect on disease progression and completely omitted the use of MRI. Despite this, compared to more contemporary treatments, the effect size was so great on relapse reduction with the immunomodulators that it exceeds even the placebo rate of more recent studies, making it very difficult to compare efficacy. Nevertheless, most of these immunomodulators have been re-tested in more contemporary studies as either an active or direct comparator to a newer agent and they continue to show benefit.

Despite their long and exalted safety record, with only rare reported concerns, they have one quality that puts them in disfavor – they require to be injected. Some newer therapies also need to be injected, though less frequently and at times intravenously. Advances in the delivery techniques have helped ease the discomfort, but many patients still prefer the simplest form of treatment such as a pill, even though such an agent may pose greater toxicity. A virtue that is becoming increasingly evident is that immunomodulators can be used in any sequence, either before or after any newer therapy with complete confidence that there will be no undue toxicity. In fact, they can even be given in conjunction with newer treatments and may even generate a synergistic response.

Many of the newer therapies are plagued with side effects and toxicities never noted with immunomodulators, especially infections. This has been attributed to the immunosuppressive nature of the various treatments, something that has never been attributed to the immunomodulators. It is true that they are not effective in all patients, but the same can be said of all contemporary therapies. With few exceptions (e.g. alemtuzumab, ocrelizumab) there has been a general lack of head to head trials proving succinctly that newer treatments are more efficacious than immunomodulators. Therefore immunomodulation should remain as a main mode of controlling early relapsing disease safely for the long term.



L7. Efficacy and safety of immunosuppressants in RR MS

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Multiple sclerosis (MS) is the most common non-traumatic disabling condition to afflict young adults. Although the prognosis of MS is highly variable, given sufficient time the majority of people with MS will become disabled. In the case of established MS disease-modifying therapies (DMTs) the long-term impact of these therapies on MS prognosis is not fully defined, but appears promising. In general DMTs can be classified as being immunomodulatory or immunosuppressive. The problem associated with using immunosuppressive therapies is that they come with greater known risks as well as undefined longterm risks. Chemotherapy induced premature ovarian failure and accelerated disease progression, steroid-induced osteoporosis and avascular necrosis, mitoxantrone-related leukaemia and cardiomyopathy, natalizumab-associated progressive multifocal leukoencephalopathy (PML), alemtuzumab-associated autoimmune diseases, opportunistic infections and possibly treatment-related malignancies, fingolimod associated PRES, macular oedema, cardiac conduction abnormalities and possibly sudden death. How do we balance the risks of these therapies with their potential long-term benefits? In this talk I will review licensed immunosuppressive DMTs and provide strategies for de-risking these therapies for people with MS. In addition, the talk will stress the importance of education and the role of the professional patient in helping make the right decisions regarding individualised treatment plans.



L8. Treatment individualization and new treatment algorithms

Giancarlo Comi

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Current disease-modifying therapies for multiple sclerosis (MS) include interferon (IFN) beta (subcutaneous [sc] and intramuscular [im]) glatiramer acetate, mitoxantrone, and natalizumab, are characterized by specific safety and efficacy profile. These therapies have demonstrated clear efficacy in clinical trials and in postmarketing studies; however the full response on long term is rare. This opens the requirement of alternative therapies in order to achieve the goal of obtaining full control of the disease. Fingolimod has been recently approved by Regulatory Authorities and other potential new treatments are in different phases of development. The availability of multiple therapeutic options permits the ambitious target of a full control of disease activity in multiple sclerosis. MS evolution is quite variable from patient to patient with possibility of a very aggressive course from the onset.

Early and accurate assessments may help to identify patients who require more aggressive therapeutic options. The definition of individual prognostic factor with the history of previous treatments will contribute to define the best candidate therapy for a given patient at a specific time of disease evolution. In the future, it may become possible to use also pharmacogenomic information to individualize treatment. Recent studies have confirmed the association between glypican 5 gene polymorphisms and response to IFN-beta treatment. Close monitoring of the response to treatment with clinical biomarkers will be fundamental in order to allow rapid shift from a treatment to another. Patient adherence to prescribed treatment is hugely variable and can influence decision-making. An assessment of each patient's benefit-to-risk preferences may also help to identify those patients who are willing to accept additional risks in exchange for potentially greater clinical efficacy.



L9. Pharmacological and non pharmacological approach to progressive MS

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Progressive multiple sclerosis (PMS) leads to the gradual accumulation of disability and results from diffuse immune mechanisms and neurodegeneration¹. Approximately 15% of patients begin with a progressive disease course from onset, termed primary progressive MS (PPMS), while around 70% develop progression 10–15 years after an initial relapsing-remitting (RR) course, termed secondary progressive MS (SPMS). Given the global prevalence of MS, estimated at 2.3 million in 2013, around 1.3 million people have progressive MS.

The gradually worsening disability in PPMS and SPMS most often relates to motor impairment with a pattern suggesting a myelopathy but progressive hemiparesis, ataxia, visual dysfunction, or cognitive impairment also occurs. While the onset of progression commonly occurs at 40–50 years in both groups, SPMS follows an initial RR phase. Patients with PPMS have an equal gender balance, while SPMS more commonly affects women. The current consensus is that PPMS is biologically part of the MS spectrum, and the clinical, imaging, and pathological differences between PPMS and SPMS are relative rather than absolute.

The hallmark of progression is the gradual accumulation of disability for a minimum of 12 months, independent of relapses. In primary progressive MS, this is the presenting pattern whereas in secondary progressive MS it follows a period of relapses and remissions and diagnosis is usually made retrospectively. In PPMS few and smaller lesions are seen on MRI with less enhancement than RRMS. However, the same imaging criteria are used for all forms of MS to provide evidence for dissemination in space in the 2010 McDonald diagnostic criteria. In SPMS, there tends to be expansion of existing MRI lesions rather than new lesions. Extensive grey matter involvement is seen in both forms of progressive MS.

Effective therapies for PMS that prevent worsening, reverse damage, and restore function represent a major unmet need and many of the agents which have been successful in RRMS such as Glatiramer Acetate, Fingolimod and Natalizumab, have failed to show efficacy in PMS. However, the recent positive phase III study of Ocrelizumab in PPMS has introduced new therapeutic optimism. Other positive studies, including a Phase II trial of simvastatin and a trial of Biotin have reinforced that view. Although there are still relatively few trials in PMS, new trials designs focusing on neuroprotective agents are now well underway.

Over and above these specific interventions, the management of the increasing disability and wide-range of complex interacting symptoms in PMS, falls to pharmacologic treatments for these symptoms² together with restorative and rehabilitation approaches. There is some evidence to suggest that exercise, incorporating endurance or resistance training, is feasible and beneficial in PMS. The need to raise the profile of PMS and improve the lot of those affected, by reducing the time to deliver new treatments form the mission statement of the newly established Progressive MS Alliance³ - a global alliance of MS Societies, academia and industry which has already had a useful impact.

References:

1. Ontaneda D, Thompson AJ, Fox RJ, Cohen JA Progressive multiple sclerosis: prospects for disease therapy, repair and restoration of function. *Lancet* (in press)
2. Thompson AJ, Toosy AT, Ciccarelli O. Pharmacological management of symptoms in multiple sclerosis: current approaches and future directions. *Lancet Neurol* 2010; **9**(12): 1182–99
3. Fox RJ, Thompson A, Baker D, *et al.* Setting a research agenda for progressive multiple sclerosis: the International Collaborative on Progressive MS. *Mult Scler J* 2012; **18**: 1534–40



L10. Future therapies

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Abstract not in hand at the time of printing.

NOTES



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