3rd Annual Meeting of the Lupus Academy

Abstract Book

Hotel Maritim
Berlin
Germany
7–9th March 2014

LupusAcademy
Communicate. Educate. Treat.

European Accreditation Council for Continuing Medical Education (EACCME) Accreditation

The 3rd Annual Meeting of the Lupus Academy 2014 is accredited by the European Accreditation Council for Continuing Medical Education (EACCME) Event Code: 10336, and is designated for a maximum of 10 European CME credits (ECMECs). Each medical specialist should claim only those credits that he/she actually spent in the educational activity. The EACCME is an institution of the European Union of Medical Specialists (UEMS), www.uems.net.

Delegates from Europe

EACCME is an institution of the European Union of Medical Specialists (UEMS) and operates by reciprocal agreement for recognising CME credits across Europe. More information can be found at www.uems.net.

Delegates from USA

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.

Delegates from Canada

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Delegates from other countries

CME accreditation by EACCME and ECMECs are recognised internationally by many national authorities across the globe. Please check with your local authority to confirm its validity for your purposes.

Meeting organisation

This meeting has been developed and presented by Lupus Academy under the control of the Course Director and Steering Committee Chair, Professor Ronald van Vollenhoven, Professor and Chief, Unit for Clinical Therapy Research, Inflammatory Diseases (ClinTRID), Karolinska Institute, Sweden, Secretariat support provided by Adevez, and the CME compliance and fulfilment overseen by European CME Forum.

European CME Forum

Financial supporters

Lupus Academy has received financial support by means of independent educational grants from GSK and UCB, neither company has had any influence over the development or presentation of any aspect of this meeting.

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Welcome

Dear Friends and Colleagues,

We are delighted to welcome you to the 3rd Annual Meeting of The Lupus Academy, which we hope will be one of the most thought-provoking and fulfilling meetings you will attend this year.

Now in its third year, the Lupus Academy continues to grow in its commitment to providing high quality and clinically relevant education that will support you in your strive for better patient outcomes in SLE. This Annual Meeting, which has full Continuing Medical Education (CME) accreditation, aims to provide cutting edge insights into advances in global research and clinical practice in lupus and allied diseases. Delegate feedback from our 2nd Annual Meeting in Buenos Aires (2013) has guided us in our selection of topics and speakers to ensure that a top-class educational programme is provided.

The scientific component of this programme, developed by our Steering Committee of nine international experts in Lupus, is designed to create a highly interactive forum through which we can develop a logical approach to the management of lupus across the globe. It will give you the opportunity to meet world-leading clinicians and scientists and, through the sharing of clinical experience, develop your knowledge in this high-profile therapeutic area.

We sincerely hope that the meeting will provide you with new ideas for your clinical work, enhanced enthusiasm for collaborative research, and fruitful discussions with your colleagues who care for patients with lupus.

We look forward to meeting and talking with you here in Berlin.

With kind regards,

The Lupus Academy Steering Committee

Professor Ronald F. van Vollenhoven
Lupus Academy Chair (2014)

Professor Sandra V. Navarra and Professor Thomas Dörner
Lupus Academy Programme Directors and Co-chairs (2014)

Professor Zahir Amoura; Professor Ricard Cervera; Professor Andrea Doria; Professor David A. Isenberg, Professor Roger A. Levy; Professor Munther A. Khamashta

Mission Statement

The Lupus Academy is a long-term initiative committed to improving patient outcomes in SLE and allied diseases. By providing a highly interactive educational forum, the Lupus Academy is dedicated to sharing best clinical practice through the dissemination and discussion of cutting edge scientific and clinical research.

Programme

Friday 7th March

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18:30	Opening Address	Thomas Dörner (*Germany*)	
Keynote Lectures		*Moderator:* Ronald F. van Vollenhoven *(Sweden)*	
18:50	Low disease activity: a realistic therapeutic goal in SLE?	Eric Morand (*Australia*)	22
19:30	NETs: from infection to autoimmunity	Arturo Zychlinsky (*Germany*)	24
20:30	Welcome Dinner		

Saturday 8th March

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07:00–08:15	Breakfast		
Plenary I: Disease monitoring and management updates		*Moderator:* Thomas Dörner *(Germany)*	
08:30	Update on the diagnosis and management of neuropsychiatric SLE	Tom W.J. Huizinga *(The Netherlands)*	26
09:00	Update on the management of lupus nephritis	Bevra H. Hahn *(United States)*	28
09:30	Use of activity indices to assess clinical involvement in lupus	David A. Isenberg *(United Kingdom)*	30
10:00	Discussion		
10:30	Coffee		
Case Study Workshops (AM)			
11:00	*Moderator:* Murray B. Urowitz (*Canada*) Difficult lupus	Sandra V. Navarra (*Philippines*) & Eric Morand (*Australia*)	34
11:00	*Moderator:* Andrea Doria (*Italy*) Cardiovascular disease in SLE	Elisabet Svenungsson (*Sweden*) & Ian N. Bruce (*United Kingdom*)	36
11:00	*Moderator:* Roger A. Levy (*Brazil*) Bone health and vitamin D	Ricard Cervera (*Spain*) & Zahir Amoura (*France*)	38
11:00	*Moderator:* Bevra H. Hahn (*United States*) Lupus nephritis	Falk Hiepe (*Germany*) & Richard A. Furie (*United States*)	40
12:15	Lunch		

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Case Study Workshops (PM)			
13.30	*Moderator:* Murray B. Urowitz *(Canada)* Difficult lupus	Sandra V. Navarra *(Philippines)* & Eric Morand *(Australia)*	34
13.30	*Moderator:* Andrea Doria *(Italy)* Cardiovascular disease in SLE	Elisabet Svenungsson *(Sweden)* & Ian N. Bruce *(United Kingdom)*	36
13.30	*Moderator:* Roger A. Levy *(Brazil)* Bone health and vitamin D	Ricard Cervera *(Spain)* & Zahir Amoura *(France)*	38
13.30	*Moderator:* Bevra H. Hahn *(United States)* Lupus nephritis	Falk Hiepe *(Germany)* & Richard A. Furie *(United States)*	40
14.45	Coffee		
Plenary II: From basic science to clinical trials		*Moderator:* Munther A. Khamashta *(United Kingdom)*	
15.10	Interferon as a therapeutic target in SLE: why and how?	Lars Rönnblom *(Sweden)*	42
15.40	Doing small open trials in lupus: experiences with anti-TNF	Martin Aringer *(Germany)*	44
16.10	Is there a place for kinase blockers in SLE?	Liz Jury *(United Kingdom)*	46
17.00	Discussion		
17.30	**Close**		

Sunday 9th March

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07:00–08:15	Breakfast		
Plenary III: Challenges in treatment		*Moderator:* Roger A. Levy *(Brazil)*	
08.30	Treat-to-target in SLE	Marta Mosca *(Italy)*	48
09.15	Pregnancy issues in SLE	Rebecca Fischer-Betz *(Germany)*	50
09.45	Optimal management of hypercoagulability states in SLE	Roger A. Levy *(Brazil)*	52
10.15	Coffee		
Plenary IV: Treatment in 2014 and beyond		*Moderator:* Sandra V. Navarra *(Philippines)*	
10.45	Glucocorticoid-free treatment for lupus nephritis: a paradigm shift in the making?	Liz Lightstone *(United Kingdom)*	54
11.15	Optimising outcomes in SLE: best practice	Andrea Doria *(Italy)*	56
11.45	Biologics: the future of SLE treatment?	Ronald F. van Vollenhoven *(Sweden)*	58
12.15	Discussion		
12.30	**Summary and close**	Sandra V. Navarra *(Philippines)* Ronald F. van Vollenhoven *(Sweden)*	

Biographies

Professor Zahir Amoura, MD, MSc

Pitie-Salpetriere Hospital, Paris, France

Zahir Amoura is Professor of Internal Medicine at the French National Reference Centre for Systemic Lupus Erythematosus at Pitié-Salpêtrière Hospital, a role that he has held since 2003. In 2009, Professor Amoura became Head of the Department of Internal Medicine in the same institution. Professor Amoura completed his Paris Hospital Medical Internship in 1988, obtained a Master's degree in Immunopharmacology in 1989, and was subsequently awarded his MD (silver medal) in 1993 and his qualifying certification in internal medicine in 1994. Professor Amoura joined the Department of Internal Medicine at Pitié-Salpêtrière Hospital in 1995 as a Senior Lecturer and Senior Practitioner.

In the last 10 years, Professor Amoura has published over 321 peer-reviewed papers, of which 137 focused on the immunopathological features of lupus.

Disclosures

Grant/Research:
Amgen, AstraZeneca, Biogen Idec, Bristol Myers Squibb, Merck, Roche, Teva

Consultant/Advisor:
Bristol Myers Squibb, GlaxoSmithKline, UCB

Professor Amoura is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Professor Dr Martin Aringer, MD

Technical University of Dresden, Germany

Martin Aringer is Professor of Medicine (Rheumatology) and Chief of the Division of Rheumatology, University Medical Centre and Medical Faculty at the Technical University of Dresden. Professor Aringer received his MD from Vienna University in 1992. In the same year he began his Internal Medicine training at Vienna General Hospital, was board certified in 1999, and went on to train in rheumatology with Professor Josef Smolen at the Department of Rheumatology at the Medical University of Vienna. From 1997 to 1999 Professor Aringer received a Max Kade Postdoctoral Research Exchange Grant followed by a National Institutes of Health fellowship award to work in the laboratory of Dr John O'Shea at the National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, in Bethesda, Maryland, USA. Back in Vienna, he finished his Rheumatology training and in 2003 became Associate Professor of Rheumatology, Department of Rheumatology, Internal Medicine III, Medical University of Vienna. At the beginning of 2007, Professor Aringer was appointed to his current position as Professor of Medicine and Chief of the division of Rheumatology at the Technical University of Dresden.

Professor Aringer's main scientific interests include systemic lupus erythematosus and other systemic autoimmune diseases, early arthritis, and cellular and clinical aspects of cytokines and cytokine signal transduction. He is author of 115 publications, 24 book chapters and editor of three books. Professor Aringer is married and father of two boys.

Disclosures

Grant/Research:
Centocor

Consultant/Advisor:
AbbVie, MSD, Pfizer

Speakers' Bureau:
AbbVie, MSD, Pfizer, UCB

Professor Ian N. Bruce, MD, FRCP

University of Manchester, United Kingdom

Disclosures

Grant/Research:
Genzyme, GlaxoSmithKline, Human Genome Sciences, Roche, UCB

Consultant/Advisor:
GlaxoSmithKline, MedImmune, Pfizer, Roche, UCB

Speakers' Bureau:
GlaxoSmithKline, MedImmune, Pfizer, Roche, UCB

Ian Bruce is a National Institute of Health Research (NIHR) Senior Investigator and Professor of Rheumatology at the Arthritis Research UK Centre for Epidemiology, Institute of Inflammation and Repair, University of Manchester. He is Director of The NIHR Manchester Wellcome Trust Clinical Research Facility. Professor Bruce qualified in medicine from Queen's University Belfast in 1988 and gained his MRCP in 1991. He trained in medicine and rheumatology in Northern Ireland and completed his MD thesis on the pathogenesis of systemic vasculitis in 1995. He was the Geoff Carr Lupus Fellow at the University of Toronto, before moving to Manchester in 1998 as an NHS consultant, transferring to the University in 2003.

Professor Bruce is on the Editorial Board of the journal *Lupus Science & Medicine*. He is a Chair of the Systemic Lupus International Collaborating Clinics (SLICC) and a member of the British Isles Lupus Assessment Group. Professor Bruce participates in a number of national and international multicentre studies that are seeking to refine our understanding of systemic lupus erythematosus (SLE). He leads a Cardiovascular Research Group and is joint Principal Investigator on the Norfolk Arthritis Registry (NOAR), Cardiovascular Sub-study. He also serves on Data Safety Steering Committees in several commercial and academic clinical trials and contributes to the British Society for Rheumatology Biologics Registry Control Consortium.

Professor Bruce's major research focus is on the association between inflammatory rheumatic diseases and premature atherosclerosis/coronary heart disease. In particular, his focus is on SLE and rheumatoid arthritis. He has published 148 papers in his field.

Professor Ricard Cervera, MD, PhD, FRCP

Hospital Clínic, Barcelona, Catalonia, Spain

Disclosures

Consultant/Advisor:
Eli Lilly, GlaxoSmithKline, MedImmune, UCB

Professor Cervera is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Ricard Cervera is Head of the Department of Autoimmune Diseases (which he co-founded in 1995), at Hospital Clínic, Barcelona. He is also Group Leader of the Research Group on Systemic Autoimmune Diseases at the Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) and Professor at the University of Barcelona where he coordinates the Master's on Autoimmune Diseases. He qualified in medicine in 1983 from the University of Barcelona and received his PhD in 1988 for his thesis on anticardiolipin antibodies. He spent 2 years at the Lupus Research Unit at The Rayne Institute, St Thomas' Hospital, London.

Professor Cervera is an Associate Editor of the journal *Lupus Science & Medicine* and is on the Editorial Boards of 20 medical journals. He is coordinator of the European Forum on Antiphospholipid Antibodies and of the European Working Party on Systemic Lupus Erythematosus (SLE) (Euro-Lupus Group). He is Chairman of the Medical Advisory Board of the Catalan Association of Lupus Patients and Medical Advisor to Lupus Europe. He chaired the 6th and 8th International Congress on Autoimmunity, the 1st and 2nd Latin-American Congresses on Autoimmunity, the 5th Meeting of the European Forum on Antiphospholipid Antibodies and the 8th European Lupus Congress.

Professor Cervera's research interests include clinical and epidemiological aspects of systemic autoimmune diseases, particularly SLE and antiphospholipid syndrome, with special focus on its 'catastrophic' variant. He has presented over 300 invited lectures and published more than 800 scientific papers (H-factor, 57), including original articles at the *New England Journal of Medicine, The Lancet, Annals of Rheumatic Diseases, Arthritis & Rheumatism, American Journal of Medicine* and *Medicine* (Baltimore). He is co-Editor of 25 books, including 'The Antiphospholipid Syndrome', 'Vascular Manifestations of Systemic Autoimmune Diseases' and 'Diagnostic Criteria in Autoimmune Diseases'.

Biographies

Professor Andrea Doria, MD

University of Padova, Italy

Disclosures

Consultant/Advisor:
GlaxoSmithKline
Speakers' Bureau:
GlaxoSmithKline

Professor Doria is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Andrea Doria is Associate Professor of Rheumatology, Director of the Academic Postgraduate School of Rheumatology and Head of the Unit of Connective Tissue Disease and Rare Rheumatic Diseases, School of Medicine, University of Padova. Professor Doria received his medical degree and qualification in rheumatology from the University of Padova. He currently is a Council member of Italian Society of Rheumatology (SIR) and he was Council member of SIR (2007–2010) and of Italian College of Rheumatology (CRO) (1999–2005). He is also a member of American College of Rheumatology (ACR).

Professor Doria has organised over 10 international conferences on autoimmunity and was involved as "expert" in the European League Against Rheumatism (EULAR) Standing Committee for the development of clinical and therapeutic recommendations: (1) EULAR recommendations for the management of systemic lupus erythematosus (SLE)—Assessment of the SLE patient (2008–2009); (2) EULAR recommendations for the management of SLE Part II—Neuropsychiatric disease (2008–2009); (3) Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis (2012).

Professor Doria is on the Editorial Boards of several rheumatology and immunology journals, including *Lupus, Autoimmunity, Clinical and Experimental Rheumatology, Autoimmunity Reviews, Journal of Autoimmunity, Experimental Biology and Medicine, Rheumatology Reports, Journal Autoimmunity Highlights and Reumatismo* (the official journal of SIR). He has authored over 250 ISI publications on SLE and other connective tissue diseases. These include clinical studies describing new manifestations or subgroups of autoimmune disorders, prognostic risk factors, diagnostic tests and therapeutic interventions as well as immunochemical studies that evaluate autoantibodies, epitopes and complementary epitopes of autoantigens. In addition, he has authored and co-authored three books, over 90 book chapters and conference proceedings, and over 200 abstracts to national and international conferences.

Professor Doria has a longstanding experience in the clinical management of patients with connective tissue disease. The unit in which he works is a 3rd referral rheumatology centre (within Italy) for the diagnosis and management of patients affected with systemic connective tissue diseases. In addition, he has expertise in the management and follow-up of pregnant patients with systemic rheumatic diseases. Professor Doria has also trained over 30 students in rheumatology.

Professor Dr Thomas Dörner, MD

Charité University Hospitals, Berlin, Germany

Disclosures

Grant/Research:
Roche/Chugai, Sanofi, UCB

Consultant/Advisor:
Eli Lilly, Roche/Chugai, Takeda, UCB

Speakers' Bureau:
Roche/Chugai, Takeda, UCB

Professor Dörner is Programme Director and co-Chair of the Lupus Academy (2014) and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Thomas Dörner is a board certified Rheumatologist and Professor of Rheumatology and Hemostaseology at Charité University Hospitals, Berlin, and group leader at the German Research Center of Rheumatology, Berlin (DRFZ). He qualified in medicine in 1990 at Charité University Hospitals, Berlin, and received his board certification in internal medicine in 1995 before undertaking a postdoctoral fellowship at the University of Texas, Southwestern Medical Center at Dallas, where he researched delineating molecular aspects of the B-cell receptor gene usage in autoimmune diseases.

Professor Dörner has received a number of international and national awards, including the Senior Scholar Award of the American College of Rheumatology, the H Schultze Award of the German League Against Rheumatism, Randy Fischer Prize for Excellence in flow cytometry and the Schoen Award of the German Society of Rheumatology.

Professor Dörner has served as a member of Editorial Boards of leading journals in rheumatology and immunology, including *Arthritis & Rheumatism, Arthritis Research & Therapy, Annals of the Rheumatic Diseases, Global Arthritis Research Network (GARN), Current Reviews in Rheumatology, Brazilian Journal of Rheumatology, European Journal of Immunology, Lupus Science & Medicine* and *Rheumatology Reviews*.

Professor Dörner has led various clinical trials of rheumatic diseases, including systemic lupus erythematosus, Sjögren's syndrome, rheumatoid arthritis and seronegative spondyloarthropathies. His research interests focus on the characterisation of disturbances of humoral autoimmunity and abnormalities of B cell subsets in the blood *versus* tissue (lupus, neonatal lupus syndromes, Sjögren's syndrome), exploring innovative therapeutic approaches with particular focus on B-cell directed therapy as well as improving diagnostic tools in autoimmune diseases.

Dr Rebecca Fischer-Betz, MD

Heinrich-Heine-University, Düsseldorf, Germany

Disclosures

Consultant/Advisor:
Abbott, AbbVie, Actelion, Chugai, GlaxoSmithKline, MSD, Pfizer, Roche, Sobi, UCB

Rebecca Fischer-Betz is Deputy Director of the Department of Rheumatology at Heinrich-Heine-University Hospital in Düsseldorf. Following Medical School at Westfalian-Wilhelms-University Münster, Germany and Boston University, USA, she took up a residency at Westfalian-Wilhelms-University Hospital and at Heinrich-Heine-University Hospital in the departments of gastroenterology, endocrinology and rheumatology before being appointed to her current position. Dr Fischer-Betz has also attended a programme in clinical effectiveness at the Harvard School of Public Health, USA.

Dr Fischer-Betz sits on the Board of the German Society of Rheumatology, is Chair of the Pregnancy in Rheumatic Disease Study Group, and is on the Steering Committee of the European League Against Rheumatism (EULAR) task force for "Points to consider for use of antirheumatic drugs before pregnancy and during pregnancy and lactation". She is also on the Editorial Boards for the *Zeitschrift für Rheumatologie* and *Lupus Science & Medicine*.

Dr Fischer-Betz's primary research interests include systemic lupus erythematosus and pregnancy in autoimmune diseases.

Biographies

Professor Richard A. Furie, MD

Hofstra North Shore-LIJ School of Medicine, New York, United States

Richard Furie is Chief of the Division of Rheumatology and Allergy-Clinical Immunology at North Shore-Long Island Jewish (LIJ) Health System, New York, and Professor of Medicine at the Hofstra North Shore-LIJ School of Medicine. He is a Rheumatologist whose activities for the last several decades have focused on patient care, physician education and clinical research in the area of antirheumatic drug development. He directs The Program in Novel Therapeutics—the Health System's clinical research programme in musculoskeletal disease. He also directs the hospital's Systemic Lupus Erythematosus (SLE) and Autoimmune Disease Treatment Center, which has become internationally recognised for its role in the development of new therapies for SLE.

Regarded as one the senior Rheumatologists in the New York metropolitan area, Professor Furie has been on the Boards of Directors of the local chapters of the Arthritis Foundation and the Lupus Alliance of America and is a member of the Medical-Scientific Advisory Council of the Lupus Foundation of America as well as its Lupus News Editorial Board. He also is on the Medical and Scientific Advisory Board of the SLE Foundation as well as the Alliance for Lupus Research Scientific Advisory Board. Professor Furie has served on many committees of the American College of Rheumatology and is currently serving on the College's Board of Directors.

Professor Furie's interests focus on the management of patients with lupus and antiphospholipid antibody syndrome. He is particularly active in clinical research aimed at advancing new therapies for patients with rheumatic diseases.

Disclosures

Grant/Research:
Anthera, AstraZeneca, Biogen Idec, Bristol Myers Squibb, Boehringer-Ingelheim, Celgene, Dynavax, Eli Lilly, Exagen, Genentech, GlaxoSmithKline, MedImmune, NIAID, Novartis, Novo Nordisk, Pfizer, Questcor, Rigel, UCB

Consultant/Advisor:
Amgen, Anthera, Biogen Idec, Bristol Myers Squibb, Celgene, Eisai, Eli Lilly, EMD Serono, Exagen, GlaxoSmithKline, MedImmune, Merck, Novartis, Novo Nordisk, Onyx, Pfizer, Questcor, Rigel, Takeda, UCB

Professor Bevra H. Hahn, MD

University of California, Los Angeles, United States

Bevra Hahn is Professor of Medicine (Emeritus, recalled for part time work) in the Division of Rheumatology at the University of California, Los Angeles (UCLA). She received her medical degree and Rheumatology training at Johns Hopkins University School of Medicine in Baltimore, Maryland. She was Chief of Rheumatology at UCLA for 30 years.

Professor Hahn has published research in clinical investigations and basic studies of immune tolerance (including the invention of a tolerizing peptide) and T cell biology as they apply to systemic lupus erythematosus. For these works she and her colleagues have received several awards, including the Carol-Nachman International Award for Rheumatology Research, awards from the British Society for Rheumatology and the Dutch Society for Rheumatology, the James Klinenberg Medal of the US Arthritis Foundation, an award from the Canadian Rheumatism Society, and the Gold Medal of the American College of Rheumatology (ACR). Professor Hahn was President of the ACR (1999–2000). She is co-Editor, with Daniel Wallace, of the 'Dubois' Lupus Erythematosus' textbook and is first author of the ACR guidelines for the management of lupus nephritis. She continues to work in clinical and basic research devoted to the study of SLE.

Disclosures

Grant/Research:
Teva

Consultant/Advisor:
Eisas, Eli Lilly, GlaxoSmithKline

Professor Dr Falk Hiepe, MD

Charité University Hospitals, Berlin, Germany

Disclosures

Grant/Research:
Deutsche Forschungsgemeinschaft

Consultant/Advisor:
Actelion, Bristol Myers Squibb, Cephalon, Eli Lilly, GlaxoSmithKline, Merck, Novo Nordisk, Roche, UCB

Falk Hiepe is Professor of Medicine and Deputy Director of the Department of Rheumatology and Clinical Immunology, Charité University Hospitals, Berlin. He is also Group Leader of the Autoimmunology Group, German Rheumatism Research Center, Berlin—an Institute of the Leibniz Association. Professor Hiepe received his MD from the Faculty of Medicine, Humboldt University, Berlin (1976), he went on to receive certification in internal medicine in 1983 and completed his postdoctoral work at the same university in 1988. In 1987, Professor Hiepe was visiting Professor at the Second Department of Medicine at Teikyo University and Department of Medicine and Physical Therapy at the University of Tokyo, Japan. In 1995 he took a research fellowship at the W.M. Keck Autoimmune Disease Center, The Scripps Research Institute, La Jolla, California.

Professor Hiepe holds several awards, including research awards from Charité Hospital (1992) and the Wolfgang Schultze Foundation (2004). He sits on the IUIS/WHO/AF/CDC Committee for the Standardization of Autoantibodies and the International Advisory Board of Modern Rheumatology for The Japan Rheumatism Association. He is Editor of the journal *Autoimmunity Highlights*.

Professor Hiepe's research interests include systemic autoimmune diseases, diagnostic and pathogenic relevance of autoantibodies, biomarkers, the role of long-lived plasma cells in autoimmunity, B cells and plasma cells as therapeutic targets in autoimmune diseases and innovative cell therapies, including autologous haematopoietic stem cell transplantation in refractory autoimmune diseases.

Professor Dr Tom W.J. Huizinga, MD, PhD

Leiden University Medical Center, The Netherlands

Disclosures

None

Tom Huizinga is Chairman of Rheumatology at Leiden University Medical Center, the oldest university in the Netherlands. He received his MD from the University of Amsterdam in 1986, after which he joined the Army as a blood transfusion specialist from 1986 to 1987. Professor Huizinga went on to receive his PhD *cum laude* on the biochemical and functional characterisation of Fc-gamma receptors. In 1990 he worked as a postdoctoral researcher in Dartmouth Medical School, New Hampshire, USA and in 1991 he was ratified as an immunologist and started his training in internal medicine. He finished his rheumatology training in 1997.

Between 1994 and 1999 Professor Huizinga received a fellowship of the Royal Academy of Arts and Sciences to study: "Regulation of TNFα-production in rheumatoid arthritis". In 1998 he became Associate Professor in Rheumatology and has served as full Professor since 2000. In 2006 he became Chairman of Rheumatology at Leiden University Medical Center.

Professor Huizinga has received a number of prizes for his work including the Boerhaave prize for outstanding contributions to Immunology and the Howard and Martha Holley Award: American College of Rheumatology (ACR) Southeast Regional Meeting "Cytokine polymorphisms in disease".

He has served on a number of committees, including the Annual Meeting Planning Committee of the ACR (2000–2003) and the Annual Meeting Planning Committee of the European League Against Rheumatism (EULAR) (2004–2007).

Professor Huizinga serves on the board of the Dutch Society for Rheumatology as well as on a number of journal Editorial Boards including *Genes and Immunity, International Journal of Advances in Rheumatology, Joint Bone Spine Revue du Rheumatism* International Edition, *Annals of Rheumatic Diseases, PLOS Medicine* and *Current Rheumatology Reviews*.

He has co-authored over 500 peer-reviewed articles, (H-factor 66) and he has written over 10 book chapters.

Biographies

Professor David A. Isenberg, MD, FRCP, FAMS

University College London, United Kingdom

David Isenberg is the Arthritis Research UK Diamond Jubilee Professor of Rheumatology at University College London (UCL). He graduated from St. Bartholomew's Hospital, London, in 1973, and trained in general medicine, rheumatology, neurology, psychiatry and gastroenterology, becoming a Research Fellow at UCL/The Middlesex Hospital in 1979. He was awarded his MD in 1984, based on his studies of myositis. During a year of research at Tufts University, Boston, he became interested in autoantibody structure/function and origin. He was appointed Consultant Rheumatologist in 1984, Professor in 1991 and became the arc Diamond Jubilee Chair of Rheumatology at UCL in 1996. He has fellowships of both the Royal College of Physicians and the Academy of Medical Sciences.

Professor Isenberg is on the Editorial Boards of five journals, including the *Journal of Rheumatology*. He is Chair of the British Isles Lupus Assessment Group (BILAG) and Lupus UK's Research Committee and was Chair of the Systemic Lupus International Collaborating Clinics group (SLICC) (1998–2003). During the past 20 years, Professor Isenberg has undertaken many roles at Arthritis Research UK and currently sits on the Executive Board. He is past-President of the British Society for Rheumatology (2004–2006) and he chaired the Society's Biologics Register Committee for 5 years (2006–2011). Professor Isenberg is the 2010 recipient of the Evelyn V. Hess Prize from the Lupus Foundation of America for his contribution to lupus research and treatment. He has authored over 500 original articles, 250 reviews/chapters and 16 books, many on topics related to Lupus.

Professor Isenberg's principal clinical interests are the development of disease activity and damage assessment tools in patients with lupus. His specialist interest is autoimmune rheumatic diseases, notably systemic lupus erythematosus, Sjögren's syndrome, myositis and antiphospholipid antibody syndrome.

Disclosures

Professor Isenberg does not accept personal honoraria but asks that an equivalent sum is given to an arthritis charity of his choosing.

Professor Isenberg is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Dr Elizabeth Jury, PhD

University College London, United Kingdom

Elizabeth Jury is a Principal Research Associate and Arthritis Research UK Career Progression Fellow at the Centre for Rheumatology Research, University College London. Dr Jury started her career at St Bartholomew's Hospital developing the Immunopathology service specialising in the diagnosis of autoimmunity, immunodeficiency and immunophenotyping. She moved to a more research-focused career joining Professor David Isenberg's team in 2000 and now leads her own research group. Dr Jury's work has developed new areas of research into signalling abnormalities in T and B cells from patients with systemic lupus erythematosus (SLE) and has made a significant contribution towards understanding the nature of these abnormalities and how they relate to disease pathogenesis. The main focus of her research is to understand the role of plasma membrane and cellular and serum lipids on immune cell activation. Dr Jury was one of the first to identify defects in plasma membrane lipids in T cells from patients with SLE and her recent work has identified a defect in lipid metabolism that results in increased levels of a particular type of lipid called glycosphingolipids (GSLs). Furthermore, she found inhibiting GSL biosynthesis using a clinically approved inhibitor restored correct lipid metabolism and corrected functional defects in T cells from SLE patients. This work provides an emerging picture of a possible underlying defect in lipid metabolism in SLE patients and supports further the hypothesis that targeting lipid biosynthesis pathways could be a novel therapeutic strategy for SLE.

Disclosures

None

Professor Munther A. Khamashta, MD, PhD, FRCP

St. Thomas' Hospital, London, United Kingdom

Disclosures

Consultant/Advisor:
GlaxoSmithKline, Inova, MedImmune, UCB

Professor Khamashta is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Munther Khamashta is Professor, Consultant Physician and Director of The Graham Hughes Lupus Research Laboratory at St. Thomas' Hospital, London, and he runs a large lupus pregnancy clinic. He studied medicine in Barcelona and internal medicine in Madrid, Spain, where he developed an interest in connective tissue diseases and received his PhD. He was awarded the MRCP in 1999 and FRCP in 2002. He joined the Lupus Unit in London 25 years ago and has been instrumental in developing it into an internationally recognised tertiary centre receiving referrals from all over the United Kingdom.

Professor Khamashta has served on the Editorial Boards of many journals, including *Clinical & Experimental Rheumatology, Lupus* and *Current Rheumatology Reviews*. He is a member of several professional societies, including the International Society of Internal Medicine, the American College of Rheumatology and the Spanish Society of Rheumatology. He is a member of the Steering Committee of the International Board on the Study of Antiphospholipid Antibodies and of the Steering Committee of the International Advisory Board for Systemic Lupus Erythematosus. He has received several international awards for his work in lupus, including The European League Against Rheumatism (EULAR) and International League Against Rheumatism (ILAR) prizes.

Professor Khamashta has a strong research interest in lupus and connective tissue diseases, with a special interest in pregnancy and antiphospholipid syndrome. He has published extensively in lupus, Hughes' syndrome and related areas, with more than 600 original papers.

Biographies

Professor Roger A. Levy, MD, PhD

The State University of Rio de Janeiro, Brazil

Disclosures

Research Grants:
Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ), Coordenação de Aperfeiçoamento de Pessoal de Nivel Superior (CAPES), and Federico Foundation, Liechtenstein

Consultant/Advisor:
AbbVie, AstraZeneca, GlaxoSmithKline, Janssen, Pfizer

Speakers' Bureau:
AbbVie, GlaxoSmithKline, Janssen, Roche

Professor Levy is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Roger Levy is Associate Professor of Rheumatology at The State University of Rio de Janeiro. Graduating from medical school at the Federal University of Rio de Janeiro in 1986, he subsequently completed a fellowship programme at the Hospital for Special Surgery, Cornell Medical College, New York in 1989 and received his PhD in Biological Sciences from the Biophysics Institute – Immunology, at the Federal University of Rio de Janeiro in 1994. That same year he joined the staff at State University Hospital and started the pregnancy clinic dedicated to patients with rheumatic conditions.

Professor Levy holds positions on a number of Editorial Boards including the journals of *Arthritis and Rheumatology, Arthritis Care and Research, Clinical Rheumatology, Lupus, Lupus Science & Medicine, Seminars of Arthritis and Rheumatism, Rheumatology, Autoimmunity Reviews* and *The Brazilian Journal of Rheumatology* (of which he is a former Editor). He was the Scientific Director of the XXV Brazilian Congress of Rheumatology and chaired the 2nd Latin American Congress of Autoimmunity (Rio de Janeiro, 2006). Professor Levy is past-President of the Rio de Janeiro Rheumatology Society (2007–2008) and is currently the Scientific Director. He has coordinated the Vasculitis and Thrombophilias Committee of the Brazilian Society of Rheumatology since 2009 and chaired the extremely successful XIV International Antiphospholipid Congress (APLA) and IV Latin American Congress of Autoimmunity (LACA) that was held in Rio de Janeiro in September 2013 for almost 700 attendees.

Professor Levy's research is based around the clinical and immunologic aspects of systemic lupus erythematosus, antiphospholipid syndrome, Sjögren's syndrome and pregnancy in rheumatic patients. He has published 100 articles in medical journals, over 200 abstracts, two books, 20 book chapters and has lectured in many countries.

Dr Liz Lightstone, PhD, FRCP

Imperial College London, United Kingdom

Disclosures

Consultant/Advisor:
Anthera, Aspreva Pharmaceuticals, Biogen Idec, EMD Serono, Genentech, GlaxoSmithKline, MedImmune, Merck, Roche, Teva, Vifor

Liz Lightstone is a Reader in Renal Medicine in the Division of Immunology and Inflammation, Department of Medicine, Imperial College London, and an Honorary Consultant Renal Physician in the Imperial College Healthcare NHS Trust Renal and Transplant Centre (ICHNT RTC). After an undergraduate degree at Cambridge, she graduated in medicine from the University of London in 1983 and trained in nephrology at the Royal Postgraduate Medical School. She won a Medical Research Council (MRC) Training Fellowship in 1988 and undertook a PhD in immunology at University College London. This was followed by a MRC Clinician Scientist Fellowship at the Royal Postgraduate Medical School. She was appointed Senior Lecturer and Honorary Consultant Physician in 1995.

Dr Lightstone has major roles in undergraduate and postgraduate medicine at Imperial College, in particular as Director of the Academic Foundation programme within the North West Thames Foundation School. She is a member of the LUPUS UK Peer Review Panel. She was an elected member of the UK Renal Association Executive and remains active in the Renal Association Programme Planning group and Equal Opportunities Committee. She is on the EU executive of the Lupus Nephritis Trials Network, was an author on the 2012 European League Against Rheumatism (EULAR) recommendations for the treatment of lupus nephritis and regularly advises on the design of trials in lupus nephritis.

Dr Lightstone's research is now focused on Lupus Nephritis as well as Pregnancy in Women with Kidney Disease. Together with colleagues in the ICHNT RTC, she pioneered the use of steroid-minimising regimens in lupus nephritis. She is Chief Investigator on the planned international multicentre randomised RITUXILUP trial funded by Arthritis Research UK. She is particularly interested in developing better ways of predicting outcomes, not least by improving adherence to therapy. To this end she has established a new assay of hydroxychloroquine levels as a marker of adherence to therapy. She is also working on identifying urine biomarkers and histological features that better predict the outcome of lupus nephritis. She is the inaugural National Coordinator of the newly established Pregnancy and Chronic Kidney Disease—Rare Disease Group and has pioneered the use of tacrolimus in the treatment of lupus nephritis in pregnancy.

Her main clinical interests are in lupus nephritis (she jointly manages a combined renal/rheumatology lupus clinic following over 300 patients with lupus nephritis) and the management of women with kidney disease in pregnancy—she established and runs a renal obstetric clinic and a preconception counselling clinic.

Biographies

Professor Eric Morand, MBBS(Hons), PhD, FRACP

Monash University, Clayton, Melbourne, Australia

Disclosures

Grant/Research:
AbbVie, AstraZeneca, CSL, Eli Lilly, GlaxoSmithKline, UCB, Roche

Consultant/Advisor:
CSL, Eli Lilly, Roche

Speakers' Bureau:
AbbVie, Pfizer

Eric Morand is Director of Rheumatology at Monash Health, and Professor and Head of the Southern Clinical School, Faculty of Medicine, Nursing and Health Sciences at Monash University, Melbourne. Trained as a specialist physician in rheumatology in Australia and at the Royal National Hospital for Rheumatic Diseases UK, Professor Morand has led the rheumatic diseases group of the Monash Centre for Inflammatory Diseases since the mid-1990s.

Professor Morand is founder of the Lupus Clinic at Monash Health, which is home to Australia's largest longitudinally studied lupus cohort. His laboratory focusses on the effects of glucocorticoid-induced proteins on inflammation in systemic lupus erythematosus and rheumatoid arthritis.

He has held programme and project grants from the National Health and Medical Research Council, National Institutes of Health and Royal Australasian College of Physicians, and has served on the Council of the Australian Rheumatology Association and chaired its Scientific Program and Research Committee. He is also Chair of the AsiaPacific Lupus Collaboration, a regional group of lupus clinical investigators. He has published over 120 peer-reviewed publications, book chapters and patents.

Professor Marta Mosca, MD

University of Pisa, Italy

Disclosures

Consultant/Advisor:
GlaxoSmithKline, UCB

Speakers' Bureau:
Eli Lilly, GlaxoSmithKline, UCB

Marta Mosca is Associate Professor of Rheumatology at the Department of Internal Medicine, University of Pisa. Professor Mosca graduated from Medical School at the University of Pisa in 1992.

Professor Mosca's research interests are represented by systemic lupus erythematosus (SLE) and undifferentiated connective tissue diseases, with particular interest in clinimetrics. Recently she worked on the development of European League Against Rheumatism (EULAR) recommendations for monitoring SLE patients in clinical practice and observational studies", quality measures in SLE, and a core set of measures to be used in clinical practice to standardise patient care.

Professor Mosca's clinical activity includes the follow up of patients with connective tissue diseases at the Rheumatology Unit, where she runs the Lupus Clinic and the Pregnancy Clinic.

Professor Sandra V. Navarra, MD, FPCP, FPRA

University of Santo Tomas, Manila, Philippines

Disclosures

Consultant/Advisor:
Pfizer

Speakers' Bureau:
GlaxoSmithKline, Pfizer, Roche

Professor Navarra is Programme Director and co-Chair of the Lupus Academy (2014) and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Sandra Navarra is Professor and Head of Rheumatology at University of Santo Tomas and Consultant Rheumatologist at St. Luke's Medical Center in the Philippines. She served as Secretary-General, Head of the Education Committee, chaired the special interest group on systemic lupus erythematosus (SLE) of the Asia Pacific League of Associations for Rheumatology (APLAR) and was Associate Editor of the *International Journal of Rheumatic Diseases*. She is a past-President of the Philippine Rheumatology Association.

Professor Navarra co-founded the Arthritis Care and Research Foundation of the Philippines, where she is currently Scientific Programmes Director, and the Lupus Foundation of the Philippines where she has served as Medical Director. Currently President and CEO of the Rheumatology Educational Trust Foundation Inc. (RETFI), she is the prime mover of the Lupus Inspired Advocacy (LUISA) Project for lupus education and research, and the People Empowerment for Arthritis and Lupus (PEARL) Movement for lay education and medical assistance programmes.

Professor Navarra is an experienced clinical trials investigator and has published widely in the field of lupus and other rheumatic diseases. She is a well-known lecturer in a broad range of topics in rheumatology and has received several university and national awards for her contributions to education and research.

Professor Navarra has organised several national and regional educational meetings including the Ten Topics in Rheumatology—Asia (November 2009) and the first Asian Lupus Summit (November 2012), both held in Manila.

Professor Lars Rönnblom, MD, PhD

Uppsala University, Sweden

Disclosures

Consultant/Advisor:
UCB

Lars Rönnblom is Professor of Rheumatology at the Department of Medical Sciences, Uppsala University. He received his PhD in immunology in 1983 and board certification in internal medicine in 1989. He has been board certified Rheumatologist since 1994 and was appointed Professor of Rheumatology at Uppsala University in 2006. Professor Rönnblom is a Senior Consultant in Rheumatology and responsible for the lupus clinic at Uppsala University Hospital. He is group leader for the Rheumatology Section at the Department of Medical Sciences and coordinates the Swedish systemic lupus erythematosus (SLE) network.

Professor Rönnblom has received a number of awards for his research, including the Scandinavian Research Foundation/*Scandinavian Journal of Rheumatology* award for research in rheumatology, The Wyeth Prize for Clinical Research in Rheumatology and the Thuréus prize from The Royal Society of Science. He has served on a number of Editorial Boards and currently is an Associate Editor of *Lupus Science & Medicine*.

Professor Rönnblom has been working on the etiopathogenesis of SLE for more than 20 years and his main research focus is the role of the type I interferon system in the development of SLE and other systemic autoimmune diseases. He first described the mechanisms behind the activation of plasmacytoid dendritic cells and the increased type I interferon production in SLE. Professor Rönnblom's other research interests include the genetic background to disease susceptibility and clinical manifestations. His group have made seminal contributions to the identification of a number of risk genes of importance in SLE, including IRF5, TYK2, STAT4 and IRF8.

Biographies

Professor Elisabet Svenungsson, MD, PhD

The Karolinska Institute, Stockholm, Sweden

Disclosures

Consultant/Advisor:
GlaxoSmithKline, UCB
Stock/Shareholder:
Pfizer

Elisabet Svenungsson is Senior Consultant and Associate Professor of Rheumatology at Karolinska University Hospital/Karolinska Institute in Stockholm. She obtained her medical education at the Karolinska Institute and is a specialist in internal medicine and rheumatology. She has, for many years, been head of the inpatient rheumatology ward at Karolinska University Hospital. Her main clinical expertise is in systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS) and cardiovascular comorbidity associated with systemic autoimmune diseases. Professor Svenungsson is Principal Investigator of the Karolinska SLE cohort, which started in 1995 and presently comprises 500 SLE patients and matched population controls. She chairs the cardiovascular study group in The Swedish Society for Rheumatology.

Professor Svenungsson´s research is based on clinical studies of the systemic autoimmune diseases, mainly SLE, APS and systemic sclerosis. The main focus of her studies has been to understand why patients with autoimmune diseases are affected with premature cardiovascular diseases (CVD). She has, for many years, taken part in genetic studies of SLE and has recently demonstrated the importance of genetic susceptibility to SLE-related CVD.

Ongoing studies are focused on CVD, autoantibodies and genetics as well as on neurological and renal manifestations and quality of life issues. Recently, Professor Svenungsson has taken a more general research interest in the pathogenesis, sub-phenotypes and diagnostic entities of systemic autoimmunity.

Professor Murray B. Urowitz, MD

University of Toronto, Canada

Disclosures

Consultant/Advisor:
Eli Lilly, GlaxoSmithKline, UCB

Murray Urowitz is Professor of Medicine at the University of Toronto and Director of the Centre for Prognosis Studies in the Rheumatic Diseases and the University of Toronto and the Lupus Clinic at the Toronto Western Hospital. Professor Urowitz received his MD from the University of Toronto and completed his postgraduate training in rheumatology at the Johns Hopkins University, Baltimore and at the University of Toronto. He was a Staff Rheumatologist at the Wellesley Hospital in Toronto from 1974 to 1987 and Physician in Chief from 1987 to 1995. He has also been a Senior Staff Rheumatologist at the Toronto Western Hospital and Senior Scientist at the Toronto Western Research Institute since 1995.

Professor Urowitz established the University of Toronto Lupus Clinic and Lupus Databank Research Program in 1970. This extensive longitudinal database is one of the largest such databanks in the world with over 1800 patients and has allowed for numerous findings that have changed the way lupus is diagnosed and managed. His teaching excellence is exemplified by having won the outstanding clinical teacher award in the medical school for a remarkable eight times. He was the Associate Dean of Postgraduate Medical Education at the University of Toronto between 1995 and 2005. This lifelong commitment to medical education has resulted in him being the recipient of the Royal College of Physicians and Surgeons of Canada 2004 Duncan Graham Award.

Professor Urowitz is a founding member of the Ontario Lupus Association (now Lupus Ontario) and past-President of the Lupus Council of the American Rheumatology Association. He is a founding member of the Systemic Lupus International Collaborating Clinics (SLICC) group and currently directs the SLICC Registry for Atherosclerosis. In 1995 he was the recipient of the Distinguished Rheumatologist Award of the Canadian Rheumatology Association and in 2009 he was recipient of the Evelyn V. HESS Award for outstanding contributions to lupus research, awarded by the Lupus Foundation of America. In 2012 he was awarded a Queen Elizabeth Diamond Jubilee Medal (nominated by the Canadian Rheumatology Association) in recognition of his longstanding contributions to lupus research and his work in the field of rheumatology.

Professor Urowitz has published over 300 peer reviewed papers and 40 book chapters, and has supervised the training of over 100 fellows in rheumatology, mainly in systemic lupus erythematosus. He has been an invited speaker around the world.

Biographies

Professor Ronald F. van Vollenhoven, MD, PhD

The Karolinska Institute, Stockholm, Sweden

Disclosures

Research Grants:
AbbVie, Bristol Myers Squibb, GlaxoSmithKline, Pfizer, Roche, UCB
Consultant/Advisor:
AbbVie, Biotest, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Merck, Pfizer, Roche, UCB, Vertex

Professor van Vollenhoven is Chairman of the Lupus Academy (2014) and has been involved in the planning and development of the 3rd Annual Meeting programme and materials.

Ronald F. van Vollenhoven is Chief of the Unit for Clinical Therapy Research, Inflammatory Diseases (ClinTRID) at the Karolinska Institute and Chief of the Clinical Trials Unit in Rheumatology at Karolinska University Hospital, Stockholm.

He received his medical and PhD degrees from the University of Leiden in the Netherlands. After graduating in 1984 he pursued immunology research at Cornell Medical College in New York, followed by specialty training in Internal Medicine at the State University of New York at Stony Brook and a fellowship in Rheumatology at Stanford University in Palo Alto, following which he received American Board of Internal Medicine certification in both Internal Medicine and Rheumatology.

From 1993 to 1998 Professor van Vollenhoven held a faculty appointment as Assistant Professor of Medicine in the Division of Immunology and Rheumatology at Stanford University and from 1995 he was the Medical Services Chief and Fellowship Director in that division.

In 1998 Professor van Vollenhoven moved to Stockholm, Sweden, where he worked as a Senior Physician and Chief of the Clinical Trials Unit in the Department of Rheumatology at Karolinska University Hospital, and Associate Professor of Rheumatology. In 2010, he was appointed to his current position as Professor and Unit Chief at the Karolinska Institute.

Professor van Vollenhoven's research interests focus around the development and systematic evaluation of biologic and immunomodulatory treatments for the rheumatic diseases. With his co-workers, he has established the Stockholm registry for biologic therapies (the STURE database) for this purpose, which has supported research projects relating to clinical efficacy, pharmacology, outcomes and pharmacoeconomics. He has been Principal Investigator in many clinical trials of novel therapies in rheumatic diseases and has contributed to a number of important investigator-initiated trials including the recently published SWEFOT (Swedish Farmacotherapy) trial. He has published over 200 original papers, book chapters and reviews, he is editor of the textbook 'Targeted Treatment of the Rheumatic Diseases' and associate-Editor of 'Dubois' Lupus Erythematosus'. In 2004, Professor van Vollenhoven was awarded the Scandinavian Research Foundation Prize for excellence in clinical research in rheumatology and is an honorary member of several rheumatological societies. He is the Editor-in-Chief of *Lupus Science & Medicine*, member of many journal Editorial Boards, Chair of the Swedish Rheumatology Society Professors' Council and of the health economics working group HeraS, co-founder of the IRBIS registry for biologics in systemic lupus erythematosus, the CERERRA registries collaboration and the NORD-STAR collaboration for Nordic trials in the rheumatic diseases and is the initiator of the Treat-to-Target-in-SLE initiative. Professor van Vollenhoven lives just north of Stockholm with his wife and two children aged 18 and 14 years. Outside his professional life he is an avid classical pianist.

Professor Arturo Zychlinsky, PhD

Max Planck Institute for Infection Biology, Berlin, Germany

Disclosures

None

Arturo Zychlinsky is Director of the Department of Cellular Microbiology at the Max Planck Institute for Infection Biology, Berlin. He studied chemistry, bacteriology and parasitology at the Instituto Politécnico Nacional in Mexico City and received his PhD in immunology from the Rockefeller University, New York City. He performed his his postdoctoral studies in the lab of Philippe Sansonetti at the Institut Pasteur in Paris. From 1993 to 2001 he was a Professor at the Skirball Institute and Department of Microbiology at the New York University School of Medicine.

In addition to research on the inflammasome and the link between immunity and development, one main research line of the Zychlinsky lab is the role of neutrophils in immune defense. The Zychlinsky lab discovered neutrophil extracellular traps (NETs), a novel mechanism by neutrophils to fight pathogens. NETs are structures made of chromatin and specific proteins that are released from the neutrophil after a unique cell death programme. They allow neutrophils to trap and kill even large microorganisms such as fungi. However, NETs also may trigger autoimmune responses if their formation and removal is not properly regulated. The Zychlinsky lab showed that in some groups of patients with lupus, antibodies are made against NETs, preventing their efficient removal after an infection and resulting in autoimmune reactions. There is also strong evidence that in patients with lupus, both insufficient NET removal and excessive NET formation leads to an accumulation of NETs and exacerbation of the disease.

Abstracts

Keynote Lecture

Moderator: Professor Ronald F. van Vollenhoven (Sweden)

Professor Eric Morand, MBBS(Hons), PhD, FRACP
Monash University, Clayton, Melbourne, Australia

Low disease activity: a realistic therapeutic goal in SLE?

The use of empiric measures of effectiveness to drive physicians' decisions to adjust therapy was initially used in common conditions such as hypertension and diabetes mellitus. More recently, the application of such goal-based approaches, including the definition of a low disease activity state, has led to a paradigm shift in the treatment of rheumatoid arthritis (RA), which arose independent of the adoption of biologic therapies.[1] The low disease activity paradigm in RA is supported by studies demonstrating the impact of achieving this endpoint on long-term outcomes.

Patients with systemic lupus erythematosus (SLE) suffer a heterogeneous range of clinical manifestations. Clinical development and even fundamental research, such as the search for biomarkers, are impacted on by the difficulties inherent in quantifying such a heterogeneous disease. Measuring treatment response or defining a treatment goal potentially presents similar difficulties. Hence, there is no agreement on methods to define a goal of treatment in SLE, for use either in clinical trials or in clinical practice.

In order for a treat-to-target approach to be taken in SLE, definition and validation of a treatment target are required. A recently published definition of remission was met by less than 2% of patients, suggesting this definition is too stringent for routine use.[2] A definition of low disease activity, rather than remission, in SLE could be more feasible as a treatment target in clinical practice as well as an outcome measure in observational and interventional studies.

The AsiaPacific Lupus Collaboration (APLC) has recently generated a definition of 'lupus low disease activity state' (LLDAS), defined conceptually as 'a state which, if sustained, is associated with a low likelihood of adverse outcome'.[3] From 56 unique items, a definition of LLDAS comprising five disease activity and treatment variables was derived using two rounds of Delphi and nominal group techniques. The APLC has now begun a multicentre longitudinal study to validate this measure against outcomes including damage and death. Preliminary validation using retrospective analysis of longitudinal cohort data suggested this goal is achievable and is associated with significantly improved outcomes.[3] The results of this work will be reported when the study is complete.

Learning Objectives

At the end of the presentation, participants will be able to:

- Understand the application of treatment goals in diseases other than SLE.
- Know the difference between low disease activity and remission.
- Reach a view on the value of a low disease activity measure in SLE.
- Understand gaps in knowledge in regard to the definition of treatment goals in SLE.

References

1. Grigor C, Capell H, Stirling A, *et al*. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. *Lancet*. 2004 Jul 17–23;364(9430):263–9.

2. Urowitz MB, Feletar M, Bruce IN, *et al*. Prolonged remission in systemic lupus erythematosus. *J Rheumatol*. 2005 Aug;32(8):1467–72.

3. Morand EF, Franklyn K, Lau CS, *et al*. Consensus definition and preliminary validation of a low disease activity state in systemic lupus erythematosus. *Arthritis and Rheumatism*. 2013;65:S664–S5.

Notes

Abstracts

Keynote Lecture **Moderator:** Professor Ronald F. van Vollenhoven (Sweden)

Professor Arturo Zychlinsky, PhD
Max Planck Institute for Infection Biology, Berlin, Germany

NETs: from infection to autoimmunity

Neutrophils are one of the first lines of defence of the immune system against microbes. These cells kill microorganisms effectively by phagocytosis and by the formation of extracellular structures, called neutrophil extracellular traps (NETs). NETs are made of chromatin and specific neutrophil proteins, and are released after a unique cell death programme that requires the production of radical oxygen species and the relocation of neutrophil elastase to the nucleus.[1–4] NETs help limit and control infection and also can activate the acquired immune system. Thus, formation of NETs appears to be necessary for an efficient clearing of microbes but can also initiate and exacerbate autoimmune responses.[5]

Learning Objectives

At the end of the presentation, participants will be able to:

- Analyse the mechanism of NET formation.
- Recognise the evolutionary relevance of NETs.
- Understand the role of NETs in infections.
- Identify the potential role of NETs in autoimmune diseases.

References

1. Brinkmann V, Reichard U, Goosmann C, *et al*. A. Neutrophil extracellular traps kill bacteria. *Science*. 2004 Mar 5;303(5663):1532–5.

2. Brinkmann V, Zychlinsky A. Neutrophil extracellular traps: is immunity the second function of chromatin? *J Cell Biol*. 2012 Sep 3;198(5):773–83.

3. Amulic B, Cazalet C, Hayes GL, *et al*. Neutrophil function: from mechanisms to disease. *Annu Rev Immunol*. 2012;30:459–89.

4. Metzler KD, Fuchs TA, Nauseef WM, *et al*. Myeloperoxidase is required for neutrophil extracellular trap formation: implications for innate immunity. *Blood*. 2011 Jan 20;117(3):953–9.

5. Hakkim A, Fürnrohr BG, Amann K, *et al*. Impairment of neutrophil extracellular trap degradation is associated with lupus nephritis. *Proc Natl Acad Sci* USA. 2010 May 25;107(21):9813–8.

Notes

Abstracts

Plenary I: Disease monitoring and management updates **Moderator:** Professor Dr Thomas Dörner (Germany)

Professor Dr Tom W.J. Huizinga, MD, PhD
Leiden University Medical Center, The Netherlands

Update on the diagnosis and management of neuropsychiatric SLE

Neuropsychiatric systemic lupus erythematosus (NPSLE) can be divided in focal *versus* diffuse manifestations. The pathogenesis of focal manifestations is mediated via antibodies that interfere with coagulation, while diffuse manifestations are most likely caused via antibodies binding to brain tissue antigens. Although many antibodies that identify brain antigens have been recognised, no specific antigens are currently known, leading to lack of diagnostic serological support in clinical decision making.

An animal model of this last mechanism has been published with anti-NMDA antibodies.[1] This model shows that these antibodies can only mediate their detrimental effect if the blood brain barrier is damaged, allowing the antibodies to enter the brain. The relevance of anti-NMDA antibodies in humans is less clear, but associated studies support that similar mechanisms are operating in humans, leading to diffuse NPSLE.[2]

Pathology studies clearly show that complement activation is involved in clinical diffuse neuropsychological manifestations, even in areas of the brain where studies with 7Tesla magnetic resonance imaging (MRI) show no abnormalities.[3] In patients, the relevance of new MRI techniques like magnetisation transfer imaging also supports that diffuse brain involvement is leading to pathology. Interestingly, the presence of antiphospholipid antibodies is also associated with diffuse NPSLE, suggesting that a multiple hit model of antiphospholipid antibodies, leading to damage of the blood brain barrier, and subsequently a second hit by antineuronal antibodies, are the mechanisms for diffuse NPSLE.

Based on clinical symptomatology, treatment is guided by interfering in coagulation, immune suppression and therapy based on specific symptomatology.[4]

Learning Objectives

At the end of the presentation, participants will be able to:

- Know that focal and diffuse NPSLE are different entities.
- Recognise the pathogenesis of focal and diffuse NPSLE.
- Understand the therapeutic approaches in the management of NPSLE.

References

1. Faust TW, Chang EH, Kowal C, *et al*. Neurotoxic lupus autoantibodies alter brain function through two distinct mechanisms. *Proc Natl Acad Sci U S A*. 2010 Oct 26;107(43):18569–74.

2. Steup-Beekman GM, Zirkzee EJ, Cohen D, *et al*. Neuropsychiatric manifestations in patients with systemic lupus erythematosus: epidemiology and radiology pointing to an immune-mediated cause. *Ann Rheum Dis*. 2013 Apr;72 Suppl 2:ii76–9.

3. Luyendijk J, Steens SC, Ouwendijk WJ, *et al*. Neuropsychiatric systemic lupus erythematosus: lessons learned from magnetic resonance imaging. *Arthritis Rheum*. 2011 Mar;63(3):722–32.

4. Bertsias GK, Ioannidis JP, Aringer M, *et al*. EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: report of a task force of the EULAR standing committee for clinical affairs. *Ann Rheum Dis*. 2010 Dec;69(12):2074–82.

Notes

Abstracts

Plenary I: Disease monitoring and management updates **Moderator:** Professor Dr Thomas Dörner (Germany)

Professor Bevra H. Hahn, MD
University of California, Los Angeles, United States

Update on the management of lupus nephritis

Lupus nephritis (LN) results from a complex interaction between the innate and adaptive immune systems, beginning as deposition of autoantibodies and immune complexes that activate complement, followed by activation and infiltration of multiple immune cells (including B, T and dendritic cells, and macrophages) into renal glomeruli and interstitium.[1] Multiple renal target cells are injured, including endothelial, mesangial, renal tubular and podocyte cells, and pathways that lead to proliferation, necrosis, ischaemia, injury and scarring are activated. Treatment, therefore, must suppress many of these pathways.

Current EULAR and ACR guidelines for treatment of LN will be reviewed.[2,3] Therapy may be viewed as **induction** of improvement, followed by **maintenance** of improvement and **prevention** of damage. Recommended induction treatment of Class III, IV and V LN combines high dose glucocorticoids with another immunosuppressive, usually mycophenolate mofetil (MMF) or cyclophosphamide (CYT) for at least 6 months, during which glucocorticoid doses should be tapered as low as possible. After 8 weeks, a 25% reduction in proteinuria and improvement in serum complement indicate response to treatment is likely to be good. At 6 months response occurs in approximately 50% of patients (complete response in 20% of those) and at 12 months response is achieved in 75% of patients. Low-dose CYT (500 mg i.v. every 2 weeks x 6) then maintenance with MMF or azathioprine, may be as effective as high dose CYT (750 mg/m2 i.v. monthly for 6 months) in certain races.

In non-responders, ACR recommends therapy be changed either to the immunosuppressive that was not chosen initially (i.e. MMF changes to CYT, or CYT changes to MMF); EULAR recommends either that change, or the addition of rituximab. EULAR recommends that therapy for LN be continued for at least 3 years. Azathioprine is acceptable as an immunosuppressive for either induction or maintenance, although it is associated with higher flare rates and more cytopaenias than MMF or CYT over the long term. All patients should also receive hydroxychloroquine (which reduces renal damage) and an ACE inhibitor or ARB (which lowers proteinuria and reduces the chance of end stage renal disease [ESRD]).

Since these strategies do not have 100% efficacy, and renal scarring with ESRD still occurs in 15% of patients, new approaches are under aggressive study and we will briefly review them. They include targets for B or T cells (belimumab, epratuzumab, abatacept), inhibition of C5a (eculizumab), inhibition of inflammatory macrophages (laquinimod), inhibition of toll-like receptor activation, T/B cell activation pathways (TOR, JAK kinase, Tyk), proteasomes and PDG4.[4,5] Finally, we will review recent data suggesting that pulse glucocorticoids, plus rituximab, plus daily MMF, without additional daily glucocorticoids, may be sufficient treatment for some cases of LN, thus reducing steroid morbidity.[6]

Learning Objectives

At the end of the presentation, participants will be able to:

- Understand the pathogenesis of LN.
- Be familiar with current European and American guidelines for management of lupus nephritis.
- Understand the limitations of current therapies.
- Be familiar with current experimental therapies being studied for LN.

References

1. Lech M, Anders HJ. The pathogenesis of lupus nephritis. *J Am Soc Nephrol*. 2013 Sep;24(9):1357–66.

2. Hahn BH, McMahon MA, Wilkinson A, *et al*. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care Res* (Hoboken). 2012 Jun;64(6):797–808.

3. Bertsias GK, Tektonidou M, Amoura Z, *et al*. Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. *Ann Rheum Dis*. 2012 Nov;71(11):1771–82.

4. Rovin BH, Parikh SV. Lupus Nephritis: The evolving role of novel therapeutics. *Am J Kid Dis*. 2013: [Epub ahead of print].

5. Houssiau FA, Lauwerys BR. Current management of lupus nephritis. *Best Pract Res Clin Rheumatol*. 2013 Jun;27(3):319–28.

6. Lightstone L. Minimising steroids in lupus nephritis--will B cell depletion pave the way? *Lupus*. 2013 Apr;22(4):390–9.

Notes

Abstracts

Plenary I: Disease monitoring and management updates **Moderator:** Professor Dr Thomas Dörner (Germany)

Professor David A. Isenberg, MD, FRCP, FAMS
University College London, United Kingdom

Use of activity indices to assess clinical involvement in lupus

Until the mid-1980s disease activity assessments in lupus could best be described as naïve and ill thought-out. In the past 30 years they have been optimised with the introduction of the BILAG (British Isles Lupus Assessment Group) system (based on the physician's intention to treat capturing activity in, currently, nine organs and systems) and the SLEDAI (Systemic Lupus Erythematosus Disease Activity Index), the best of the global score indices.[1,2] Both indices have been updated and substantial studies involving hundreds of patients have indicated that they are reliable, valid and sensitive to change.

Lupus is not a straightforward disease, and the importance of using these validated indices is to encourage commonality in the way lupus activity data are collected. By doing this genuine comparisons can be made between patients treated at different centres and, of course, in multinational clinical trials where accurate identification of clinical features genuinely due to activity (and not to damage or a concomitant disease) is absolutely vital. The use of the indices is therefore to be commended and the development of computerised systems makes them easier to introduce and sustain.

Learning Objectives

At the end of the presentation, participants will be able to:

- Understand the value and robustness of the BILAG and SLEDAI disease activity indices.
- Recognise the importance and relevance of using these validated indices throughout clinical practices and in clinical trials.

References

1. Isenberg DA, Rahman A, Allen E, *et al*. BILAG 2004. Development and initial validation of an updated version of the British Isles Lupus Assessment Group's disease activity index for patients with systemic lupus erythematosus. *Rheumatology* (Oxford). 2005 Jul;44(7):902–6.

2. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. *J Rheumatol*. 2002 Feb;29(2):288–91.

Notes

Notes

Case Study Workshops

Saturday 8th March

Morning (11:00) & Afternoon (13:30) Case Study Workshops

Moderator: Murray B.Urowitz *(Canada)* Difficult lupus	▲	Sandra V. Navarra (*Philippines)* & Eric Morand (*Australia)*
Moderator: Andrea Doria (*Italy)* Cardiovascular disease in SLE	◗	Elisabet Svenungsson (*Sweden)* & Ian N. Bruce (*United Kingdom)*
Moderator: Roger A. Levy (*Brazil)* Bone health and vitamin D	■	Ricard Cervera (*Spain)* & Zahir Amoura (*France)*
Moderator: Bevra H. Hahn (*United States)* Lupus nephritis	●	Falk Hiepe (*Germany)* & Richard A. Furie (*United States)*

Please Note

These workshops will be held in breakout rooms. Please follow the appropriate signs/symbols corresponding to the workshops you are registered to attend. Please note workshops are repeated at 11:00 and 13:30 hours.

Case Study Workshop

Moderator: Professor Murray B. Urowitz (Canada)

Presenters: Professor Sandra V. Navarra & Professor Eric Morand

Difficult lupus

Professor Sandra V. Navarra, MD, FPCP, FPRA &
Professor Eric Morand, MBBS(Hons), PhD, FRACP

Case 1: It's not all lupus–cases with a twist

A 30-year-old female has had stable systemic lupus erythematosus (SLE) while maintained on prednisone 10 mg/day, hydroxychloroquine and losartan. She was admitted to the emergency department with fever, chills, profuse diarrhoea and consequent dehydration, and Raynaud's was apparent on most fingers and toes. Fluid resuscitation and empiric antibiotics were started while awaiting diagnostic test results. A few hours later, she developed hypotension, became oliguric with increasing serum creatinine and signs of pulmonary congestion. Haemodialysis and vasopressors were initiated. During her stay at intensive care, there was worsening digital ischemia, progressing to gangrene in some digits.

Discussion point: *contributory factors to symmetrical peripheral gangrene.*

Case 2: It's not all lupus–cases with a twist

A 48-year-old female has had lupus nephritis for 20 years, with progression to end stage renal disease requiring regular haemodialysis during the past year. She is maintained on prednisone 5 mg/day, amlodipine, and calcium and iron supplements. She consulted because of fever and headaches, followed 3 days later by development of painful vesicular lesions of herpes zoster (HZ) over the left side of her forehead. Valacyclovir was started at 500 mg/day. In the next 5 days, she had episodes of disorientation, incoherence and transient slurring of speech. There were no focal neurologic deficits and cranial magnetic resonance imaging (MRI) findings were non-specific. Discontinuation of valacyclovir was almost immediately followed by resolution of neurological symptoms. She was discharged on prednisone 10 mg/day, and maintained on other medications and regular haemodialysis. The HZ lesions had completely healed a week later, with residual but tolerable post-herpetic neuralgia.

Discussion point: *diagnostic considerations for central nervous system manifestations in a patient with lupus.*

Case 3: It's not all lupus–cases with a twist

A 33-year-old nulligravid female has had stable SLE for the last 5 years while maintained on hydroxychloroquine (HCQ) and prednisone 5 mg/day. Three years ago, she was also diagnosed with antiphospholipid syndrome (APS) presenting as steroid-responsive haemolytic anemia with thrombocytopaenia, livedo reticularis and high titer anticardiolipin antibodies. Two weeks before presentation, she developed fever and intermittent diplopia and was admitted to hospital. Pertinent medical history disclosed recurrent throat and gingival infections treated with various antibiotics. Physical examination revealed a temperature of 38.2°C, malar rash, livedo reticularis, heart murmur and right cranial nerve VI palsy. Haemoglobin was 92 g/L, leucocyte 11.4 x 109/L, platelet 241 x 109/L; ESR 130 mm/hr, C3 complement 0.70g/L (NV 0.9–1.8); anti-dsDNA, urinalysis, renal and liver functions were normal. Cranial MRI revealed an enhancing foci at the pontomedullary area indicative of an infarct. Transthoracic and transoesophageal echocardiogram revealed echodense structures/vegetations on the mitral valve. Blood cultures did not grow any organism. Prednisone was increased to 20 mg/day and HCQ was continued. She completed 4 weeks of i.v. penicillin plus gentamicin, and was started on tinzaparin later overlapped/shifted to warfarin. On clinic follow-up a month after discharge, she was well with normal blood counts, ESR 36 mm/hr and no neurologic deficit.

Discussion point: *distinguishing between active SLE* versus *infection (infective* versus *Libman Sacks endocarditis).*

Case 4: Materno-foetal morbidity in a patient with APS and positive Ro antibody
A 30-year-old female with SLE and APS with strongly positive anti-Ro/SSA serology has had two foetal losses each at 24 to 25 weeks gestation, with pregnancy complications of preeclampsia and postpartum cardiomyopathy. A third successful pregnancy delivered a premature but healthy baby boy following intensive anticoagulation and foetal monitoring during pregnancy. The most recent pregnancy was delivered at 31 weeks gestation because of foetal distress, with the baby showing evidence of neonatal lupus syndrome (pleuropericarditis, thrombocytopaenia, bradyarrhythmia, hepatosplenomegaly and anti-Ro/SSA positive antibodies).
Discussion points: *challenges and management approach to APS-complicated pregnancy and neonatal lupus syndrome.*

Learning Objectives

At the end of the workshop, participants will be able to:

- Recognise medical problems mimicking lupus complications that have specific treatments.
- Effectively address potentially life- or organ-threatening complications in an SLE patient.
- Review pregnancy and neonatal complications in SLE and APS.

Notes

Case Study Workshop

Moderator: Professor Andrea Doria (Italy)

Presenters: Professor Elisabet Svenungsson & Professor Ian N. Bruce

Cardiovascular disease in SLE

Professor Elisabet Svenungsson, MD, PhD

Case 1

Alexander is a 21-year-old male adopted from Brazil and living with his parents. He has had asthma since childhood, but has steadily improved and now rarely has symptoms. He works in a supermarket and smokes 10 cigarettes a day.

Alexander was referred to rheumatology because of a few months of joint pain, fatigue and sicknesses, and has noted shortness of breath when running and climbing stairs.

Alexander presents with asymmetrical polyarthritis affecting mainly small joints and X-ray showed discrete pleuritis. Laboratory tests revealed hemoglobin 120 g/L, ESR 15 mm/h, CRP <3 mg/L, +ANA (high titers) and +anti-dsDNA (low tier), low complement C4 and slightly elevated C3d.

Case 2

Gabriella is a 35-year-old single female with two children. She works irregular hours in a hotel as a receptionist and smokes 15 cigarettes a day.

She was healthy until the age of 30 years when she was diagnosed with systemic lupus erythematosus (SLE). Manifestations include polyarthritis, lymphopaenia, Raynaud´s phenomenon and laboratory tests revealed +ANA (high titer) and +anti-dsDNA (high titer) and low complement C4.

At age 35 years there was onset of proteinuria 1.5 g/24h, and SLE nephritis was confirmed with a renal biopsy demonstrating a focal glomerulonephritis with immune complex depositions, WHO III with active lesions. Gabriella was treated with steroids and cyclophosphamide according to the Euro-Lupus protocol.

After 3 months of treatment cardiovascular risk factors are assessed. She is taking azathioprine 100 mg, prednisone 20 mg and enalapril (ACE inhibitor) 20 mg/day.

Heart auscultation is normal, blood pressure 140/80 mmHg, BMI 28 kg/m2, creatinine 95 µmol/L, estimated GFR 60 ml/min, cholesterol 4.4 mmol/L, LDL 2.0 mmol/L, HDL 1.0 mmol/L, triglycerides 2.1 mmol/L and fasting glucose 4.9 mmol/L.

Case 3

Ann is an 18-year-old, whose mother has diabetes and had a myocardial infarction at age 52 years.

Ann was diagnosed with SLE at age 11 years. Diagnosis was based on polyarthritis, butterfly erythema, photosensitivity, +ANA, +anti-dsDNA and +anti-Sm antibodies.

At age 15 years she presents with proteinuria 1.5 g/L, active sediment and a transient rise in creatinine to 105 µmol/L. Renal biopsy demonstrates a vasculopathy with microthrombosis and no immune complex depositions. Ann is treated with steroids and azathioprine 100 mg/day.

Now 18-years-old, Ann is transferring to adult rheumatology. She is presently taking azathioprine, the dose has been tapered to 50 mg/day, hydroxychloroquine 200 mg/day and prednisone 5 mg/day.
Discussion point: *what additional investigations would you like to perform, and how could these three patients be treated in order to minimise cardiovascular risks?*

Professor Ian N. Bruce, MD, FRCP

Case 4

A 29-year-old female presents with a 5-year history of SLE characterised by polyarthritis, recurrent oral ulceration, myositis, serositis and nephrotic syndrome. She has had +ANA, +anti-dsDNA and +Sm antibodies and low C4 complement. Her proteinuria (originally 3.8 g/day) improved on initial treatment with steroids and azathioprine. At the time of this review (8 weeks postpartum) she is taking prednisone 12.5 mg/day, azathioprine 100 mg/day and methyldopa 500 µg three times daily. Her creatinine is 85 µmol/L, anti-dsDNA titre is 38 U (<10) and C4 complement is normal. Currently, her proteinuria is 2.1 g/day, her total cholesterol is 5.1 mmol/L and blood pressure is 140/90 mmHg.

Discussion point: *what additional check would you perform at this stage and how would you plan to manage her?*

Case 5

A 38-year-old women is referred with a 6-year history of SLE. She initially presented with arthritis photosensitivity, malar rash, serositis and class II nephritis on biopsy. She had a +ANA, +anti-dsDNA and low C4 complement. Two years ago she had an acute coronary syndrome and had two drug eluting stents inserted. Her original treatment was with azathioprine, prednisone and hydroxychloroquine, however she stopped azathioprine because of nausea and a low white cell count. Mycophenolate mofetil was started 18 months ago but she stopped this of her own volition 12 months later. She now presents and is 8 weeks pregnant.

Discussion point: *what factors would you consider when planning this patient's care over the next 6 months?*

Case 6

A 31-year-old woman of African descent presented with SLE 5 years ago characterised by arthritis, rashes, alopecia and profound thrombocytopaenia. She had +ANA, +anti-dsDNA and +Sm antibodies as well as low C3 and C4 complement. Her subsequent course has been complicated by osteomyelitis. She also has had three pregnancies (with two live births and one miscarriage) during this time. Two years ago she presented with class IV lupus nephritis and was treated with prednisone and mycophenolate mofetil.

Discussion point: *at what point would you begin to introduce the topic of cardiovascular disease prevention to this lady?*

Learning Objectives

At the end of the workshop, participants will be able to:

- Be aware that cardiovascular disease risk is increased in patients with SLE.
- Understand that ischaemic heart, cerebrovascular and peripheral vascular diseases all contribute to the high incidence rates of vascular diseases in SLE.
- Recognise that SLE is a heterogeneous disease and the vascular risk is not evenly distributed among SLE sub-phenotypes.
- Distinguish differences in the risk factors for ischaemic heart disease and ischaemic cerebrovascular disease.
- Remember that they should screen all newly diagnosed SLE patients broadly for cardiovascular risk factors, and not forget antiphospholipid antibodies. Treat when indicated!
- Pay particular attention to the enhanced cardiovascular risk associated with nephritis, the treatment of nephritis and impaired renal function.
- Understand that from early in the disease, metabolic syndrome is more common in patients with SLE.
- Know that corticosteroid therapy is likely to have a detrimental effect on the cardiovascular system.
- Appreciate that antimalarial drugs have potential beneficial effects on the cardiovascular system.
- Be mindful that a targeted approach to cardiovascular modification is recommended.

Case Study Workshop

Moderator: Professor Roger A. Levy (Brazil)

Presenters: Professor Ricard Cervera & Professor Zahir Amoura

Bone health and vitamin D

Professor Ricard Cervera, MD, PhD, FRCP

Case 1

A 73-year-old Caucasian female with history of systemic lupus erythematosus (SLE) was admitted to the Hospital Clínic of Barcelona with acute back pain. Diagnosis of SLE had been made 13 years before based on photosensitivity, pleuritis, thrombocytopaenia and detection of antinuclear, anti-dsDNA, and IgG and IgM anti-β2-glycoprotein-I antibodies. She had required low-to-moderate doses of prednisone over these years. One month before this current admission, the patient had been hospitalised because of community-acquired pneumonia caused by *Streptococcus pneumoniae*.

The patient reported 6 days of dorsal back pain. No previous history of any trauma was reported by the patient. Her medications on admission included hydroxychloroquine 200 mg/day, prednisone 5 mg/day, calcium-Vitamin D and several pain-killers.

The patient was in a regular state. Back examination revealed a selective point of pain in the thoracic dorsal spine. Laboratory tests showed a low platelet count (21x109/L). Lateral X-ray of the thoracic spine revealed a reduction in vertebral height indicative of fracture at the D9 vertebra.

Professor Zahir Amoura, MD, MSc

Case 2

A 54-year-old Caucasian woman with history of SLE was admitted with intense diffuse pain and fatigue. Diagnosis of SLE had been made 30 years before based on photosensitivity, polyarthritis, and detection of antinuclear and anti-dsDNA antibodies. Nine years earlier, she had lupus nephritis (Class IV ISN/RPS), which was treated with monthly cyclophosphamide pulses for 6 months followed by mycophenolate mofetil 2 g for 2 years, resulting in normalisation of proteinuria. She experienced premature ovarian failure at the age of 35 years.

Clinical examination revealed an 8-week history of pain and swelling in the hands and wrists, a 5-day period of right groin and buttock pain, and chronic (>6 months) dorsal back pain. No previous history of any trauma/accident was reported by the patient.

Routine laboratory tests were normal with a normal serum creatinine level (54 µM), GFR was 94 mL/min, CRP was 9 mg/dL (N<5) and a urine dipstick result was negative.

Her medications on admission included hydroxychloroquine 400 mg/day, prednisone 5 mg/day, methotrexate 15 mg oral/week (started 6 months before for refractory polyarthritis), calcium-Vitamin D, ACE inhibitor, proton pump inhibitor and several painkillers.

Learning Objectives

At the end of the workshop, participants will be able to:

- Recognise clinical, laboratory and imaging features, which help assess bone health and pathology in patients with SLE.
- Describe the role of steroids and other drugs in increasing susceptibility to osteoporosis.
- Outline principles and strategies in the management and prevention of osteoporosis in SLE.
- Enhance clinical awareness of potential severe complications of osteoporosis in SLE.

Notes

Case Study Workshop

Moderator: Professor Bevra H. Hahn (United States)

Presenters: Professor Dr Falk Hiepe & Professor Richard A. Furie

Lupus nephritis

Professor Dr Falk Hiepe, MD

Case 1

A 28-year-old female with a 10-year history of lupus nephritis had been in remission after treatment with cyclophosphamide followed by mycophenolate mofetil (2 g/d) until December in 2012. Since that time, she had an increase in proteinuria and anti-dsDNA antibodies as well as a decrease in complement levels. Clinically, she felt well and did not have any symptoms. Laboratory findings in September 2013 revealed creatinine 0.80 mg/dL, serum albumin 35.7 g/L, protein 61 g/L, complement C3 750 mg/dL, C4 60 mg/dL, anti-dsDNA ELISA >200U/mL (<20), and anti-dsDNA Crithidia-IFA 1:40; urinalysis revealed proteinuria 3141 mg/day.

Renal biopsy revealed diffuse proliferative lupus nephritis class IV-G (A/C), global glomerulosclerosis (4/15 glomeruli). Medications at the time of renal biopsy included methylprednisolone 6 mg/d, mycophenolate mofetil 2 g/day, hydroxychloroquine 400 mg/day, Vitamin D3 400 IU/day and calcium 500 mg/day.

Discussion points:

Would you change the treatment?
What therapeutic intervention would you perform?
Which therapeutic options are available?

Professor Richard A. Furie, MD

Case 2

A 27-year-old female with a 5-year history of systemic lupus erythematosus (SLE) was admitted to the hospital because of confusion and fever. Past manifestations of SLE included arthritis, rash, pericarditis, and anemia (but no nephritis: baseline creatinine 0.7 mg/dL). At the time of admission, medicines included hydroxychloroquine 400 mg/day, prednisone 15 mg/day and calcium. Her examination was notable for blood pressure of 150/90, temperature of 39°C, altered mental status, petechiae, Jaccoud's arthropathy and bilateral Babinski's. Laboratory tests revealed Hb 6.8 g/dL; Plt 12 K/uL; PT/PTT 12/26 seconds; **creatinine 1.9 mg/dL; urinalysis 5 WBC, 20 RBC; Pr/Cr 0.6 g/g**; DNA 87 (<30 IU/ml); complement (C3/C4) was normal.

Despite broad spectrum antibiotics, methylprednisolone 60 mg/day, and then pulse steroids, the patient became comatose, and there was no improvement whatsoever in her haematologic and renal parameters.

Discussion points:

What is your differential diagnosis?
Would you perform a biopsy? If so, what organ?
What additional diagnostic tests would you perform?
What therapeutic interventions might you try?

Case 3

A 52-year-old female with a history of stroke and maintained on warfarin was hospitalised for evaluation of 2 months of fever, diarrhoea and weight loss. Her examination was notable for blood pressure of 135/85; temperature of 39.8°C; mild proximal interphalangeal synovitis. Laboratory tests revealed WBC 1.2 (50% PMN's; 50% L); Hb 7.6; Plt 66; PT/PTT 15/38; AST 173; ALT 104; **creatinine: 1.4 (pre-morbid creatinine 0.7 mg/dL); urinalysis: 8 RBC; no casts; Pr/Cr 0.3 g/g; ANA: 1:320;** DNA: 562; aPL Ab: negative. Despite methylprednisolone 60 mg/day, there was no improvement whatsoever in her haematologic, hepatic and renal parameters.

Discussion points:

What is your differential diagnosis?
Would you perform a biopsy? If so, what organ?
What additional diagnostic tests would you perform?
What therapeutic interventions might you try?

Learning Objectives

At the end of the workshop, participants will be able to:

- Discuss therapeutic options in refractory lupus nephritis.
- Discuss the treat-to-target concept in lupus nephritis.
- Discuss uncommon non-nephritic causes of renal disease in SLE patients.
- Describe appropriate diagnostic evaluations.
- Discuss treatment regimens for such patients.

Notes

Abstracts

Plenary II: From basic science to clinical trials

Moderator: Professor Munther A. Khamashta (United Kingdom)

Professor Lars Rönnblom, MD, PhD
Uppsala University, Sweden

Interferon as a therapeutic target in SLE: why and how?

There are several observations suggesting an important role for the type I interferon (IFN) system in the aetiopathogenesis of systemic lupus erythematosus (SLE). Among these are the reported development of SLE during treatment with IFN-α, a prominent increase in the expression of type I IFN regulated genes (an IFN signature) in SLE, the existence of endogenous IFN inducers in SLE patients and a genetic association between SLE and gene variants within the type I IFN signalling pathway.[1]

The type I IFN system consists of a large number of different IFNs (>15) and is closely connected to a number of cytokine and chemokine pathways, which all can contribute to both the IFN signature and the type I IFN effects. Important type I IFN effects include maturation and differentiation of dendritic cells, activation of T and B cells with enhanced antibody production and induction of increased expression of autoantigens.

Consequently, type I IFNs can act as an immune adjuvant and promote an autoimmune process.[2] Recent data have also shown that the regulation of the type I IFN system is abnormal in SLE, which altogether suggests that inhibition of the type I IFN system could be beneficial in SLE. Many different therapeutic targets exist and several studies are in progress aiming to block, or down-regulate, the activated type I IFN system in SLE.[3] A number of studies with monoclonal anti-IFN-α antibodies are ongoing, and a small study investigating vaccination with an interferon-α-kinoid against IFN-α has been published.[4] Trials targeting the type I IFN receptors are also under way. The results so far show that it is possible to partially suppress the IFN signature and improve several biomarkers in SLE patients with moderate disease activity.[3,5] No major safety problems have been observed to date. However, only modest clinical efficacy has been noted and improved strategies for modulating the interferon system in SLE should be developed.

Learning Objectives

At the end of the presentation, participants will:

- Understand the evidence for an important role of the interferon system in SLE.
- Realise the complexity of the interferon system.
- Associate the type I interferon system with the pathogenesis of SLE and possible reasons behind an IFN signature.
- Be aware of the many possibilities to modulate the interferon system in SLE.
- Recognise possible adverse effects of type I IFN inhibition.

References

1. Rönnblom L, Alm GV, Eloranta ML. The type I interferon system in the development of lupus. *Semin Immunol*. 2011 Apr;23(2):113–21.

2. Eloranta ML, Alm GV, Rönnblom L. Disease mechanisms in rheumatology--tools and pathways: plasmacytoid dendritic cells and their role in autoimmune rheumatic diseases. *Arthritis Rheum*. 2013 Apr;65(4):853–63.

3. Kirou KA, Gkrouzman E. Anti-interferon alpha treatment in SLE. *Clin Immunol*. 2013 Sep;148(3):303–12.

4. Lauwerys BR, Hachulla E, Spertini F, *et al*. Down-regulation of interferon signature in systemic lupus erythematosus patients by active immunization with interferon α-kinoid. *Arthritis Rheum*. 2013 Feb;65(2):447–56.

5. Petri M, Wallace DJ, Spindler A, *et al*. Sifalimumab, a human anti-interferon-α monoclonal antibody, in systemic lupus erythematosus: a phase I randomized, controlled, dose-escalation study. *Arthritis Rheum*. 2013 Apr;65(4):1011–21.

Notes

Abstracts

Plenary II: From basic science to clinical trials

Moderator: Professor Munther A. Khamashta (United Kingdom)

Professor Martin Aringer, MD
Technical University of Dresden, Germany

Doing small open trials in lupus: experiences with anti-TNF

It is obvious that controlled clinical trials are an absolute requirement for getting a drug approved for any indication today. Why would one then even consider doing uncontrolled trials? Although tumour necrosis factor (TNF) blockers have not yet been tested in controlled trials, the experience with these substances, and infliximab in particular, gives some answers to this question. Small trials are useful if they help overcome obstacles. With regard to TNF blockade, they were fourfold. Safety was disputed, based on murine data from NZB/W mice,[1] and on the occasional emergence of drug-induced lupus in TNF-blocker treated inflammatory disease.[2] Efficacy was not seen as likely by many groups and there was no information on potential efficacy in nephritis. TNF-blocker treatment was very successful in several more common rheumatic diseases, as well as in Crohn's disease, which curbed the enthusiasm of the pharmaceutical industry to run big clinical trials in systemic lupus erythematosus (SLE). Moreover, funding for a medium-to-large sized trial with a biologic was not available. In contrast, an investigator-driven, small open trial was feasible, and TNF blockers were known to act rapidly. Given that we had cytokine data suggesting that TNF was associated with disease activity,[2] such a trial was initiated. This small open trial established at least some safety data. Lupus flares were not seen and the increase in autoantibodies was transient.[3,4] However, there were some other safety issues of unclear significance.[5] The trial also indicated probable long-term efficacy in lupus nephritis, which was unexpected. In addition, it was suggested that an effect on lupus arthritis was present but transient. In retrospect, it worked well to look at well-established markers of two common inflammatory manifestations of the disease on top of SLE activity scores and serology. With these safety and efficacy data combined, the small trial brought forward arguments to formally test TNF blockade in SLE. Two small controlled trials were in fact started, but failed due to recruitment issues, which were mostly due to the prominence of safety concerns. Unfortunately, the risks for a drug associated with a complex disease such as SLE have so far prevented the initiation of pivotal trials.

Learning Objectives

At the end of the presentation, participants will:

- Be aware that serious safety concerns may be alleviated by small open trials.
- Understand safety precautions and constant surveillance are essential to prevent undue risks.
- Recognise the underlying pathomechanisms (here autoantibodies) need to be studied in parallel.
- Have learnt that two to three obvious and rather common organ manifestations should be investigated.
- Appreciate that preliminary efficacy data may only be realistic when the drug's mode of action is rapid.

References

1. Jacob CO, McDevitt HO. Tumour necrosis factor-alpha in murine autoimmune 'lupus' nephritis. *Nature*. 1988 Jan 28;331(6154):356–8.

2. Aringer M, Smolen JS. Therapeutic blockade of TNF in patients with SLE-promising or crazy? *Autoimmun Rev*. 2012 Mar;11(5):321–5.

3. Aringer M, Graninger WB, Steiner G, *et al*. Safety and efficacy of tumor necrosis factor alpha blockade in systemic lupus erythematosus: an open-label study. *Arthritis Rheum*. 2004 Oct;50(10):3161–9.

4. Aringer M, Steiner G, Graninger WB, *et al*. Effects of short-term infliximab therapy on autoantibodies in systemic lupus erythematosus. *Arthritis Rheum*. 2007 Jan;56(1):274–9.

5. Aringer M, Houssiau F, Gordon C, *et al*. Adverse events and efficacy of TNF-alpha blockade with infliximab in patients with systemic lupus erythematosus: long-term follow-up of 13 patients. *Rheumatology* (Oxford). 2009 Nov;48(11):1451–4.

Notes

Abstracts

Plenary II: From basic science to clinical trials

Moderator: Professor Munther A. Khamashta (United Kingdom)

Dr Elizabeth Jury, PhD
University College London, United Kingdom

Is there a place for kinase blockers in SLE?

Non-specific, relatively toxic, immunosuppression continues to be the standard treatment for patients with systemic lupus erythematosus (SLE). However, by understanding the mechanisms underlying the pathogenesis of SLE, new and more targeted treatments are emerging as demonstrated by the success of biologic therapies, including rituximab and belimumab, that target autoantibody-producing B-lymphocytes.[1–3] In recent years, a large body of work has identified defects in the way that T and B lymphocytes from patients with SLE respond to their environment via so called 'cell signalling'.[4] Some of these defects are associated with genetic abnormalities in patients, whereas some are acquired due to the proinflammatory environment associated with lupus disease.[5,6] Importantly, understanding these complex intracellular processes is providing new prospects for treating patients. In particular, small molecules that are directed against intracellular enzymes, called kinases and phosphatases, are now being tested for efficacy in animal models of lupus and in clinical trials in patients with SLE.[7]

Kinases and phosphatases control the flow of crucial signalling messages transmitted to the nucleus; such messages inform cells how to respond to their environment (e.g. to proliferate, undergo apoptosis and to produce cytokines). Key targets being considered include Janus kinases (JAK) involved in cytokine signalling, phosphatidylinositol 3-kinases (PI3K) involved in coordinating multiple cell growth and survival signals, mammalian target of rapamycin (mTOR) involved in cell metabolism, and Rho kinases (ROCK) that regulate the cell cytoskeleton, amongst others.[7]

The benefit of using kinase blockers could be significant. Compared to biologic therapies they are inexpensive, can be administered orally rather than by infusion/injection and do not trigger immunogenicity. Furthermore, since the success of kinase blockers is now established in the treatment of some cancers, they could represent a valuable addition to the more targeted therapies available to patients with SLE.

Learning Objectives

At the end of the presentation, participants will be able to:

- Understand how cell signalling abnormalities affect SLE pathogenesis.
- Identify the key intracellular target molecules in lymphocytes.
- Understand the benefits and risks associated with blocking signalling pathways.

References

1. Stohl W. Future prospects in biologic therapy for systemic lupus erythematosus. *Nat Rev Rheumatol*. 2013 Dec;9(12):705–20.

2. Fattah Z, Isenberg DA. Recent developments in the treatment of patients with systemic lupus erythematosus: focusing on biologic therapies. *Expert Opin Biol Ther*. 2014 Jan 6: [Epub ahead of print].

3. Thanou A, Merrill JT. Treatment of systemic lupus erythematosus: new therapeutic avenues and blind alleys. *Nat Rev Rheumatol*. 2014 Jan;10(1):23–34.

4. Moulton VR, Tsokos GC. Abnormalities of T cell signaling in systemic lupus erythematosus. *Arthritis Res Ther*. 2011 Mar 17;13(2):207.

5. Pascual V, Chaussabel D, Banchereau J. A genomic approach to human autoimmune diseases. *Annu Rev Immunol*. 2010;28:535–71.

6. Perl A. Systems biology of lupus: mapping the impact of genomic and environmental factors on gene expression signatures, cellular signaling, metabolic pathways, hormonal and cytokine imbalance, and selecting targets for treatment. *Autoimmunity*. 2010 Feb;43(1):32–47.

7. Markopoulou A, Kyttaris VC. Small molecules in the treatment of systemic lupus erythematosus. *Clin Immunol*. 2013 Sep;148(3):359–68.

Notes

Abstracts

Plenary III: Challenges in treatment

Moderator: Professor Roger A. Levy (Brazil)

Professor Marta Mosca, MD
University of Pisa, Italy

Treat-to-target in SLE

The principle of treat-to-target has been applied to many diseases, and recently to rheumatoid arthritis, leading to improved care and outcomes.

The clinical picture of systemic lupus erythematosus (SLE) develops from the interaction of many different aspects including disease activity (affecting different organs and systems with various degrees of severity and with a flaring/remitting pattern), damage accrual, the patient's perspective, comorbidities, drug toxicity and the patient's quality of life.[1] All these aspects may represent important targets to treatment and should be taken into consideration in clinical trials as well as in clinical practice.

An international task force was gathered to investigate this question with the aim to develop recommendations aimed at improving the management of SLE in clinical practice.[2] A systematic literature review was conducted and four overarching principles and 11 recommendations for treating-to-target in SLE were developed. The main areas of these recommendations include targeting remission, preventing damage and improving quality of life.

This literature review and the following discussion highlighted a number of unsolved issues, which constitute a future research agenda.

Learning Objectives

At the end of the presentation, participants will be able to:

- Consider if a treat-to-target approach in SLE may be useful.
- Identify potential targets for SLE therapy/management.
- Apply the treat-to-target approach in routine clinical practice.

References

1. Urowitz MB, Gladman DD, Tom BD, *et al*. Changing patterns in mortality and disease outcomes for patients with systemic lupus erythematosus. *J Rheumatol*. 2008 Nov;35(11):2152–8.

2. Mosca M, Boumpas DT, Bruce IN, *et al*. Treat-to-target in systemic lupus erythematosus: where are we today? *Clin Exp Rheumatol*. 2012 Jul-Aug;30(4 Suppl 73):S112–5.

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Abstracts

Plenary III: Challenges in treatment

Moderator: Professor Roger A. Levy (Brazil)

Dr Rebecca Fischer-Betz, MD
Heinrich-Heine-University, Düsseldorf, Germany

Pregnancy issues in SLE

Modern multidisciplinary care has improved pregnancy outcomes in patients with systemic lupus erythematosus (SLE), but not eliminated the increased risk for foetal and maternal mortality and morbidity.[1] Foetal complications include higher rates of miscarriages, preterm birth, intrauterine growth restriction and neonatal lupus syndromes.[2] Maternal complications include flares and a two-to-four fold increased risk of preeclampsia. However, not all women with lupus have the same risk. Thus, prepregnancy counselling is essential to estimate and reduce the chance of both foetal and maternal problems. This is also the time to evaluate the safety of the treatment received by the patient.

It is widely accepted that the risk for flares is especially increased in women with active SLE in the months prior to pregnancy.[3] Disease activity has also shown a clear association with foetal loss and prematurity. One factor that has unfavourable effects on the rate of flares and pregnancy complications is the discontinuation of hydroxychloroquine (HCQ). Given its excellent safety profile, HCQ should not be discontinued when women wish to become pregnant, even if their disease is stable.[4] Specific preconception care should be offered to women with renal involvement to optimise and increase chances of a successful pregnancy. Pregnancy should be ideally planned in patients with inactive lupus nephritis, proteinuria <3 g/day, normal renal function and normal blood pressure. Several studies have found adverse pregnancy outcomes are significantly related to the presence of antiphospholipid antibodies.[5] In particular, lupus anticoagulant has emerged as a consistent predictor for pregnancy complications. In addition, previous thromboembolic events are risk factors for pregnancy complications in aPL-positive women.[5] The most important requirement is to identify patients at risk in order to bring more of those pregnancies to a successful conclusion.

In summary, adequate pregnancy management in SLE should include preconception counselling, coordinated medical-obstetric care and an agreed and well-defined management protocol. Recent studies support the beneficial effect of close monitoring and therapy with significantly improved live-birth rates.

Learning Objectives

At the end of the presentation, participants will be able to:

- Demonstrate knowledge of the influence of SLE on pregnancy and *vice versa*.
- Describe main predictors of pregnancy complications in women with SLE.
- Be familiar with the currently accepted management of SLE prior to conception and during pregnancy.
- Understand the importance of pregnancy counselling in women with SLE.

References

1. Clowse ME, Jamison M, Myers E, *et al*. A national study of the complications of lupus in pregnancy. *Am J Obstet Gynecol*. 2008 Aug;199(2):127.e1–6.

2. Clowse ME, Chakravarty E, Costenbader KH, *et al*. Effects of infertility, pregnancy loss, and patient concerns on family size of women with rheumatoid arthritis and systemic lupus erythematosus. *Arthritis Care Res* (Hoboken). 2012 May;64(5):668–74.

3. Fischer-Betz R, Specker C, Brinks R, *et al*. Low risk of renal flares and negative outcomes in women with lupus nephritis conceiving after switching from mycophenolate mofetil to azathioprine. *Rheumatology* (Oxford). 2013 Jun;52(6):1070–6.

4. Bertsias GK, Tektonidou M, Amoura Z, *et al*. Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. *Ann Rheum Dis*. 2012 Nov;71(11):1771–82.

5. Lateef A, Petri M. Managing lupus patients during pregnancy. *Best Pract Res Clin Rheumatol*. 2013 Jun;27(3):435–47.

Notes

Abstracts

Plenary III: Challenges in treatment

Moderator: Professor Roger A. Levy (Brazil)

Professor Roger A. Levy, MD, PhD
The State University of Rio de Janeiro, Brazil

Optimal management of hypercoagulability states in SLE

Before indicating anticoagulation treatment for people with lupus, one should first identify if there is a high risk of thrombosis. Among the thrombophilias, the most prevalent is antiphospholipid antibody (Hughes') syndrome (APS)[1] and the inherited mutations may occur more rarely. Atherosclerosis and metabolic syndrome are more prevalent in patients with lupus; other important risk factors when anticoagulation is indicated include nephrotic syndrome, placement of a central vein catheter, post-major surgical procedures (e.g. hip replacement) and some cases of vasculitis, pregnancy, prolonged bed rest and immobilisation. Adherence to treatment recommendations is crucial for a successful therapeutic outcome, since the chronic use of vitamin K antagonists (AVK) require change of diet and life-habits and rigorous monitoring.[2]

Diagnosing APS can be challenging, the antibodies may be found in asymptomatic patients and be indicative of disease. Conversely, patients may have the classical features of APS, as well as characteristic but non-classical/criteria clinical features, yet their laboratory tests are negative, constituting the so-called seronegative APS.[3] For APS patients with previous venous thrombosis, AVK treatment targeting an INR of 2.5 is recommended, while for those with past arterial events the target aimed is 3.5.[4] In high-risk situations, and when an invasive procedure is necessary, oral anticoagulation is replaced by short-term subcutaneous anticoagulation with low-molecular weight heparin (LMWH). Also, when pregnancy is detected in women with thrombotic APS, AVK is switched to full dose LMWH combined with low-dose aspirin. This treatment has improved life-birth rates, but the frequency of gestational complications remains high.[5] Long-term treatment with AVK is troublesome as it requires frequent monitoring and strict compliance to medication and dietary habits. The new generation of oral anticoagulants is still being studied for APS, and it is too early to recommend their use. Other forms of anticoagulation as well as agents such as hydroxychloroquine, statins, B-cell inhibitors and peptides are being studied for APS.[6]

Learning Objectives

At the end of the presentation, participants will be able to:

- Recognise risk factors and potential triggers of thrombosis.
- Identify the markers related to thrombosis in lupus.
- Understand when treatment targeting the clotting system is necessary in SLE.
- Decide on short- or long-term treatment protocol.
- Decide how to proceed in emergency and specific situations.

References

1. Miyakis S, Lockshin MD, Atsumi T, *et al*. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost*. 2006 Feb;4(2):295–306.

2. Schiro TA, Sakowski J, Romanelli RJ, *et al*. Improving adherence to best-practice guidelines for venous thromboembolism risk assessment and prevention. *Am J Health Syst Pharm*. 2011 Nov 15;68(22):2184–9.

3. Conti F, Alessandri C, Sorice M, *et al*. Thin-layer chromatography immunostaining in detecting anti-phospholipid antibodies in seronegative anti-phospholipid syndrome. *Clin Exp Immunol*. 2012 Mar;167(3):429–37.

4. Ansell J, Hirsh J, Hylek E, *et al*; American College of Chest Physicians. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest*. 2008 Jun;133(6 Suppl):160S–198S.

5. de Jesús GR, Rodrigues G, de Jesús NR, *et al*. Pregnancy morbidity in antiphospholipid syndrome: what is the impact of treatment? *Curr Rheumatol Rep*. 2014 Feb;16(2):403–9.

6. Erkan D, Aguiar CL, Andrade D, *et al.* 14th International Congress on Antiphospholipid Antibodies Task Force Report on Antiphospholipid Syndrome Treatment Trends. *Autoimmun Rev.* 2014 Jan 24. pii: S1568–9972.

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Abstracts

Plenary IV: Treatment in 2014 and beyond

Moderator: Sandra V. Navarra (Philippines)

Dr Liz Lightstone, PhD, FRCP
Imperial College London, United Kingdom

Glucocorticoid-free treatment for lupus nephritis: a paradigm shift in the making?

The treatment of lupus nephritis (LN) was transformed in 1951 by the introduction of steroids[1]; previously, it had been an untreatable disease leading to renal failure and, in that era of no maintenance dialysis, death. However, the treatment came at a cost. Steroids have a multitude of side effects; the visible ones such as moon faces, weight gain, striae and acne deter patients from adherence, the less visible ones cause long term damage—osteoporosis, diabetes, hypertension, dyslipidaemia, cataracts and glaucoma to name just a few. Steroid doses were often very high and grew with the introduction of methylprednisolone. The toxicity of steroids is related to cumulative dose and duration of treatment and starts with doses as low as 5 mg od.[2]

Despite the introduction of steroid sparing agents—azathioprine, cyclophosphamide, and more recently mycophenolate mofetil (MMF)—steroids are perceived to be an essential part of every subsequent treatment regimen for LN. This is despite scant evidence supporting their efficacy in treating LN and even less data to suggest the correct dose.[3] The only secure data on dosing is that higher doses are associated with higher risk of infections.

There are groups who have pioneered the use of low-dose steroid regimens in managing LN; either using steroids just for extra renal manifestations or using methylprednisolone for fast onset of action and rapidly tapering oral steroids.[4,5]

It was hoped that the newer biologic agents would offer better outcomes in LN, however trials to date with anti-CD20 agents rituximab (the LUNAR trial) and ocrelizumab (the BELONG study), or with CTLA4-Ig (abatacept), the BMS study and the very recent ACCESS trial, have failed to achieve their primary endpoints or had to be stopped prematurely because of the infections (the BELONG trial). We have argued that the problem is that the biologics were being used as add on therapy rather than instead of the steroids.[6]

Following the lead of the transplantation community where the addition of a biologic allowed steroid avoiding regimens to be implemented, we developed the RITUXILUP regimen—methylprednisolone 500 mg and rituximab 1g on days 1 and 15, and MMF daily but with no oral steroids. In June 2013 we reported the very favourable outcomes of the first 50 patients treated with this regimen. At 1 year the complete renal remission rate was 52%, and overall there were low rates of adverse events, high rates of remission and only two out of the 45 patients who remained on the protocol required long term steroids.[7]

We are now undertaking a randomized multicentre controlled trial (The RITUXILUP trial) comparing the RITUXILUP regimen with the standard-of-care of methylprednisolone, MMF and oral steroids. The trial is designed as a non-inferiority study for the primary endpoint of complete renal response at 1 year but is powered to demonstrate superiority in safety outcomes at 1 and 2 years.

Over the last 5 years there has been a growing recognition of the need to reduce the use of steroids in patients with LN. The new paradigm is smart use of biological agents to minimise steroid exposure and avoid oral steroids altogether.

References

1. Heller BI, Jacobson WE, Hammarsten JF. The effect of cortisone in glomerulonephritis and the nephropathy of disseminated lupus erythematosus. *J Lab Clin Med*. 1951 Jan;37(1):133–42.

2. Urowitz MB, Gladman DD, Ibañez D, *et al*. Evolution of disease burden over five years in a multicenter inception systemic lupus erythematosus cohort. *Arthritis Care Res* (Hoboken). 2012 Jan;64(1):132–7.

3. Lightstone L. Minimising steroids in lupus nephritis--will B cell depletion pave the way? *Lupus*. 2013 Apr;22(4):390–9.

4. Fischer-Betz R, Chehab G, Sander O, *et al*. Renal outcome in patients with lupus nephritis using a steroid-free regimen of monthly intravenous cyclophosphamide: a prospective observational study. *J Rheumatol*. 2012 Nov;39(11):2111–7.

5. Ruiz-Irastorza G, Danza A, Perales I, *et al*. Prednisone in lupus nephritis: how much is enough? *Autoimmun Rev*. 2014 Feb;13(2):206–14.

6. Lightstone L. The landscape after LUNAR: rituximab's crater-filled path. *Arthritis Rheum*. 2012 Apr;64(4):962–5.

7. Condon MB, Ashby D, Pepper RJ, *et al*. Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids. *Ann Rheum Dis*. 2013 Aug;72(8):1280–6.

Learning Objectives

At the end of the presentation, participants will be aware of the:

- Historical context of the steroid-based regimens in current use.
- Adverse events associated with long-term steroid use.
- Outcomes of the steroid lower regimens in use for the treatment of LN.
- Entirely novel concept of the RITUXILUP regimen, which avoids the use of oral steroids altogether.
- Design of the RITUXILUP trial to evaluate the RITUXILUP regimen in a randomised controlled multicentre international trail against the standard-of-care treatment.

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Abstracts

Plenary IV: Treatment in 2014 and beyond

Moderator: Sandra V. Navarra (Philippines)

Professor Andrea Doria, MD
University of Padova, Italy

Optimising outcomes in SLE: best practice

Survival of patients with systemic lupus erythematosus (SLE) has improved dramatically over the last few decades; however, patients with SLE still display a four-to-five fold higher standardised mortality rate compared with the general population.[1] Persistent disease activity and drug side effects, especially with corticosteroids, are responsible for increased organ damage, which in turn is predictive of more damage and death.[2] By contrast, remission is associated with better outcomes and prolonged survival.[3] Thus, remission should be the main target in the management of patients with lupus.

From a clinical perspective, we can define clinical remission as the absence of signs, symptoms, urinary and haematological abnormalities due to the immune pathways involved in the disease in patients who are corticosteroid free and clinical-serological remission; in other words, complete remission as a clinical-serological healing in patients who are free of any treatment. However, complete remission is often hard to accomplish for the majority of patients with SLE, whereas clinical remission without corticosteroids or with a minimal dose of corticosteroids could be acceptable alternative targets. Low disease activity, even with low dose steroids, may also be a reasonable target in order to minimise development of organ damage.

New biologic agents hold promise for improving outcomes in patients with SLE, since when added to the standard of care they seem to reduce disease activity and spare the need for corticosteroids.[4] In addition, we should try to make the diagnosis earlier, thereby allowing early treatment.[5] Unfortunately, new SLICC (Systemic Lupus International Collaborating Clinics) classification criteria for SLE do not seem to help an earlier diagnosis, compared with previous ACR (American College of Rheumatology) criteria, and no single biomarker exists that can correctly identify SLE in patients at a very early stage. Thus, general practitioners, who see patients before rheumatologists, should be educated to identify any element raising the suspicion of SLE and refer patients to the specialist quickly.

Learning Objectives

At the end of the presentation, participants will be able to:

- See that persistent disease activity and drug side-effects are the two main determinants of organ damage in SLE, and that damage is predictive of more damage, worse prognosis and death.
- Learn the different definitions of clinical or clinical and serological (complete) remission, being aware that prolonged clinical and serological remissions remain very difficult to achieve.
- Recognise that the ideal although distant treatment target in SLE is complete remission, defined as the absence of disease signs and symptoms, negative serology and no treatment.
- Understand that clinical remission or even low disease activity, with minimal corticosteroid intake, are recommended.
- See that a tight balance between therapeutic harm and benefit has to be provided and prompt corticosteroid withdrawal should be performed.
- Know that early treatment prevents organ damage and is predictive of durable remission.

References

1. Doria A, Iaccarino L, Ghirardello A, *et al*. Long-term prognosis and causes of death in systemic lupus erythematosus. *Am J Med*. 2006 Aug;119(8):700–6.

2. Zen M, Bassi N, Nalotto L, *et al*. Disease activity patterns in a monocentric cohort of SLE patients: a seven-year follow-up study. *Clin Exp Rheumatol*. 2012 Nov-Dec;30(6):856–63.

3. Steiman AJ, Gladman DD, Ibañez D, *et al.* Outcomes in patients with systemic lupus erythematosus with and without a prolonged serologically active clinically quiescent period. *Arthritis Care Res* (Hoboken). 2012 Apr;64(4):511–8.

4. Doria A, Gatto M, Zen M, *et al*. Optimizing outcome in SLE: treating-to-target and definition of treatment goals. *Autoimmun Rev*. 2014 Jan 27. pii: S1568–9972

5. Doria A, Zen M, Canova M, *et al.* SLE diagnosis and treatment: when early is early. *Autoimmun Rev*. 2010 Nov;10(1):55–60.

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Abstracts

Plenary IV: Treatment in 2014 and beyond

Moderator: Sandra V. Navarra (Philippines)

Professor Ronald F. van Vollenhoven
The Karolinska Institute, Stockholm, Sweden

Biologics: the future of SLE treatment?

Biologic therapies have revolutionised the care of patients across a range of autoimmune diseases, including rheumatoid arthritis, inflammatory bowel disease and multiple sclerosis. In contrast, in systemic lupus erythematosus (SLE) therapeutic advances have been limited and there have been some notable set-backs when trials, which were widely regarded as being almost certain to give positive results, did in fact turn out negative; however, more recently some successes have been achieved. The phase III trials with belimumab achieved their primary and secondary endpoints and supported the approval of what is currently the only registered biologic for SLE.[1,2] Phase II trials, with impressively positive results, have been published for epratuzumab[3] and some other biologics in mid-stage development are also showing promise.

Perhaps more interestingly, it is becoming clear that biologics may have benefits in many ways that are not immediately apparent in clinical trials. Exploratory and post-hoc analyses from the belimumab phase III trials have revealed that patient subsets with greater likelihood of response can be defined,[4] that an important steroid-sparing effect may be quantifiable, and that even benefits may be seen in some patients with lupus nephritis.[5] Observational data have been presented showing that the onset of effect with belimumab may be quicker than originally believed. Similarly, while two randomised trials failed to support the use of rituximab in patients with SLE, observational data continue to emerge and are strongly supportive of efficacy if the biologic is used in the correct medical setting; for example, in the patient with nephritis who has failed conventional therapies, or possibly even as a first-line therapy—an entirely novel concept that is being tested in a clinical trial at this time.[6]

The use of biologics in SLE is limited largely by cost considerations. However, it has become increasingly clear that the true cost of SLE to society is very large,[7] while the cost of biologics is likely to become less of a problem owing to technological improvements and market mechanisms, as is already seen in other fields of medicine.

Thus, for many different reasons, I predict that in the near future biologics will start playing a much bigger role in SLE treatment.

Learning Objectives

At the end of the presentation, participants will be able to:

- Recognise the failed and the successful trials of biologics for SLE.
- Identify some of the results from post-hoc exploratory analyses of trials with biologics that reveal practical issues of their use in SLE.
- Understand how biologics may come to play a bigger role in the management of SLE in the future.

References

1. Navarra SV, Guzmán RM, Gallacher AE, *et al;* BLISS-52 Study Group. Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. *Lancet*. 2011 Feb 26;377(9767):721–31.

2. Furie R, Petri M, Zamani O, *et al*; BLISS-76 Study Group. A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. *Arthritis Rheum*. 2011 Dec;63(12):3918–30.

3. Wallace DJ, Kalunian K, Petri MA, *et al*. Efficacy and safety of epratuzumab in patients with moderate/severe active systemic lupus erythematosus: results from EMBLEM, a phase IIb, randomised, double-blind, placebo-controlled, multicenter study. *Ann Rheum Dis*. 2014 Jan;73(1):183–90.

4. van Vollenhoven RF, Petri MA, *et al.* Belimumab in the treatment of systemic lupus erythematosus: high disease activity predictors of response. *Ann Rheum Dis*. 2012 Aug;71(8):1343–9.

Notes

5. Dooley MA, Houssiau F, Aranow C, *et al;* BLISS-52 and -76 Study Groups. Effect of belimumab treatment on renal outcomes: results from the phase 3 belimumab clinical trials in patients with SLE. *Lupus*. 2013 Jan;22(1):63–72.

6. Condon MB, Ashby D, Pepper RJ, *et al*. Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids. *Ann Rheum Dis*. 2013 Aug;72(8):1280–6.

7. Bexelius C, Wachtmeister K, Skare P, *et al*. Drivers of cost and health-related quality of life in patients with systemic lupus erythematosus (SLE): a Swedish nationwide study based on patient reports. *Lupus*. 2013 Jul;22(8):793–801.

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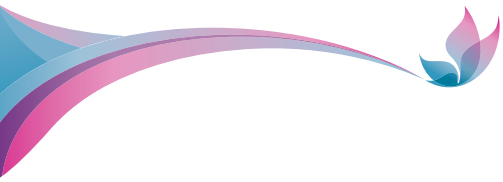

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