

4th Annual Meeting of the Lupus Academy

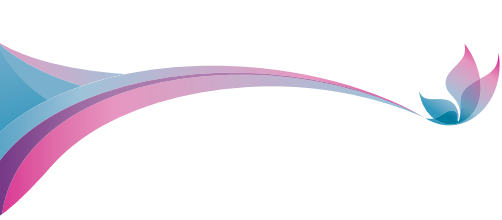
# Abstract Book

Marriott Park Hotel  
Rome, Italy  
**27th February to  
1st March 2015**



**LupusAcademy**

Communicate. Educate. Treat.



## European Accreditation Council for Continuing Medical Education (EACCME) Accreditation



The 4th Annual Meeting of the Lupus Academy is accredited by the European Accreditation Council for Continuing Medical Education (EACCME) Event Code: 11715, and is designated for a maximum of 11 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](http://www.uems.net).

### Participants from Europe

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### Participants from USA

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### Participants from Canada

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

### Participants 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

The content for this activity has been developed under the control of the meeting Chairs: Professor Andrea Doria, Padova, Italy, and Professor Roger Levy, Rio de Janeiro, Brazil, on behalf of the Steering Committee of the Lupus Academy. No supporting companies have had any influence over the presentation of any aspects of this meeting. For information about financial and in-kind support received to assist Lupus Academy in the delivery of its educational programme, please visit the website [www.lupus-academy.org](http://www.lupus-academy.org). CME compliance, accreditation and fulfilment has been facilitated by European CME Forum, on behalf of the Lupus Academy.



### Supporters

The Lupus Academy's education programme is supported through financial and in-kind support.

For the 2015 programme we would like to acknowledge the following organisations for their support through independent educational grants:

**GlaxoSmithKline, UCB (Gold supporters) and  
Bristol Myers Squibb (Bronze supporter).**

In-kind support has been provided by:



# Welcome

## Dear Friends and Colleagues,

We are delighted to welcome you to the 4th Annual Meeting of The Lupus Academy, which we hope will be one of the most rewarding and interactive learning environments you will participate in this year.

Now in its fourth year, the Lupus Academy continues to strengthen its commitment to providing high quality, insightful and clinically relevant education. With this we aim will support you as you strive to provide best-in-class patient care and improve patient outcomes in lupus.

This Annual Meeting, which has been accredited by the European Accreditation Council for CME (EACCME), aims to provide cutting edge insights into advances in global research and clinical practice in lupus and allied diseases. Delegate feedback from our previous annual meetings continues to guide us in selecting the topics and speakers you need to ensure translation of treatment advances into your clinical practice.

The scientific component of this programme, developed by our Steering Committee of 12 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.

This meeting will give you the opportunity to meet distinguished clinicians and scientists and, through the sharing of clinical experience, develop your knowledge in this fast moving therapeutic area.

We sincerely hope that this 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 Rome.

With kind regards,

The Lupus Academy Steering Committee

### **Professor Roger A. Levy**

Lupus Academy Course Director  
and co-Chairman (2014–2015)






### **Professor Andrea Doria**

Lupus Academy Meeting Programme Director  
and co-Chairman (2014–2015)

Professor Zahir Amoura; Professor Ricard Cervera; Professor Thomas Dörner; Professor Richard Furie; Professor Bevra Hahn;  
Professor David Isenberg; Professor Munther Khamashta; Professor Sandra Navarra; Professor Murray Urowitz;  
Professor Ronald van Vollenhoven

Friday 27th February			Page
18:00	Opening Address	Andrea Doria ( <i>Italy</i> )	
<b>Keynote Lecture</b>		<i>Moderators: Andrea Doria (Italy) &amp; Roger A. Levy (Brazil)</i>	
18:20	My ten commandments in the management of lupus	Murray B. Urowitz ( <i>Canada</i> )	24
<b>Discussion Forum: Issues and Answers</b>		<i>Moderators: Munther A. Khamashta (UK) &amp; Ricard Cervera (Spain)</i>	
19:00–20:30	Vitamin D and SLE: To D or not to D? The matter of the debate (15 minutes) Pros: (20 minutes + 10 minutes rebuttal) Cons: Ian Bruce (UK) (20 minutes + 10 minutes rebuttal) Discussion (15 minutes)	Ricard Cervera ( <i>Spain</i> )  Yehuda Shoenfeld ( <i>Israel</i> ) Ian Bruce ( <i>UK</i> )	26
20:30	Welcome Dinner		

Saturday 28th February			Page
07:00	Breakfast		
<b>Plenary I: New Aspects in the Diagnosis and Management of SLE</b>		<i>Moderators: Bevra H. Hahn (USA) &amp; Zahir Amoura (France)</i>	
08:30	Early lupus: how early is early?	Andrea Doria ( <i>Italy</i> )	30
09:00	Treat-to-target: issues and answers	Ronald F. van Vollenhoven ( <i>Sweden</i> )	32
09:30	Biomarkers in SLE: how useful are they?	David A. Isenberg ( <i>UK</i> )	34
10:00	Discussion		
10:30	Coffee		

Case Study Workshops (AM)				
11:00	<i>Moderator: Zahir Amoura (France)</i> Investigating the febrile lupus patient		Sandra V. Navarra ( <i>Philippines</i> ) & Fabrizio Conti ( <i>Italy</i> )	38
11:00	<i>Moderator: Ricard Cervera (Spain)</i> Haematologic challenges: cytopaenias		Michelle Petri ( <i>USA</i> ) & David A. Isenberg ( <i>UK</i> )	40
11:00	<i>Moderator: Roger A. Levy (Brazil)</i> CNS lupus		Munther A. Khamashta ( <i>UK</i> ) & Angela Tincani ( <i>Italy</i> )	42
11:00	<i>Moderator: Murray B. Urowitz (Canada)</i> Difficult skin disease		Annegret Kuhn ( <i>Germany</i> ) & Marta Mosca ( <i>Italy</i> )	44
11:00	<i>Moderator: Bevra H. Hahn (USA)</i> Lupus nephritis		Richard A. Furie ( <i>USA</i> ) & Gabriella Moroni ( <i>Italy</i> )	46
12:30	Lunch			

<b>Saturday 28th February <i>continued</i></b>			Page
<b>Case Study Workshops (PM)</b>			
13:30	<i>Moderator: Zahir Amoura (France)</i> Investigating the febrile lupus patient		Sandra V. Navarra ( <i>Philippines</i> ) & Fabrizio Conti ( <i>Italy</i> ) 38
13:30	<i>Moderator: Ricard Cervera (Spain)</i> Haematologic challenges: cytopaenias		Michelle Petri ( <i>USA</i> ) & David A. Isenberg ( <i>UK</i> ) 40
13:30	<i>Moderator: Roger A. Levy (Brazil)</i> CNS lupus		Munther A. Khamashta ( <i>UK</i> ) & Angela Tincani ( <i>Italy</i> ) 42
13:30	<i>Moderator: Murray B. Urowitz (Canada)</i> Difficult skin disease		Annegret Kuhn ( <i>Germany</i> ) & Marta Mosca ( <i>Italy</i> ) 44
11:00	<i>Moderator: Bevra H. Hahn (USA)</i> Lupus nephritis		Richard A. Furie ( <i>USA</i> ) & Gabriella Moroni ( <i>Italy</i> ) 46
15:00	Coffee		
<b>Plenary II: Clinical Manifestations and Management</b>		<i>Moderators: David A. Isenberg (UK) &amp; Ronald F. van Vollenhoven (Sweden)</i>	
15:30	New trends in the treatment of nephritis		Gabriella Moroni ( <i>Italy</i> ) 48
16:00	Renal transplantation in SLE: outcomes and prognostic factors		Federico Oppenheimer ( <i>Spain</i> ) 50
16:30	Osteonecrosis and osteoporosis in SLE: early diagnosis and prevention		Bevra H. Hahn ( <i>USA</i> ) 52
17:00	Discussion		
17:30	<b>Close</b>		
<b>Sunday 1st March</b>			Page
07:00	Breakfast with the Professor		Steering Committee (x11)
<b>Plenary III: From Conception Through Adolescence: Issues in SLE and APS</b>		<i>Moderators: Murray B. Urowitz (Canada) &amp; Ricard Cervera (Spain)</i>	
08:00	Planning and managing pregnancy in SLE		Munther A. Khamashta ( <i>UK</i> ) 54
08:30	Outcomes in children from mothers with SLE and APS		Angela Tincani ( <i>Italy</i> ) 56
09:00	Transition of childhood onset SLE into adulthood		Alberto Martini ( <i>Italy</i> ) 58
09:30	Discussion		
10:00	Coffee		
<b>Plenary IV: Management of SLE and APS: Today and Tomorrow</b>		<i>Moderators: Gianfranco Ferraccioli (Italy) &amp; Sandra V. Navarra (Philippines)</i>	
10:15	Future treatments for APS		Roger A. Levy ( <i>Brazil</i> ) 60
10:45	Plasma exchange and IVIG in SLE and APS		Ricard Cervera ( <i>Spain</i> ) 62
11:15	Managing SLE today and in 2025		Richard A. Furie ( <i>USA</i> ) 64
11:45	Discussion		
12:15	<b>Summary and close</b>		Roger A. Levy ( <i>Brazil</i> ) & Andrea Doria ( <i>Italy</i> )

## Biographies



**Professor Zahir Amoura, MD, MSc**  
Pitié Salpêtrière 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

#### Grants/Research

#### Support:

Amgen; Eli Lilly; GSK; Roche

#### Consultant/Advisor:

Amgen; Eli Lilly; GSK

#### Meeting Honorarium/

Expenses: Actelion; GSK; LFB

*Professor Amoura is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th Annual Meeting programme and materials.*



**Professor Ian N. Bruce, MD, FRCP**  
University of Manchester, UK

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 Musculoskeletal Biomedical Research Unit and Deputy Director of the NIHR/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.

Professor Bruce is Chair of the Systemic Lupus International Collaborating Clinics (SLICC), is a member of the British Isles Lupus Assessment Group and leads the BILAG Biologics Register. He participates in a number of national and international multicentre studies that are seeking to refine our understanding of SLE. He also leads a Lupus 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. Professor Bruce's research is focused on the association between inflammatory rheumatic diseases and premature atherosclerosis/coronary heart disease as well as stratified medicine in SLE.

### Disclosures

#### Grants/Research

Support: Genzyme/Sanofi; GSK; Roche; UCB

#### Consultant/Advisor Fees:

Eli Lilly; GSK; Medimmune; Merck Serono; UCB

#### Participation in Speakers' Bureau:

GSK; UCB

#### Meeting Honorarium/

Expenses: GSK; Roche; UCB



**Professor Ricard Cervera, MD, PhD, FRCP**  
Hospital Clinic, Barcelona, Catalonia, Spain

**Disclosures**

Consultant/Advisor Fees:  
GSK

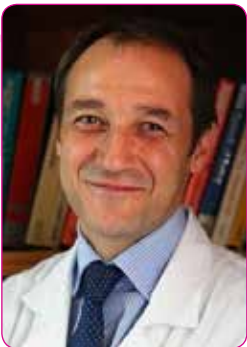
*Professor Cervera is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th Annual Meeting programme and materials.*

Ricard Cervera is Head of the Department of Autoimmune Diseases (which he co-founded in 1995), at Hospital Clinic, Barcelona. He is also Team Leader of the Research Team 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 Masters 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, 60), 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'.



**Professor Fabrizio Conti, MD, PhD**  
Sapienza University of Rome, Rome, Italy

**Disclosures**

Consultant/Advisor Fees:  
Regeneron

Fabrizio Conti is an Associate Professor of Rheumatology at the Sapienza University of Rome, Italy. Professor Conti qualified in Medicine and Surgery from Sapienza University of Rome, Italy, and gained his PhD in Experimental Immunology.

Since September 2008, Professor Conti has been the manager of the Lupus Clinic, Policlinico Umberto I, Sapienza University of Rome, Italy. He is a fellow of the Italian Society of Rheumatology (SIR), a member of the Standing Committee of SIR and a member of the SIR study group on neuropsychiatric systemic lupus erythematosus.

Professor Conti was visiting Professor at the Arthritis Research UK Centre for Epidemiology, Institute of Inflammation and Repair, University of Manchester. He participates in a number of national and international multicentre studies on neuropsychiatric and renal manifestations in systemic lupus erythematosus (SLE). Professor Conti has led various clinical trials on autoimmune rheumatic diseases, including SLE.

Professor Conti's major research focus is on SLE as well as on antiphospholipid syndrome, rheumatoid arthritis and other autoimmune rheumatic diseases (aetiopathogenesis, clinical features and treatment). Professor Conti has authored over 100 publications on issues relating to SLE and other autoimmune rheumatic diseases.

## Biographies



### Professor Andrea Doria, MD

University of Padova, Italy

#### Disclosures

##### Consultant/Advisor:

Eli Lilly; GSK; Pfizer

##### Speakers' Bureau:

Eli Lilly; GSK

*Professor Doria is Programme Director and co-Chairman of the Lupus Academy (2015) and has been involved in the planning and development of the 4th Annual Meeting programme and materials.*

Andrea Doria is 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 the Italian Society of Rheumatology (SIR) and he was Council member of SIR (2007–2010) and of the Italian College of Rheumatology (CRO) (1999–2005). He is also a member of the 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 tertiary 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 Thomas Dörner, MD**  
Charité University Hospitals Berlin, Germany

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 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, the 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.

**Disclosures**

Professor Dörner is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th Annual Meeting programme and materials.



**Professor Gianfranco Ferraccioli, MD**  
Catholic University of the Sacred Heart, Rome, Italy

Gianfranco Ferraccioli is Professor of Rheumatology, Director of the Division of Rheumatology and Internal Medicine–CIC, Chairman of the Institute of Rheumatology and Affine Sciences, and Postgraduate School of Rheumatology at the School of Medicine of the Catholic University of the Sacred Heart, in Rome, Italy. Winner of the 2° Ogrzyzlo Fellowship Award of the Canadian Society of Rheumatology, he trained at the Division of Clinical Immunology and Rheumatology at McGill University in Montreal 1981–1982. He became research associate at the Division of Rheumatology of the University of Parma in 1983 and moved to the Department of Internal Medicine at the University of Udine in 1992. He became Professor of Rheumatology at the same university in 1999, and Director of the Division of Rheumatology and Chairman of the Department of Internal Medicine at the University of Udine between 2000 and 2003, until he took up his current post.

His specific interests include clinical–biological prognostic indexes in rheumatoid arthritis;

molecular mechanisms of B cells as biomarkers in autoimmune diseases, rheumatoid arthritis, systemic lupus erythematosus (SLE) and systemic sclerosis, and their clonal expansion in Sjögren's syndrome and cryoglobulinemia. Another focus of his research is on biomarkers in SLE, connective tissue diseases and rheumatoid arthritis, and innovative therapeutic approaches for autoimmune rheumatic diseases. He has published 330 papers in international peer review journals.

Professor Ferraccioli has served on a long list of committees and is currently a member of the European League Against Rheumatism (EULAR) as well as the Kunkel Society, Rockefeller University, USA and the Italian Society of Rheumatology.

He has been part of the group of EULAR scientists that established the Recommendation for an Early Diagnosis and Therapy of an Early Rheumatoid Patient and also part of the group that defined the new classification criteria for rheumatoid arthritis. He is Country Leader of the METEOR group and BIODAM.

**Disclosures**

**Grants/Research**

**Support:** BMS; Pfizer; Roche

**Participation in Speakers'**

**Bureau:** AbbVie; BMS; MSD; Pfizer; Roche; UCB

# Biographies



## Professor Richard A. Furie, MD

Hofstra North Shore-LIJ School of Medicine, New York, USA

### Disclosures

#### Grants/Research

**Support:** Amgen; Anthera; Biogen Idec; BMS; Boehringer-Ingelheim; Celgene; Dynavax; Eli Lilly; Exagen; Genentech/Roche; GSK; Human Genome Sciences; Medimmune; NIAID; Novartis; NovoNordisk; Pfizer; Questcor Pharmaceuticals; Rigel; Takeda; UCB

#### Consultant/Advisor:

Biogen Idec; BMS; Celgene; Eli Lilly; EMD Serono; Exagen; Genentech/Roche; GSK; Medimmune; Merck; Novartis; NovoNordisk; Onyx; Pfizer; Questcor Pharmaceuticals; Rigel; Takeda; UCB

#### Investigator:

Amgen; Anthera; Biogen Idec; BMS; Boehringer-Ingelheim; Celgene; Dynavax; Eli Lilly; Exagen; Genentech/Roche; GSK; Human Genome Sciences; Medimmune; NIAID; NovoNordisk; Pfizer; Rigel; UCB

#### Committee Member:

American College of Rheumatology; Lupus Foundation of America; Lupus Alliance of America; SLE Foundation; Alliance for Lupus Research

*Professor Furie is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th Annual Meeting programme and materials.*

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 several decades, have focused on patient care, physician education and clinical research in the area of anti-rheumatic 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 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 of 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 Bevra H. Hahn, MD**  
University of California, Los Angeles, USA

**Disclosures**

**Advisor:**

BMS; Exagen; Eli Lilly

*Professor Hahn is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th Annual Meeting programme and materials.*

Bevra Hahn is Distinguished 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.



**Professor David A. Isenberg, MD, FRCP, FAMS**  
University College London, UK

**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 4th Annual Meeting programme and materials.*

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.

## Biographies



**Professor Munther A. Khamashta, MD, PhD, FRCP**  
St. Thomas' Hospital, London, UK

### Disclosures

#### Grants/Research

**Support:** Bayer

#### Consultant/Advisor:

GSK; INOVA Diagnostics;  
Medimmune/AstraZeneca;  
UCB

#### Meeting Honorarium/

**Expenses:** GSK; INOVA  
Diagnostics; Medimmune/  
AstraZeneca

*Professor Khamashta is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th 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.



(Photo: Peter Pulkowski)

**Professor Annegret Kuhn, MD, MBA**

Interdisciplinary Center for Clinical Trials (IZKS), University Medical Center Mainz, Germany

**Disclosures**

Grants/Research

Support: GSK; Biogen

Idec

Consultant/Advisor: GSK

Annegret Kuhn is Head of the Interdisciplinary Study Center for Clinical Trials (IZKS) at the University Medical Center of the Johannes Gutenberg University of Mainz, Germany. Professor Kuhn acquired her Doctor of Medicine at the University of Düsseldorf, Germany, where she also received her German Board Certification for Dermatology and Venereology and her Qualification as University Lecturer. In 1999, Professor Kuhn was awarded a Lise-Meitner Fellowship by the Ministry for School and Education of North Rhine-Westphalia and in 2004 she was awarded a Heisenberg Fellowship by the German Research Foundation (DFG). She has worked in several University Departments and Scientific Institutions, such as the Max-Planck-Institute for Molecular Biomedicine, Münster, and the German Cancer Research Center, Heidelberg, Germany.

Her major clinical and scientific interest is translational immunology and human autoimmune diseases. Professor Kuhn is particularly interested in the pathogenesis, diagnosis, classification and

treatment of cutaneous lupus erythematosus. The IZKS performs translational research and transfers technologies from basic science to pharmaceutical application by conducting investigator-initiated and sponsor-initiated trials according to the guidelines for Good Clinical Practice. Professor Kuhn is Chair of the European Society of Cutaneous Lupus Erythematosus (EUSCLE) and member of several German and international medical societies.

Professor Kuhn is interested in Health Care and Science Management. In 2013, she completed the MBA Health Care Management Program at the University of Bayreuth, Germany. She is also member of various editorial and clinical advisory boards and reviewer of several clinical and scientific peer reviewed journals. She has published widely in high impact journals, such as *Nature Medicine*, *Nature Reviews Rheumatology*, *Annals of the Rheumatic Diseases*, and the *Journal of Investigative Dermatology*, including more than 150 original and review articles.

## Biographies



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

### Disclosures

#### Grants/Research

**Support:** GSK; Roche; Servier

#### Consultant/Advisor:

AbbVie; GSK; Pfizer; Roche

#### Speakers' Bureau:

AbbVie; Janssen; Roche

#### Meeting Honorarium/

**Expenses:** AbbVie; GSK; Janssen; Pfizer

*Professor Levy is Course Director and co-Chairman of the Lupus Academy (2015) and has been involved in the planning and development of the 4th 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, Sjogren's syndrome and pregnancy in rheumatic patients. He has published 110 articles in medical journals, over 200 abstracts, four books, 20 book chapters and has lectured in many countries.



**Professor Alberto Martini, MD**  
University of Genoa, Italy

Alberto Martini is Professor of Pediatrics at the University of Genoa and Director of Pediatria II Reumatologia (EULAR Centre of Excellence in Rheumatology 2008-13) and of the Department of Pediatrics in the G Gaslini Institute, Genoa, Italy.

Professor Martini is author of more than 350 papers in peer reviewed journals related to paediatric rheumatic diseases. His h-index (Google-scholar) is 66.

**Disclosures**

**Grants/Research**

**Support:** Abbott; Aventis; BMS; Francesco Angelini S.P.A.; GSK; Janssen Biotech Inc; Novartis; Pfizer Inc; Roche; Sanofi Aventis; Schwarz Biosciences GmbH

**Consultant/Advisor Fees:**

BMS; Centocor R&D; GSK; Novartis; Pfizer Inc; Roche; Sanofi Aventis; Schwarz Biosciences GmbH; I declare that the Gaslini Hospital which is the public Hospital where I work as full time employee has received contributions to support the PRINTO research activities from the industries above mentioned ([www.printo.it](http://www.printo.it)).

**Participation in Speakers' Bureau:**

Abbott; AbbVie; Amgen; Astellas; Biogen Idec; Boehringer; BMS; Italfarmaco; Janssen; MedImmune; Novartis; Novo Nordisk; Pfizer; Roche; Sanofi; Servier.

Professor Martini is President of the Paediatric Rheumatology European Society (PRES), Chairman of the Pediatric Rheumatology International Trial Organization (PRINTO), Chairman of the EULAR Standing Committee on Paediatric Rheumatology, Past President of the Italian Council of Academic Professor of Paediatrics (2008–2012). He is co-Editor of *Clinical and Experimental Rheumatology* and *Pediatric Rheumatology* and member of the Editorial board of *Annals of the Rheumatic Diseases*.

## Biographies



### **Dr Gabriella Moroni, MD**

Division of Nephrology and Dialysis, (IRCCS) Ospedale Maggiore, Milan, Italy

#### **Disclosures**

Consultant/Advisor Fee:  
GSK

Gabriella Moroni is Consultant Nephrologist and Head of the ward of the Unit of Nephrology, Dialysis and Renal Transplant of Fondazione Ospedale Maggiore (IRCCS) Milan. Dr Moroni graduated (*magna cum laude*) from Medical School, University of Pavia, in 1981 before completing a postgraduate degree (*magna cum laude*) in Occupational Medicine in 1985 at the same university and then a postgraduate degree (*magna cum laude*) in Nephrology at the University of Modena in 1989.

Dr Moroni has been an invited speaker to numerous international meetings, is co-author of more than 80 papers and book chapters, and sits on the Editorial Boards of *Lupus* and the *Journal of Nephrology*. She is an investigator in several clinical trials including patients with Lupus Nephritis.

Dr Moroni has a longstanding experience in the histological and clinical management of lupus nephritis, renal systemic vasculitis, and renal involvement in other connective tissue diseases. Her other main scientific interests include primitive and secondary glomerulonephritis in particular evaluation of their renal histology, treatment and prognosis, recurrence and *de novo* glomerular diseases of kidney transplant, idiopathic and secondary retroperitoneal fibrosis.



### **Professor Marta Mosca, MD, PhD**

University of Pisa, Italy

#### **Disclosures**

Meeting Honorarium/  
Expenses: Eli Lilly; GSK;  
UCB  
Speakers' Bureau: GSK

Marta Mosca is Associate Professor of Rheumatology at the Department of Internal Medicine, University of Pisa and Chief of the Rheumatology Unit of the Azienda Ospedaliera Universitaria Pisana. Professor Mosca graduated from Medical School at the University of Pisa in 1992.

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 Mosca's research interests are represented by systemic lupus erythematosus (SLE) and undifferentiated connective tissue diseases. 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 Sandra V. Navarra, MD, FPCP, FPRA**  
University of Santo Tomas, Manila, Philippines

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 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 Adviser. 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), the first Asian Lupus Summit (November 2012), and the Asian Lupus Summit by the Lupus Academy (March–April 2014), all held in the Philippines.

**Disclosures**

**Grants/Research**

**Support:** GSK; Pfizer

**Consultant/Advisor:** GSK; Pfizer; Roche

**Speakers' Bureau:** GSK; Pfizer; Roche

**Meeting Honorarium/**

**Expenses:** Pfizer

*Professor Navarra is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th Annual Meeting programme and materials.*



**Dr Federico Oppenheimer, MD, PhD**  
Hospital Clinic, Barcelona, Catalonia, Spain

Federico Oppenheimer has been Chief of the Renal Transplant Unit at Hospital Clinic, Barcelona, where he has worked for over 30 years, and very recently has been appointed to the position of Director of the Nephrology and Urology Institute at the same hospital. Dr Oppenheimer graduated from the Faculty of Medicine at the Universidad Autónoma de Barcelona in 1978, and then completed postgraduate training in Nephrology at the Hospital Clinic, Barcelona.

Dr Oppenheimer is a member of several professional societies including Societat Catalana de Trasplantament, Sociedad Española de Trasplantes, The Transplantation Society and the European Society for Organ Transplantation. He has been the President of The Societat Catalana de Trasplantament and Council Member of the European Society for Organ Transplantation and Sociedad Española de Trasplantes.

Dr Oppenheimer is a reviewer for major international transplant journals. He has published many articles in peer-reviewed journals and is a Principal Investigator in numerous clinical studies. His current research interest includes the use of new immunosuppressants, ischaemia reperfusion injury, ABO-incompatible transplantation and desensitisation strategies.

**Disclosures**

**Consultant/Advisor:**

Astellas; Novartis; Sandoz; Pfizer

**Speakers' Bureau:**

Astellas; Novartis

## Biographies



### Professor Michelle Petri, MD, MPH

Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

#### Disclosures

##### Grants/Research

**Support:** Anthera; GSK; MedImmune; Pfizer; UCB

##### Consultant/Advisor:

Pfizer; UCB

Michelle Petri is a Professor of Medicine in the Division of Rheumatology and Director of the Lupus Center at the Johns Hopkins University School of Medicine and Johns Hopkins Hospital in Baltimore, Maryland. She earned her medical degree from Harvard Medical School in Boston, Massachusetts, and completed her internship and residency in Internal medicine at Massachusetts General Hospital. Thereafter, Professor Petri completed her Postdoctoral Fellowship in Allergy, Immunology, and Rheumatology at the University of California, San Francisco. She subsequently earned her master's in Public Health and Epidemiology from Johns Hopkins University Bloomberg School of Public Health.

Professor Petri's research focuses on several aspects of systemic lupus erythematosus (SLE), including atherosclerosis, antiphospholipid syndrome (APS), lupus nephritis and pregnancy. The Hopkins Lupus Cohort, started by Professor Petri in 1987, is a longitudinal study of the incidence and pathogenesis of thrombotic events and coronary artery disease in SLE. Its serum and plasma bank is a useful resource for

other SLE-related research. The Hopkins Lupus Pregnancy Center, of which Professor Petri is a Co-Director, has a database of over 400 pregnant patients, providing information on lupus activity, antiphospholipid tests and pregnancy outcomes. As part of the Systemic Lupus International Collaborating Clinics, Hopkins participates in studies of atherosclerosis, malignancy and neuropsychiatric lupus. Professor Petri has served as study Chair or Principal Investigator for several of these studies on the SLE patient population.

Professor Petri has authored over 300 papers and chapters on SLE and APS. She is on the editorial board of *Arthritis and Rheumatism*, *The Journal of Rheumatology*, and *Journal of Clinical Rheumatology*. Dr. Petri serves as an ad hoc reviewer for *Annals of Internal Medicine*, *The American Journal of Medicine*, *Medicine*, *The Lancet*, *JAMA*, *Southern Medical Journal* and *Fertility and Sterility*. She served on the Medical Advisory Board of the Lupus Foundation of America, is a member of the American College of Rheumatology, and was Chair of the Lupus Now Education Program.



**Professor Yehuda Shoenfeld, MD, FRCP, MaACR**  
Sheba Medical Center, Tel Hashomer, Tel Aviv University, Israel

**Disclosures**

None

Yehuda Shoenfeld is the founder and head of the Zabludowicz Center for Autoimmune Diseases, at the Sheba Medical Center, which is affiliated to the Sackler Faculty of Medicine in Tel-Aviv University in Israel. Professor Shoenfeld is also the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases at the Tel-Aviv University.

Professor Shoenfeld's clinical and scientific works focus on autoimmune and rheumatic diseases, and he has published more than 1750 papers in journals such as *New Eng J Med*, *Nature*, *The Lancet*, *Proc Nat Acad Sci*, *J Clin Invest*, *J Immunol*, *Blood*, *FASEB*, *J Exp Med*, *Circulation*, *Cancer* and others. His articles have had over 45,000 citations. He has written more than 350 chapters in books, and has authored and edited 35 books, some of which became cornerstones in science and clinical practice, such as "The Mosaic of Autoimmunity", "Infections and Autoimmunity", and the textbooks "Autoantibodies" and "Diagnostic criteria of autoimmune diseases", all of which were published by Elsevier and sold thousands of copies.

Professor Shoenfeld is on the editorial boards of 43 journals in the fields of rheumatology and autoimmunity and is the founder and the editor of the *IMAJ (Israel Medical Association Journal)*,

the representative journal of science and medicine in the English language in Israel, and also is the founder and Editor of *Autoimmunity Reviews* (Elsevier) (Impact factor 7.1) and co-Editor of the *Journal of Autoimmunity* (Impact factor 7.0). For the past twenty years Yehuda has been the Editor of "Harefuah" – *The Israel Journal in Medicine* (Hebrew).

Professor Shoenfeld received the EULAR prize in 2005, in Vienna, Austria: "The infectious etiology of anti-phospholipid syndrome", and received a gold medal from the Slovak Society of Physicians for his contribution to Israel–Slovakia collaboration (March 2006). He is also an honorary member of the Hungarian Association of Rheumatology and the Royal Society of Physicians (UK). In UC Davis, USA, Professor Shoenfeld received the Nelson's Prize for Humanity and Science for 2008. In 2009 he was honoured as *Doctoris Honoris Causa*, from Debrecen University (Hungary), and from 2009 an honorary member of the Slovenian National Academy of Sciences. He was recently awarded a Life Contribution Prize in Internal Medicine in Israel, 2012 as well as the ACR Master Award in 2013.

Professor Shoenfeld has educated a long list of students, with >27 becoming heads of departments and institutes.

## Biographies



### Professor Angela Tincani, MD

Brescia General Hospital and University of Brescia, Italy

#### Disclosures

##### Grants/Research

**Support:** AbbVie; Actelion;  
BMS; IL Pharma; MSD;  
Pfizer

##### Consultant/Advisor:

AbbVie; GSK; Pfizer; UCB

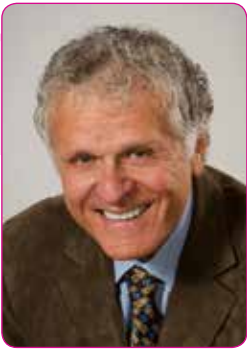
##### Meeting Honorarium/

**Expenses:** BMS; GSK;  
Pfizer

Angela Tincani is Professor of Rheumatology, University of Brescia and Head of Rheumatology and Clinical Immunology, Brescia General Hospital, Italy.

After receiving her MD from the University of Milan in 1974, Professor Tincani continued postgraduate studies in Allergology and Clinical Immunology (1977), Haematology (1979) and Rheumatology (1983), before taking up several senior positions in Rheumatology and Clinical Immunology. Professor Tincani has served on many international committees for research and education in lupus, most recently the EULAR committee “Points to consider for use of antirheumatic drugs before pregnancy and during pregnancy and lactation” (2013–14) and, as co-Chair, “Recommendations for the management of family planning, assisted reproduction, gestation, delivery and menopause in patients with Systemic Lupus Erythematosus and Antiphospholipid Syndrome” (2014–15).

In the last 10 years, Professor Tincani has participated in 10 (Phase II–III) studies of lupus. Her main clinical and research interests include pathogenesis, diagnosis and treatment of systemic autoimmune diseases, problems connected to pregnancy in patients with rheumatic diseases, evolution of autoantibody determination, and reliability and clinical significance of emerging new technology. Professor Tincani is a widely published author. She is the regional Editor (Europe) of the journal *Autoimmunity* and sits on the Editorial Boards of *Clinical and Experimental Rheumatology* and *Autoimmunity Reviews*.



**Professor Murray B. Urowitz, MD**  
University of Toronto, Canada

**Disclosures**

**Grants/Research**

**Support:** GSK; Sanofi

**Consultant/Advisor:** BMS; GSK; Teva; UCB

**Meeting Honorarium/**

**Expenses:** GSK

*Professor Urowitz is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th Annual Meeting programme and materials.*

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 1974–1987 and Physician in Chief from 1987–1995. 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

#### Grants/Research

**Support:** AbbVie; BMS; GSK; Pfizer; Roche; UCB

#### Consultant/Advisor:

AbbVie; Biotest; BMS; Crescendo; GSK; Janssen; Eli Lilly; Merck; Pfizer; Roche; UCB; Vertex

*Professor van Vollenhoven is a founding member of the Lupus Academy Steering Committee and has been involved in the planning and development of the 4th Annual Meeting programme and materials.*

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

He received his MD 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 residency (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 the Karolinska University Hospital and Associate Professor of Rheumatology; and 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 biological and immunomodulatory treatments for the rheumatic diseases. With his co-workers, he has established the Stockholm registry for biological 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 trial. He has published over 240 original papers, book chapters and reviews, and 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 he is an honorary member of several rheumatological societies. He is the Editor-in-Chief of *Lupus Science & Medicine*, Chair-elect of the EULAR Standing Committee on Clinical Affairs, member of many editorial boards, past-Chair of the Swedish Rheumatology Society Professors' Council, co-founder of the IRBIS registry for biologics in SLE, the CERERRA registries collaboration and the NORD-STAR collaboration for Nordic trials in the rheumatic diseases, and the initiator of the Treat-to-Target-in-SLE initiative. Professor van Vollenhoven lives just north of Stockholm with his wife and children aged 19 and 15. Outside his professional life he is an avid classical pianist.



Keynote Lecture

Moderators: Professor Andrea Doria (Italy) & Professor Roger A. Levy (Brazil)



## Professor Murray B. Urowitz, MD

University of Toronto, Canada

### My ten commandments in the management of lupus

Systemic lupus erythematosus is a complex multisystem disease with diverse phenotypes among patients, which are variable over time and have variable response to standard of care. Thus, hard specific goals for the management of lupus are difficult to define. However, general principles of management both 'thou shalt' and 'thou shalt not' can be developed.

My ten commandments in the management of lupus are as follows:

1. Classify/diagnose the patient properly
  - a. Merits of ACR & SLICC criteria
2. Phenotype the disease
  - a. Clinically
  - b. Disease activity state
  - c. Pathogenic mechanism
  - d. Biomarkers
3. Establish a treatment target
  - a. Choose a target
4. Prescribe an antimalarial
  - a. For all
5. Consider a defined corticosteroid dose/duration approach
  - a. Define a treatment algorithm
  - b. Beware of damage accrual
6. Add an immunosuppressive agent
  - a. When? Which? How long?
  - b. Combination therapy
  - c. Withdrawal possibilities
7. Consider the newer biologics
  - a. A newer possibility
8. Monitor for and treat the comorbidities
  - a. Cardiovascular comorbidities
  - b. Cognitive dysfunction
  - c. Bone disease
9. Don't forget patient-related outcomes
  - a. SF-36 and LUPUSQoL
10. Monitor patients regularly: How often? What measures?
  - a. Guidelines

Professor Urowitz shall present commentaries to be considered for each of the commandments.

#### Learning Objectives

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

- Appreciate the merits of key diagnostic criteria in the classification and diagnosis of lupus.
- Identify disease characteristics and treat to target, with due consideration of the treatment options available today.
- Better monitor and manage comorbid disease, and monitor patients' quality of life using health outcome measures.







**Professor Yehuda Shoenfeld, MD, FRCP, MaACR**  
Sheba Medical Center, Tel Hashomer, Tel Aviv University, Israel

## Vitamin D and SLE: To D or not to D? (Pros)

### References

1. Amital H, Szekanecz Z, Szucs G, et al. Serum concentrations of 25-OH vitamin D in patients with systemic lupus erythematosus (SLE) are inversely related to disease activity: is it time to routinely supplement patients with SLE with vitamin D? *Ann Rheum Dis* 2010; 69(6): 1155-7.
2. Amson Y, Amital H, Shoenfeld Y. Vitamin D and autoimmunity: new aetiological and therapeutic considerations. *Ann Rheum Dis* 2007; 66(9): 1137-42.
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4. Toubi E, Shoenfeld Y. The role of vitamin D in regulating immune responses. *Isr Med Assoc J* 2010; 12(3): 174-5.
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During recent decades numerous studies have established vitamin D's immune regulatory and anti-inflammatory properties in addition to its classical ones.<sup>1-3</sup> Most of the known biological effects of vitamin D are mediated through the vitamin-D receptor (VDR), vitamin-D binding protein and the cytochrome p450 27B1 (CYP27B1) hydroxylase. The immune-modulation properties of vitamin D are gained by its effect on cells of both the innate and adaptive immune systems, which harbor VDRs. The main components of the innate immune response that are affected by vitamin D include dendritic cells (DCs), macrophages and Toll-like receptors (TLRs).

*In vitro*, 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) suppresses the differentiation of monocytes into DCs as well as their capacity to secrete the Th1-polarizing cytokine interleukin (IL)-12. Inhibition of IL-12 secretion is achieved through the direct interaction of 1,25(OH)2D3 bound to VDR with nuclear factor kappa B (NFκB), suppressing NFκB induced transcription of IL-12. Treatment of DCs with 1,25(OH)2D3 leads to

a marked up-regulation of immunoglobulin-like transcripts-3 (ILT3), and ILT3 expressed by DCs is involved in induction of CD4 + forkhead family transcriptional factors (Foxp3) + regulatory T cells. Thus, vitamin-D induced DCs with a tolerogenic phenotype inhibit DC-dependent T-cell activation and favour the induction of regulatory, rather than effector T cells. Furthermore, TLR (mainly TLR2 and 4) expression on monocytes is inhibited by 1,25(OH)2D3, leading to decreased response to bacteria.<sup>4</sup> There were several studies in 2014 that showed low vitamin D in patients with SLE<sup>1-4</sup> and APS.<sup>5</sup> In many of these studies, this was correlated with disease expression and activity, including atherosclerosis,<sup>1</sup> both in adults and children; and in one, repair of endothelial damage was ameliorated. The results of interventional studies are limited, yet promising. There is a need for more experiments to confirm the beneficial effects of vitamin D in SLE.

Conclusion: Vitamin-D deficiency is common among patients with SLE and APS and is associated with clinically active events.

### Learning Objectives

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

- Identify an association between vitamin-D levels and SLE (APS) activity, expression, exacerbations.
- Recognise the mechanisms by which vitamin D may affect autoimmunity in general and SLE/APS activity specifically.
- Understand the effect of vitamin D on tissue factor in APS.
- Decide when to/or not to treat with vitamin D.
- Appreciate the benefits of vitamin D: Cheap, no side effects, many theoretical beneficial effects, no physicians' prescription.





**Professor Ian N. Bruce, MD, FRCP**  
University of Manchester, UK

## Vitamin D and SLE: To D or not to D? (Cons)

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1. Theodoratou E, Tzoulaki I, Zgaga L, Ioannidis JP. Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. *BMJ* 2014; 348: g2035.
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3. Petri M, Bello KJ, Fang H, Magder LS. Vitamin D in systemic lupus erythematosus: modest association with disease activity and the urine protein-to-creatinine ratio. *Arthritis Rheum* 2013; 65(7): 1865-71.
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In the past 2–3 decades there has been increasing interest in the role of vitamin D in the aetiology and pathogenesis of systemic lupus erythematosus (SLE). Interest in vitamin-D status is not confined to SLE. Indeed, a recent meta-analysis examined 137 different health outcomes and their putative association with vitamin D!<sup>1</sup> In the context of lupus, observational studies have suggested low vitamin D is associated with an increased risk of future development of SLE. Similarly, a range of observational studies of varying size and quality have suggested that low vitamin-D status is associated with higher disease activity, increased cardiovascular risk and higher proteinuria.<sup>2-4</sup> *In vitro* studies have also found effects of vitamin D that are of potential relevance to the aetiopathogenesis of lupus.

Such observational data does, however, need to be scrutinised before we rush into recommending vitamin D supplementation for everyone with SLE

and, importantly, we need to be clear in how we educate our patients so as not to over claim the health benefits of vitamin D supplementation. Also, no intervention is free from adverse effects. Clinical trials in SLE do not show convincing effects of vitamin D on disease activity or flares and non-randomised studies suggest (if anything) only very modest effects on disease expression.<sup>3,5</sup>

Translating this to the routine clinical setting, there is no robust evidence to support any claims of health benefits of vitamin D beyond its use in bone health. Larger scale randomised trials are needed to determine if there are clear unequivocal benefits of widespread vitamin D supplementation in lupus as well as to inform the correct dosing regimens, etc. Until then, we owe it to our patients to exercise caution in recommending further medical interventions/supplements in a condition where polypharmacy carries its own burden for patients.

### Learning Objectives

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

- Appreciate how vitamin-D research follows the typical pattern of observational epidemiology.
- Review the evidence for vitamin-D status in the aetiology and pathogenesis of SLE.
- Evaluate the evidence for low vitamin D being associated with a range of adverse health outcomes of potential relevance to SLE.
- Consider evidence from interventional studies of vitamin D conducted in SLE to date.
- Understand the limits of our current evidence base and provide patients with an informed opinion on the role of vitamin-D supplementation in SLE.



# Abstracts

Plenary I: New Aspects in the Diagnosis and Management of SLE **Moderators:** Professor Bevra H. Hahn (USA) & Professor Zahir Amoura (France)



**Professor Andrea Doria, MD**  
University of Padova, Italy

## Early lupus: How early is early?

### References

1. Doria A, Zen M, Canova M, et al. SLE diagnosis and treatment: when early is early. *Autoimmun Rev* 2010; 10(1): 55-60.
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3. Doria A, Gatto M. Nephritogenic-antinephritogenic antibody network in lupus glomerulonephritis. *Lupus* 2012; 21(14): 1492-6.
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In clinical practice the diagnosis of systemic lupus erythematosus (SLE) is usually made in a patient who has developed a combination of clinical and immunologic features consistent with SLE. Of course, diseases which can mimic SLE have to be concomitantly ruled out.

In around 1980, antinuclear antibody testing became widely used in routine laboratory practice leading to a tapering in the lag time between SLE onset and diagnosis: in fact, before 1980, time to diagnosis was approximately 50 months yet after 1980 this reduced to approximately 25–26 months. However, since then nothing relevant has been introduced which could help us in making the diagnosis of SLE any earlier.<sup>1</sup>

Notably, there is increasing evidence that early diagnosis and treatment could increase SLE remission rate and improve patient prognosis.

Although it has been shown that autoantibodies appear before clinical manifestations in SLE patients, currently we cannot predict which autoantibody-positive subjects will eventually develop the disease. Thus, great effort should be made in order to identify new biomarkers capable of improving our diagnostic potential. For example, anti-C1q and anti-PTX3 antibodies have emerged as promising biomarkers for lupus glomerulonephritis, but they need to be validated.<sup>2-4</sup>

In recent years, some therapeutic options have been proposed as appropriate interventions for early SLE treatment including antimalarial drugs, vitamin D and statins. All these immune modulators seem to be particularly useful when introduced in an early stage of the disease. Notably, reducing disease activity and achieving remission in SLE leads to an improvement in disease prognosis and a decrease in direct medical costs.<sup>5</sup>

### Learning Objectives

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

- Understand the difference in immunologic, pathology and clinical onset of SLE.
- Appreciate the importance of biomarkers in helping us to identify SLE patients at an early stage of the disease.
- Recognise that early SLE diagnosis is crucial for an early therapeutic intervention which can increase the probability of disease remission and improve patient prognosis.
- Identify the best candidates for early therapeutic intervention in SLE.

## Notes

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# Abstracts

**Plenary I: New Aspects in the Diagnosis and Management of SLE** **Moderators:** Professor Bevra H. Hahn (USA) & Professor Zahir Amoura (France)



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

## Treat-to-target: issues and answers

### References

1. Smolen JS. Treat-to-target: rationale and strategies. *Clin Exp Rheumatol* 2012; 30(4 Suppl 73): S2-6.
2. Smolen JS, Aletaha D, Bijlsma JW, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis* 2010; 69(4): 631-7.
3. Mosca M, Boumpas DT, Bruce IN, et al. Treat-to-target in systemic lupus erythematosus: where are we today? *Clin Exp Rheumatol* 2012; 30(4 Suppl 73): S112-5.
4. van Vollenhoven RF, Mosca M, Bertias G, et al. Treat-to-target in systemic lupus erythematosus: recommendations from an international task force. *Ann Rheum Dis* 2014; 73(6): 958-67.

The principle of treating-to-target, identifying appropriate therapeutic targets and pursuing these systematically, has led to improved care for patients with several diseases and useful guidance for health care providers and administrators.<sup>1,2</sup> Thus, an initiative was launched to also develop treat-to-target guidance for systemic lupus erythematosus (SLE). Thirty-four specialists in rheumatology, nephrology, dermatology and/or clinical immunology, and a patient representative contributed.<sup>3</sup> Topics of critical importance were identified and a systematic literature review (SLR) performed. The results of the SLR were condensed and reformulated as recommendations, discussed, modified, and voted upon. The finalized bullet points were analysed for degree of agreement among the panel and the Oxford Centre level of evidence (LoE) and grade of recommendation (GoR) were determined for each recommendation.

The systematic literature searches led to eleven recommendations.<sup>4</sup> Prominent features of these recommendations are:

- Targeting remission.
- Preventing flares.
- Preventing damage.
- Minimizing glucocorticoid exposure.
- Improving quality of life.

LoE and GoR of these recommendations were variable but agreement was >0.9 in each case. Four overarching principles were also agreed upon. An extensive research agenda was identified, where one of the most important items is the need for establishing a generally applicable definition of remission in SLE – an initiative towards this objective has now been started by a large international task force, and has led to the formulation of a number of principles to guide further work.

Thus, it is clear that ‘treating-to-target’ can and will be applicable to the care of patients with SLE.

### Learning Objectives

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

- Understand the principles of treating-to-target.
- Know some of the diseases where treating-to-target has been proven to result in better outcomes.
- Be aware of the methods used for establishing treat-to-target recommendations for SLE.
- Know the key elements of treating-to-target for SLE.
- Be aware of the current initiative to define remission in SLE.





# Abstracts

**Plenary I: New Aspects in the Diagnosis and Management of SLE** **Moderators:** Professor Bevra H. Hahn (USA) & Professor Zahir Amoura (France)



**Professor David A. Isenberg, MD, FRCP, FAMS**  
University College London, UK

## Biomarkers in SLE: how useful are they?

### References

1. Bizzaro N, Villalta D, Giavarina D, Tozzoli R. Are anti-nucleosome antibodies a better diagnostic marker than anti-dsDNA antibodies for systemic lupus erythematosus? A systematic review and a study of metanalysis. *Autoimmun Rev* 2012; 12(2): 97-106.
2. Herbst R, Liu Z, Jallal B, Yao Y. Biomarkers for systemic lupus erythematosus. *Int J Rheum Dis* 2012; 15(5): 433-44.
3. Jeltsch-David H, Muller S. Neuropsychiatric systemic lupus erythematosus: pathogenesis and biomarkers. *Nat Rev Neurol* 2014; 10(10): 579-96.

Biomarkers are utilised to help diagnose and classify patients with lupus, reflect disease activity overall and within individual organs or systems, to manage patients being treated with numerous varying therapies and to provide prognostic information in some circumstances.

For many years the most widely used biomarkers have been antibodies to double-stranded DNA (which increase when the disease is active) and the serum C3 (which falls in active disease).

However, about 30% of lupus patients do not have raised antibodies to double-stranded DNA and over 50% have a normal C3. There has thus been an ongoing attempt to identify a broader range of biomarkers and some, including urinary tumour necrosis factor-like weak inducer of apoptosis (TWEAK) levels in renal disease, complement breakdown products and interferon alpha-gene profiles, have shown genuine promise.

Biomarkers also include measures of end-organ dysfunction such as a rising creatinine in patients with incipient renal failure or a high troponin in those with ischaemic heart disease (to which SLE patients are particularly prone).

Of course, the challenge remains the cost of getting tests for newer biomarkers to the market and making them affordable in a wide variety of locations. Professor Isenberg will review the range of biomarkers and attempt to identify those that might become more widely used in future.

### Learning Objectives

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

- Understand the importance of identifying new biomarkers and the short comings of some existing biomarkers for SLE.
- Be aware of the challenges faced when identifying new biomarkers and barriers to developing accessible screening for these.
- Recognise those biomarkers that may become more widely used in future.










## Case Study Workshops

### Saturday 28th February

#### Morning (11:00) Case Study Workshops

<p><i>Moderator: Zahir Amoura (France)</i> Investigating the febrile lupus patient</p>		Sandra V. Navarra ( <i>Philippines</i> ) & Fabrizio Conti ( <i>Italy</i> )
<p><i>Moderator: Ricard Cervera (Spain)</i> Haematologic challenges: cytopaenias</p>		Michelle Petri ( <i>USA</i> ) & David A. Isenberg ( <i>UK</i> )
<p><i>Moderator: Roger A. Levy (Brazil)</i> CNS lupus</p>		Munther A. Khamashta ( <i>UK</i> ) & Angela Tincani ( <i>Italy</i> )
<p><i>Moderator: Murray B. Urowitz (Canada)</i> Difficult skin disease</p>		Annegret Kuhn ( <i>Germany</i> ) & Marta Mosca ( <i>Italy</i> )
<p><i>Moderator: Bevra H. Hahn (USA)</i> Lupus nephritis</p>		Richard A. Furie ( <i>USA</i> ) & Gabriella Moroni ( <i>Italy</i> )

### 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.



**Moderator:** Professor Zahir Amoura (France)

**Presenters:** Professor Sandra V. Navarra (Philippines) & Professor Fabrizio Conti (Italy)

## Investigating the febrile lupus patient



**Professor Sandra V. Navarra, MD, FPCP, FPRA**

### Case 1: Disseminated TB in SLE

A 21-year-old male has had systemic lupus erythematosus (SLE) for 2 years, and is maintained on hydroxychloroquine and prednisone 15 mg/d. Three months ago, he developed joint and back pains accompanied by intermittent fever and dry cough, episodes of diarrhoea, and weight loss. A chest radiograph showed cavitory pulmonary tuberculosis (TB), laboratory tests revealed anaemia, normal leucocyte and platelet counts, 1+ proteinuria and pyuria >100/hpf; serum creatinine was normal. Sputum smears and needle aspirate of a fluctuant mass on the dorsal right hand tested positive for acid-fast bacilli. He was started on an anti-TB regimen consisting of isoniazid, rifampicin, pyrazinamide and ethambutol; prednisone and hydroxychloroquine (HCQ) were continued. Fever dissipated and cough improved over the next 8 weeks. Sputum and bursal fluid cultures grew *Mycobacterium TB*.

**Discussion points:** *Risk factors for infection in SLE. Manifestations of TB infection in SLE.*



Five days ago, he developed headache, hiccups, episodes of dizziness and vomiting accompanied by fever and painful swollen joints. On presentation at the emergency department, he appeared pale, weak and cachectic, tachycardic (125 beats/min), febrile (38.5 C), with orthostatic hypotension (130/80 mm Hg supine; 90/60 mmHg upright). He had early cataracts; optic disc margins were distinct with no papilloedema nor tubercles. There were few cervical lymph nodes, soft systolic heart murmur and fine crackles over both lung bases. Finger joints were warm, tender and swollen. Neurologic exam was normal.

**Discussion point:** *Distinguishing SLE disease activity versus infection.*

Haemoglobin was 90 g/L, white blood cell count  $7.3 \times 10^9/L$ , platelets  $270 \times 10^9/L$ . Urine showed 1+ albuminuria and pyuria >100/hpf. Serum creatinine was 1.51 mg/dL (ULN 1.2) (improved to 0.69 mg/dL following hydration), alanine transferase 117 (ULN 41); normal aspartate transferase, electrolytes, complement C3 1.1 g/L and anti-dsDNA. Repeat chest radiograph was unchanged. Abdominal ultrasound showed mild pelvocaliectasis on the right kidney; adrenals were not visualised. Blood and urine specimens did not grow any organism on aerobic cultures, and sputum PCR did not detect rifampicin resistance. He received high-dose steroids with significant resolution of symptoms and orthostatic hypotension. He was discharged on prednisone 40 mg/d, HCQ, isoniazid and rifampicin. He continued to improve, with prednisone gradually tapered to 20 mg/d over the next 2 months.

**Discussion points:** *Special considerations and challenges in management of TB in SLE.*

### Professor Fabrizio Conti, MD

#### Case 2: Lung and renal involvement

The patient, a 26-year-old Caucasian female, was diagnosed with SLE at age 24 years after presenting with photosensitivity, malar rash and oligoarthritis. Laboratory tests showed ANA, anti-dsDNA and anti-cardiolipin antibodies. The patient was treated with glucocorticoids plus methotrexate resulting in complete remission after 4 months.

In July 2012 she referred to our Lupus Clinic: laboratory tests showed positive anti-dsDNA, anti-cardiolipin, anti- $\beta$ 2GPI and low C3; the patient reported some mild flares of arthralgia in previous months. We started a treatment with hydroxychloroquine 200 mg bid and acetylsalicylic acid 100 mg/d.

In October 2013, the patient was admitted to our hospital with a 1-week history of continuous fever, up to 39 C, dyspnoea, non-productive cough and pleuritic chest pain. She had taken ibuprofen, paracetamol and amoxicillin without improvement. On examination, her temperature was 38.6 C, blood pressure 140/90 mmHg, HR 108, RR 18 and  $SO_2$  95.4%. The vesicular sounds were reduced in the lower lung fields, and there was oedema at the extremities of the lower limbs.

She lived with her father and brother in an urban area. She worked as a receptionist and had no recent history of insect bites. She was nulligravid and sexually active with a single partner. She had never smoked or used illicit drugs; she used to drink alcohol occasionally.

Blood tests revealed normocytic normochromic anaemia (Hb 8.9 g/dl), creatinine 1.8 mg/dl, increased CRP 24 mg/dl and ESR 140 mm/h. Urinalysis revealed proteins 100 mg/dl, 79 erythrocytes, 143 leukocytes and rare hyaline casts/hpf. Daily urine protein determination ranged from 2.7 to 4.9 g.

A chest X-ray revealed the presence of multiple confluent areas of parenchymal consolidations on the lower fields, and a chest CT showed multiple confluent areas of ground glass on the upper fields, extensive bilateral multifocal asymmetric consolidation involving all lobes, alveolar and bronchiole impairments on the upper fields, bilateral pleural effusion and a moderate pericardial effusion. Moreover, additional laboratory tests demonstrated the presence of ANA, anti-dsDNA, anti-SSA, anti-Sm, anti-RNP, anti-cardiolipin; low C3 and C4 serum levels. After 36 hours from admission haemoglobin dropped to 7.9 g/dl.

#### Discussion points:

*What diagnostic tests can help distinguish SLE disease activity from infection?*

*What are the possible causes of anaemia in this patient?*

*What diagnostic possibilities may be considered for the patient's pulmonary abnormalities?*

### Learning Objectives

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

- Review diagnostic considerations in the febrile lupus patient.
- Discuss risk factors for infection in SLE.
- Apply clinical and laboratory parameters that help distinguish infection from disease activity.
- Recognise various manifestations and special challenges in management of TB involvement in SLE.

## Notes

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**Moderator:** Professor Ricard Cervera (Spain)

**Presenters:** Professor Michelle Petri (USA) & Professor David A. Isenberg (UK)

## Haematologic challenges: cytopaenias



### Professor Michelle Petri, MD, MPH

#### Case 1: TH

Diagnosed in 2004, based on facial rash with accompanying serological abnormalities and Raynauds, this female patient was started on hydroxychloroquine.

Later in 2004 she was admitted to hospital with pneumonia and had a respiratory arrest. She was ventilated and subsequently diagnosed with Guillain-Barré syndrome. Her hospital course was complicated by seizures, which were attributed to her systemic lupus erythematosus (SLE). She was started on mycophenolate mofetil 2000 mg/d.

In 2009 she had a prolonged hospital admission. She presented following a loss of consciousness and required intubation and tracheostomy formation. She was fed by percutaneous endoscopic gastrostomy. She had an acute kidney injury that did not require renal replacement therapy. She had a lymph node excised, which was benign.

In 2011 she became pregnant while on mycophenolate mofetil, and had a foetal demise at 26 weeks.

In 2013–2014 she was not on any treatment for her SLE. In 2014 she discovered she was pregnant. Records indicate that she was proteinuric prior to her pregnancy.

In January 2015 she presented to outside health center feeling vaguely unwell. She was fatigued and nauseated. She was 22 weeks pregnant with a platelet count of  $120 \times 10^9/L$ .

### Professor David A. Isenberg, MD, FRCP, FAMS

#### Case 2: Afro-Caribbean adolescent

A 13-year-old Afro-Caribbean adolescent presented with arthritis, a photosensitive rash and serositis. She was found to be anaemic with a strongly positive antinuclear antibody and raised double-stranded (ds) DNA (dsDNA) antibodies.

She developed significant proteinuria and was treated aggressively with monthly intravenous infusions of cyclophosphamide, which were subsequently switched to mycophenolate mofetil. She remained on high doses of oral prednisolone throughout.

At the age of 17 years it was decided to treat her with B-cell depletion using rituximab and cyclophosphamide and for 8 months a sustained improvement in her clinical symptoms, haematology and immunological results was effected. Unfortunately haemoglobin and C3 began to fall again and erythrocyte sedimentation rate (ESR) to rise. A decision was made to re-treat her with B-cell depletion.

### Professor Michelle Petri, MD, MPH

#### Case 3: BH

This 35-year-old East Asian man presented in October 2014 with dyspnoea and oedema and was found to have pulmonary emboli. Heparin and then warfarin were started. He remained dyspnoeic, and was transfused for anaemia.

In January 2015 he was re-admitted to hospital. A new pulmonary embolus and a left leg deep vein thrombosis were found. He had pulmonary hypertension and his urine protein/creatinine was 2.26 g.

His antinuclear antibody (ANA) was 640, anti-DNA positive and C3 low at 77 mg/dl. Anticardiolipin and anti-beta2 glycoprotein were negative. His haemoglobin was 8 g/dl, reticulocyte count 1.24, lactate dehydrogenase 191 and ferritin was high.

### Professor David A. Isenberg, MD, FRCP, FAMS

#### Case 4: 23-year-old Vietnamese female

A 23-year-old female of Vietnamese origin presented with a maculopapular rash, jaundice, elevated liver enzymes and positive ANA. Liver biopsy confirmed acute hepatitis which was assumed to be autoimmune and she was treated successfully with steroids and azathioprine.



Four months later she presented again with a headache, a widespread petechial rash and oral mucosal bleeding. On admission a blood test revealed a thrombocytopaenia with a platelet count of  $0 \times 10^9/L$ , haemoglobin 11.2, ESR 113 mm/hr and c-reactive protein (CRP) virtually normal. A decision was made to attempt to treatment her thrombocytopaenia with intravenous immunoglobulin and oral prednisolone, but over the next 4 days her haemoglobin fell to 6.5 g/dl and she was found to be Coombs-test positive. As well as being ANA positive she was now found to be dsDNA-antibody positive. A case conference was arranged quickly to decide on how best to treat her.

### **Professor Michelle Petri, MD, MPH**

#### **Case 5: MH**

An African-American woman has had a renal transplant. She is managed with mycophenolate mofetil and tacrolimus. At her visit she reports feeling unwell. Her haematocrit (HCT) returns at 23%.

### **Professor David A. Isenberg, MD, FRCP, FAMS**

#### **Case 6: 19-year-old Afro-Caribbean**

An Afro-Caribbean girl aged 19 years presented with arthritis, discoid lupus, fatigue and ANA 1:640 anti-Sm and anti-dsDNA antibodies, and was found to have a neutropaenia of  $2.9 \times 10^9/L$  and a lymphocyte count of  $0.6 \times 10^9/L$ . It was suspected that at least part of the low white count was ethnic in origin as her mother known to the department with degenerative disease also had a low white count.

The patient was treated with hydroxychloroquine and low dose corticosteroids and seemed fairly stable for the first 3 months.

She presented acutely to the Emergency Department with a high fever, generalised lymphadenopathy and hepatosplenomegaly. She seemed a little confused. Cerebral spinal fluid (CSF) findings including a slightly elevated protein but no abnormalities, were detected and a magnetic resonance imaging (MRI) scan was reported as unremarkable.

Her haemoglobin had dropped from a normal value of 12 g/dl to 9 g/dl and her platelet count, which had been over 300, was down to  $50 \times 10^9/L$  with a total neutrophil count of just  $0.7 \times 10^9/L$ . Curiously her ESR when first seen was 80 mm/hr and on the acute admission was down to 12 mm/hr, whereas her CRP, which had been normal at 3.6 mg/L, was now over 100. A case conference was called.

### **Professor Michelle Petri, MD, MPH**

#### **Case 7: 32-year-old female**

A 32-year-old woman was diagnosed with SLE in 1996 based on the presence of polyarthritis, myositis, haemolytic anaemia, ANA and anti-Ro antibodies, and hypocomplementaemia. She was treated with oral corticosteroids. Her clinical progression was marked by the development of lupus cerebritis in 1997 and hypertension in 2000. During the 32nd week of pregnancy (in September 2001), she developed renal insufficiency, nephrotic-range proteinuria, haematuria and hypertension. Her renal disease failed to improve with high-dose corticosteroids and elective induction of labor. A postpartum kidney biopsy showed mixed World Health Organization (WHO) class IV and class V crescentic glomerulonephritis. She was treated with 6-monthly intravenous (IV) cyclophosphamide infusions, followed by maintenance therapy with mycophenolate mofetil. Her creatinine remained stable but 3+ proteinuria persisted. In April 2004 she was hospitalised with fever and intermittent right lower quadrant abdominal pain. At that time, she was receiving mycophenolate mofetil 1 g bid and prednisone 5 mg/d. Admission laboratory test results included: white blood cell (WBC) count  $1300/mm^3$  with  $200/mm^3$  neutrophils, haemoglobin 10.5 g/dl, platelets  $280 \times 10^9/L$ , creatinine 1.4 mg/dl, and normal complement levels. On computed tomographic (CT) imaging of the abdomen and pelvis, there was a right ovarian cyst with fluid in the cul-de-sac. She was treated empirically with antibiotics and mycophenolate mofetil was discontinued.

## **Learning Objectives**

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

- Review the differential diagnosis of cytopenias in SLE.
- Understand laboratory testing for cytopenias in SLE.
- Consider treatment options for cytopenias in SLE.



**Moderator:** Professor Roger A. Levy (Brazil)

**Presenters:** Professor Angela Tincani (Italy) & Professor Munther A. Khamashta (UK)

## CNS lupus

### Professor Angela Tincani, MD

#### Case 1: Peripheral neuropathy in SLE

In September 2003, a 37-year-old Caucasian female with history of systemic lupus erythematosus (SLE) was seen in our Outpatients Clinic during one of her follow-up visits.

Diagnosis of SLE and a secondary Sjogren Syndrome had been made in 1998 based on photosensitivity, polyarthritis, oral aphthosis, fatigue, leukopaenia and lymphopaenia, salivary glands biopsy and positive Schirmer test.

Antinuclear antibody, anti-Ro/SSA, anti-Sm and anti-dsDNA antibodies were strongly positive at the time of diagnosis and still positive at our first evaluation when the patient was taking corticosteroids, hydroxychloroquine (HCQ) and immunosuppressive drugs.

She first experienced dysesthesia in her hands and feet in 2009, with electroneurography revealing a demyelinating sensory and motor polyneuropathy. She was admitted to hospital and during the diagnostic work-up haematuria and proteinuria were noted. Kidney biopsy confirmed the suspected lupus nephritis (Class IV ISN/RPS), which was treated with monthly cyclophosphamide pulses for 6 months followed by mycophenolate mofetil (MMF) 3 g/day, resulting in normalisation of proteinuria and disappearance of neurologic symptoms.

In 2012, during a follow up visit, the patient mentioned the reappearance of her neurological symptoms, including diffuse paresthesia of the feet. Her medications included prednisone 5 mg/day, HCQ 5mg/kg/day, MMF 2g/day and calcium-vitamin D. Electroneurography was stable, so a diagnostic work up (including biopsy) was started. A few months later progression of symptoms such as muscle weakness and ambulation impairment was recorded.

### Professor Munther A. Khamashta, MD, PhD, FRCP

#### Case 2: Multiple sclerosis-like disease in SLE

A 42-year-old woman with a previous diagnosis of systemic lupus erythematosus (SLE) at the age of 35 years (ANA, anti-dsDNA, leucopaenia and lymphopaenia, mild thrombocytopenia, butterfly rash, recurrent mouth ulcers and persistently positive anti-cardiolipin antibodies IgG isotype at high titres) presents to accident and emergency department with numbness of the left side of her face, dysphasia and weakness in her left arm. Her lupus was well controlled (in remission) and she is currently taking hydroxychloroquine 400 mg OD, low-dose aspirin 75 mg OD and prednisolone 5 mg OD. No previous history of kidney or CNS involvement, other than occasional migraine-type headaches since her teens. No previous history of miscarriages or deep vein thrombosis. Magnetic resonance imaging showed multiple and scattered high signal intensity foci within the periventricular white matter. The patient smokes heavily and has a very strong family history for premature coronary artery disease. Carotid ultrasound and transoesophageal echocardiography did not demonstrate abnormalities to explain the neurological symptoms. Physical examination was unremarkable other than prominent livedo reticularis in her lower limbs. Laboratory testing showed mild leucopaenia and lymphopaenia, and platelet count  $110 \times 10^9/L$ . Complement C3 and C4 were within normal limits, and anti-DNA antibodies were negative. ESR 17 mm/h and CRP  $<5$ . Blood biochemistry including kidney and liver function tests all within normal range. Repeat testing for antiphospholipid antibodies showed strongly positive IgG aCL (120 GPL) and was negative for lupus anticoagulant and anti- $\beta$  2-GPI antibodies.

**Discussion point:** *What is the optimal treatment for this patient?*



# Case Study Workshop



**Moderator:** Professor Murray B. Urowitz (Canada)

**Presenters:** Professor Annegret Kuhn (Germany) & Professor Marta Mosca (Italy)

## Difficult skin disease

### Professor Annegret Kuhn, MD, MBA

#### The Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index (RCLASI)

Several disease activity scores (SLEDAI, ECLAM, BILAG) have been established for systemic lupus erythematosus (SLE) to determine disease activity of individual patients in everyday clinical practice and during clinical trials. Although the disease activity scores include dermatological criteria, such as butterfly (malar) rash, generalised erythema, and oral ulcers, the scores are not suitable for judging activity of the different subtypes of cutaneous lupus erythematosus (CLE): acute CLE (ACLE), subacute CLE (SCLE), chronic CLE (CCLE), and intermittent CLE (ICLE). To assess 'activity' and 'damage' of the various subtypes of CLE, the CLASI (cutaneous lupus erythematosus disease area and severity index) has been developed as an outcome instrument for CLE. The scoring system takes into account both anatomical regions (e.g. face, chest, arms) and morphological aspects (e.g. erythema, oedema/infiltration, scarring/atrophy). In 2010, the CLASI was revised by optimizing the compilation of parameters for the evaluation of the various CLE subtypes by increasing the accuracy of existing parameters, such as scaling/hypertrophy and dyspigmentation, and by adding several new parameters, such as oedema/infiltration and subcutaneous nodule/plaque. The revised CLASI (RCLASI) was validated in twelve patients with CLE and has proven to be a valuable tool for the clinical evaluation of activity and damage in different disease subtypes. Recently, clinical responsiveness of the RCLASI has been evaluated in prospective clinical trials.

#### Discussion points:

*Morphological criteria of skin lesions in discoid and subacute CLE.*

*Difference between diffuse and scarring alopecia and 'lupus hair'.*

*Typical signs of activity and damage in mucous membrane lesions.*

### Professor Marta Mosca, MD, PhD

#### Case 1: CLE and pregnancy

A 25-year-old female patient was diagnosed with SLE 7 years ago based on the presence of serositis, acute CLE and positive antinuclear antibodies (ANA). At physical examination she presented a diffuse subacute cutaneous rash and arthritis in her hands and wrists. The laboratory assessment showed the presence of low complement, mild proteinuria (600 mg/24 hours), positive ANA and anti-Ro/SSA antibodies. A joint ultrasound showed the presence of active wrist synovitis and proliferative tenosynovitis. The patient expressed a desire to become pregnant.

Treatment with pulse steroids, hydroxychloroquine and azathioprine was started, obtaining a complete response of cutaneous manifestations, joint involvement and proteinuria. However, with steroid tapering below 12 mg/day, a flare of skin and joint involvement was observed.

The patient refused therapy with methotrexate because of her desire to become pregnant. Over the following months the patient continued treatment with hydroxychloroquine, azathioprine and a corticosteroid dose ranging between 8 and 12 mg/daily.

#### Discussion points:

*What is the preferred therapy for cutaneous manifestations in SLE?*

*What treatment options are suitable for young women wishing to become pregnant?*

(Photo: Peter Pulkowski)



## Professor Marta Mosca, MD, PhD

### Case 2: CLE systemic and local therapy

A 29-year-old female patient presented with Raynaud's phenomenon, hand arthritis, thrombocytopaenia and haemolytic anaemia. She had low complement, positive ANA, anti-dsDNA and anti-Ro/SSA antibodies.

She was initially treated with pulse steroids, hydroxychloroquine and methotrexate. After initial control of the disease, she developed a rash on her face, V-neck, shoulders and arms.

Systemic therapy was not modified and local steroid treatment was instituted. Only transient control of skin manifestations was obtained. Consequently, systemic steroids were increased, quinacrine was added and immunosuppressive therapy was changed with the introduction of mycophenolate mofetil. Over the following months skin lesions were persistently present with various degrees of activity and development of scarring.

### Discussion points:

*Local therapy for skin disease, which one and how long?*

*Which biological therapies are suitable for skin disease?*

### Learning Objectives

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

- Recognise the heterogeneous morphological aspects of the different subtypes of CLE.
- Understand the structure of the RCLASI, its different features and parameters.
- Evaluate activity and damage of clinical manifestations in patients with CLE.
- Score the skin lesions of the disease according to the RCLASI.
- Recognise when and how use topical therapies in skin disease.
- Know first and second choice therapies for skin disease.
- Understand how to approach refractory skin disease.

## Notes

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**Moderator:** Professor Bevra H. Hahn (USA)

**Presenters:** Dr Gabriella Moroni (Italy) & Professor Richard A. Furie (USA)

## Lupus nephritis



**Dr Gabriella Moroni, MD**

### Case 1: Class IV proliferative lupus nephritis

An 18-year-old Caucasian male was admitted to the Renal Unit of Fondazione Ospedale Maggiore of Milan in November 1980 for proteinuria (0.60 g/24h) and abnormalities of urinary sediment. During the 3 months before admission he complained of arthralgias, intermittent fever and malar rash. Laboratory tests revealed normal renal function, anaemia, low C3 and C4, and positive results for lupus anticoagulant, ANA and anti-DNA antibodies. A renal biopsy showed a diagnosis of class IV proliferative lupus nephritis and the patient was treated according to the approach in use in 1980, resulting in renal remission. After achieving complete remission the patient decided of his own free will to stop all therapies. Six months later the patient was hospitalised again for rapidly progressive renal failure and severe extra-renal systemic lupus erythematosus manifestations. A second renal biopsy was taken and following treatment he achieved renal and extra-renal remission. After one year of persistent remission, the patient was lost to follow-up. He decided to stop prednisone and continued unspecified herbal therapy. Six years later, the patient came back to our Unit for clinical re-evaluation for renal dysfunction and proteinuria. During the following months a severe nephrotic syndrome developed, the patient underwent a third renal biopsy and started a new course of therapy. Nephrotic syndrome persisted and renal function progressively deteriorated resulting in end-stage renal disease.

**Discussion point:** *An interesting point of this difficult case is to compare the therapy employed in this case in the 1980s with what we could have done today.*



**Professor Richard A. Furie, MD**

### Case 2: Coma, thrombocytopaenia and azotaemia

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 anaemia (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) 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, on which organ?*

*What additional diagnostic tests would you perform?*

*What therapeutic interventions might you try?*

**Professor Richard A. Furie, MD**

### Case 3: Hepatitis, pancytopenia, and azotaemia

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 exam was notable for blood pressure of 135/85; temperature of 39.8°C; mild proximal interphalangeal synovitis. Laboratory tests revealed white blood cells

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1.2 (50% PMNs; 50% L); Hb 7.6; Plt 66; PT/PTT 15/38; AST 173; ALT 104; creatinine: 1.4 (pre-morbid creatinine 0.7); urinalysis: 8 RBC; no casts; Pr/Cr 0.3; 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, on which 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:**

- Understand the discrepancies between clinical presentation and renal histological findings.
- Know the possibility of transformation from one to another histological class during the course of the disease.
- Reach a view of the therapeutic approach to the different histological forms of lupus nephritis.
- Understand the importance of compliance for the success of treatment of patients with lupus nephritis.
- Discuss uncommon non-nephritic causes of renal disease in SLE patients.
- Describe appropriate diagnostic evaluations.
- Discuss treatment regimens for such patients.

**Notes**

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## Dr Gabriella Moroni, MD

Division of Nephrology and Dialysis, (IRCCS) Ospedale Maggiore, Milan, Italy

## New trends in the treatment of nephritis

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From the 1980s until 10 years ago the “NIH regimen” (intravenous cyclophosphamide and oral steroids) represented the standard of care for induction and maintenance treatment of lupus nephritis (LN). However, the incomplete response in a number of patients and the treatment-related toxicity with this approach promoted the search for alternative therapies.<sup>1</sup> The Euro-Lupus Nephritis trial demonstrated that, in Caucasian patients at least, the same results can be obtained with a smaller dosage of cyclophosphamide plus methylprednisolone pulses and azathioprine for maintenance.<sup>2</sup> Six trials including 686 patients compared mycophenolate mofetil with cyclophosphamide as induction therapy. A meta-analysis<sup>3</sup> of these trials demonstrated no differences in complete and partial renal remission, but mycophenolate-treated patients had significantly lower risk of ovarian failure and alopecia. An interesting result is the better efficacy of mycophenolate in African-American and Latin patients. A meta-analysis involving six controlled trials and 265 Chinese patients with active LN showed that calcineurin

inhibitors (tacrolimus in particular) were superior to cyclophosphamide for higher complete remission/total remission, and had fewer side effects.<sup>4</sup> Again, in 380 Chinese patients “multi-target therapy” (steroids, low dose mycophenolate mofetil and tacrolimus)<sup>5</sup> achieved higher complete and overall response, and shorter time to response than cyclophosphamide, with no differences in side effects. In maintenance therapy, comparing azathioprine with mycophenolate mofetil, the risk of renal relapse was significantly higher in patients taking azathioprine (3 studies, 371 patients), while no difference in the incidence of end-stage-kidney disease or adverse events except leucopaenia (higher in azathioprine) was reported. Despite the discouraging results of controlled trials, a number of non-controlled trials reported that rituximab was effective in patients with refractory LN and some patients can be treated with reduced doses or even without steroids. Altogether, the results of new trials suggest a shift from a fixed protocol to an individualised or tailored treatment regimen for patients with LN.

### Learning Objectives

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

- Understand that the approach to lupus nephritis should not be standardised.
- Know how to choose a treatment based on the clinical/histological severity of lupus nephritis.
- Know how to choose a treatment based on the different ethnicities of the patients.
- Be aware of the unmet therapeutic needs for lupus nephritis in spite of the new approaches.







**Dr Federico Oppenheimer, MD, PhD**  
Hospital Clinic, Barcelona, Catalonia, Spain

## Renal transplantation in SLE: outcomes and prognostic factors

### References

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Renal transplantation is the best therapeutic option for patients with end stage renal disease (ESRD) resulting from lupus nephritis (LN). Compared with haemodialysis or peritoneal dialysis, kidney transplantation results in higher rates of survival, better quality of life and a lower cost of the therapy. There are no specific contraindications for kidney transplantation in patients with systemic lupus erythematosus (SLE). Concerns about the systemic character of the disease and the risk of graft loss due to nephritis recurrence have progressively disappeared. Furthermore, the classical recommendation of remaining on dialysis until lupus activity diminishes results in contradiction with the evidence that shorter time on dialysis before transplantation improves long-term outcomes.<sup>1</sup> The principal differences between LN transplant recipients and recipients with other nephropathies are the cumulative effect of the history of steroids and immunosuppressive therapy, the potential presence of thrombophilic factors and an increased immunological risk. However, outcomes of patient and graft survival from deceased or living donor transplants are comparable with recipients with other causes of ESRD.

Recurrence of LN after transplantation has been reported, with rates varying widely from 0–44%.<sup>2</sup> The use of investigational indication biopsies or immunofluorescence staining and electron microscopy studies increases the rate of histological findings by up to 54%.<sup>3</sup> However, in biopsies performed for clinical reasons, the incidence of recurrence is around 7–8%.<sup>2</sup> In our own experience, only one in 50 transplant recipients with SLE has shown histological findings of recurrence.<sup>4</sup> Despite the variable rate of recurrence, the risk of graft failure due to recurrence is very low. The use of immunosuppressive therapy with similar indications in transplantation and in SLE has been suggested as the principal factor, but there is no clear evidence about the superiority of one particular drug in preventing recurrence.<sup>5</sup>

Comorbidities, usually present in SLE patients because of the long-lasting use of steroids and immunosuppressive drugs before and after transplantation, may increase the risk of infections and cardiovascular events. Maintenance therapy must be adequately adjusted using an individualised approach and with the continuous collaboration between transplant and autoimmune disease physicians caring for the patients.

### Learning Objectives

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

- Identify the principal factors affecting the outcomes of transplantation in patients with LN.
- Be familiar with the similarities in the immunosuppressive therapy employed in SLE and kidney transplantation.
- Improve their knowledge on the impact of nephritis recurrence on transplant outcomes.





**Professor Bevra H. Hahn, MD**  
University of California, Los Angeles, USA

## Osteonecrosis and osteoporosis in SLE: early diagnosis and prevention

### References

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Two major problems involving bone occur in individuals with systemic lupus erythematosus (SLE): ischaemic necrosis of bone (INB) and osteoporosis (OP) with fractures, including glucocorticoid (GC)-associated bone loss (GIOP). Between 5 and 25% of patients develop INB, most commonly in femoral heads but not infrequently in knees, wrists, ankles and shoulders. Persistent pain in one or a few joints, independent of SLE activity in other systems, is the main sign, and MRI is the best widely-available imaging technique for diagnosis.

Once INB is confirmed in a single hip, the chance of its occurring in the opposite hip is approximately 50%. Treatments are controversial, with little evidence that conservative therapies (minimal weight bearing, physical therapy) or bisphosphonates prevent progression from Stage I (MRI +, routine X-ray normal) to Stage IV (collapse of head and secondary osteoarthritis on X-ray). Surgical interventions are recommended for Stage II-IV, with total hip replacement shown to have good outcomes, but less evidence for the effectiveness of preventive surgeries for Stage II/III – such as decompression (“drilling”) with or without stem cells or bone morphogenetic proteins and/or bone chips and grafts.

Osteoporosis by bone densitometry is present in 5–15% of cases at disease onset, osteopaenia in up to 30% and fractures over the course of disease in 20–25%. In SLE fractures occur at higher bone density than in the general population. Main causes are advancing age, disease activity/ chronic inflammation, physical inactivity, and medications (e.g. GC, methotrexate, cyclosporine, anticonvulsants, heparin).

GIOP is a major problem with bone loss of approximately 6.5% in the first 6 months of treatment, followed by a 3% steady loss per year if GCs are continued and no therapies to maintain bone density are used. ACR guidelines recommend all patients be treated with vitamin D, as needed, to maintain serum 25 OH-D levels at 35–50 ng/mL plus calcium intake of 1200–1500 mg daily. All patients on GC for more than 3 months should have bone density measures, or calculation of FRAX scores or both. In SLE and GC-treated patients, as well as the general population, increasing age and low bone density (hip) are the most powerful predictors of fracture risk. In patients receiving 7.5 mg prednisone daily or equivalent, even with normal bone mass, consider anti-resorptive therapy with bisphosphonates. For patients on 7.5 prednisone or more and T-scores on osteodensitometry of –1.5 or lower, or FRAX scores of 10% or higher for 10-year risk of OP-related fractures, treatment should include either bisphosphonates or denosumab (anti-RANK-L).

A recent study in age-related OP shows that zoledronate and denosumab are superior to oral bisphosphonates in reducing vertebral fractures, probably because they are administered parenterally by medical staff, thus greatly improving compliance. Teriparatide (which stimulates bone formation) for 18–24 months, followed by bisphosphonates, should be considered for patients with very low bone density, particularly if they have already had a fracture and/or density does not improve on anti-resorptive treatments. Long-term safety of the anti-resorptive therapies for pre-menopausal women and for foetuses has not been firmly established.



## Abstracts

**Plenary III:** From Conception Through Adolescence: Issues in SLE and APS

**Moderators:** Professor Murray B. Urowitz (Canada) & Professor Ricard Cervera (Spain)



**Professor Munther A. Khamashta, MD, PhD, FRCP**  
St. Thomas' Hospital, London, UK

## Planning and managing pregnancy in SLE

### References

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Women with systemic lupus erythematosus (SLE) face significant risks when embarking on a pregnancy, but attending a multidisciplinary clinic staffed by an experienced team can improve pregnancy outcomes for women and their babies. Pregnancy in SLE should be planned, and a management strategy agreed in full consultation with the patient, prior to conception.<sup>1</sup> Pregnancy increases the likelihood of a lupus flare. It is not possible to predict when, or if, an individual patient will flare, although flare is more likely if disease has been active within 6 months of conception.<sup>2</sup> Worsening of proteinuria in pregnancy could herald a lupus flare, but the differential diagnosis also includes the physiological response to pregnancy and pre-eclampsia.<sup>3</sup> Corticosteroids,

hydroxychloroquine and azathioprine are safe to use in pregnancy, with no adverse foetal effects reported despite many years of experience with their use.<sup>4</sup> Correct identification of patients with antiphospholipid syndrome is important because treatment of affected women during pregnancy can improve foetal and maternal outcomes. Neonatal lupus, although rare, carries a significant mortality and morbidity when the foetal heart is the targeted organ (congenital heart block).<sup>5</sup> Close surveillance, with monitoring of blood pressure, proteinuria and placental blood flow by Doppler studies helps the early diagnosis and treatment of complications such as pre-eclampsia and foetal distress. Post-partum follow-up is also essential.

### Learning Objectives

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

- Understand the importance of pregnancy counselling in women with SLE.
- Describe the main predictors of pregnancy complications in women with SLE.
- Diagnose and manage antiphospholipid syndrome during pregnancy.
- Understand how to manage a pregnant woman with positive anti-Ro antibodies.
- Differentiate between pre-eclampsia and lupus nephritis flare.



## Abstracts

Plenary III: From Conception Through Adolescence: Issues in SLE and APS

Moderators: Professor Murray B. Urowitz (Canada) & Professor Ricard Cervera (Spain)



**Professor Angela Tincani, MD**

Brescia General Hospital and University of Brescia, Italy

## Outcomes in children from mothers with SLE and APS

### References

1. Andreoli L, Fredi M, Nalli C, et al. Pregnancy implications for systemic lupus erythematosus and the antiphospholipid syndrome. *J Autoimmun* 2012; 38(2-3): J197-208.

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Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are autoimmune disorders that primarily affect women of childbearing age. Because of the extraordinary progress in the management of these diseases, women with SLE and APS can now experience a successful pregnancy.<sup>1</sup> Therefore, the future of their children obviously becomes the most important issue for those patients who are going to become mothers.

Preterm delivery, a frequent complication observed in SLE and APS pregnancies (due to different disease-related mechanisms), can result in problems in the children. In particular, preterm neonates may have major physical and neurological complications when born extremely preterm ( $\leq 28$  weeks of gestation): neonatal death, medical complications and neurodevelopmental problems can occur with increased prevalence in these children as compared with those born at full term.

Patients with SLE or APS need to be treated during pregnancy: one of the most challenging tasks is to effectively treat the mother without damaging the foetus. Few studies have investigated the effect of maternal immunosuppressive drugs on the unborn child's immune system and no immune deficiency state nor lack of response to vaccinations have been documented.<sup>2</sup>

The transplacental passage of anti Ro/SS-A and/or anti La/SS-B, which are found in 40–60% of SLE patients, is known to be linked to the possible (but rare) occurrence of neonatal lupus, sometimes leading to complete congenital heart block that represents its most serious consequence.

The transplacental passage of antiphospholipid antibodies (aPL) occurs in 30% of IgG positive patients in the third trimester, but foetal thrombosis has been very rarely reported. Long-term follow-up of children born to aPL positive mothers has revealed language delay and learning disabilities suggesting a possible effect of maternal aPL on brain function.<sup>3</sup>

### Learning Objectives

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

- The high frequency of premature delivery in patients with SLE and APS and the impact of prematurity in the normal development of their children.
- The possible effect on foetal development of several drugs used to treat patients with SLE and APS.
- The link between transplacental passage of anti Ro/SS-A and/or anti La/SS-B antibodies and the occurrence of neonatal lupus.
- The long-term outcomes for children born to mothers with IgG aPL in the third trimester of their pregnancy.





## Abstracts

**Plenary III:** From Conception Through Adolescence: Issues in SLE and APS

**Moderators:** Professor Murray B. Urowitz (Canada) & Professor Ricard Cervera (Spain)



**Professor Alberto Martini, MD**  
University of Genoa, Italy

## Transition of childhood onset SLE into adulthood

### References

1. Malattia C, Martini A. Paediatric-onset systemic lupus erythematosus. *Best Pract Res Clin Rheumatol* 2013; 27(3): 351-62.
2. Robertson L. When should young people with chronic rheumatic disease move from paediatric to adult-centred care? *Best Pract Res Clin Rheumatol* 2006; 20(2): 387-97.

Paediatric-onset systemic lupus erythematosus (SLE) accounts for approximately 10–20% of all patients with SLE.<sup>1</sup> Disease onset usually occurs between the ages of 12 and 16 years and is very rare before 5 years. Unlike other rheumatic diseases such as juvenile idiopathic arthritis or juvenile dermatomyositis, which differ from their counterpart in the adults, paediatric-onset SLE, although usually more severe, is the same disease as in adults. The disease is chronic and therefore adolescents or young adults need to be transferred to adult care.

There are several differences between paediatric and adult healthcare and this can make the transition of care difficult for young patients and their families.<sup>2</sup> These differences include the fact that paediatric care is family oriented and paternalistic, while adult care is individual-focused and treatment decisions are shared with patients. Moreover, strong consideration is given in paediatric medicine to developmental aspects. Adolescents with SLE need to consolidate their

identity and self-esteem, achieve independence from their parents, find a vocation, and learn to cope with their disease and its treatment by themselves.

Transitional care services aim to provide young patients with the appropriate knowledge and skills to handle this change. Transfer is an event that occurs on one occasion when the paediatric rheumatologist sends their patient, with all the pertinent information, to the adult rheumatologist. Transition, however, is multifaceted active process that considers the medical, psychosocial and vocational needs of adolescents in order to provide them with the capacity to properly and independently manage their health.

Important aspects include a progressive preparation of the patient to transition, choosing the right time to initiate the process, and the involvement of both paediatric and adult rheumatologists.

### Learning Objectives

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

- Understand the difference between transfer and transition of care.
- Know the peculiar psychological and developmental aspects of transition from paediatric to adult care.





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

## Future treatments for APS

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Antiphospholipid Syndrome (APS) patients may present with recurrent venous or arterial thrombosis and/or pregnancy morbidity occurring in patients with persistent antiphospholipid antibodies (aPL).<sup>1</sup> Persistent circulating aPL detected as lupus anticoagulant, moderate or high titres of anti-cardiolipin or anti- $\beta$ -2 glycoprotein I, are known as risk factors for thrombosis and are predictors of early damage in lupus patients.<sup>2</sup> The current treatment approach is to maintain those patients with previous venous events with lifetime oral vitamin K antagonists at an international normalisation ratio (INR) range of 2.0 to 3.0, while for those with past arterial events, the INR target should range from 3.0 to 4.0.<sup>3</sup> In these patients, as well as those that are asymptomatic aPL carriers, the avoidance/correction of additional thrombotic risk factors is of extreme importance.<sup>4</sup> Special attention should be given to aPL/APS patients when they are submitted to high-risk situations and the treatment adapted accordingly, when low molecular weight heparin is generally used. In some patients, keeping the INR at a stable target is troublesome and both thrombotic and bleeding complications may occur,<sup>5</sup> constituting an additional unmet need for aPL/APS patients proper care.<sup>6</sup>

The 14th APLA Treatment Trends Task Force suggested that future clinical research directions ought to be:

- To determine the necessity for controlled trials in venous thromboembolism with the new generation of oral anticoagulants (inhibitors of factor X and thrombin), depending on the currently ongoing rivaroxaban in APS (RAPS) trial results, and designing additional trials in arterial and other forms of thrombotic APS;
- To continuously analyse the literature, as well as aPL/APS registries;
- To stimulate recruitment for an ongoing primary thrombosis prevention trial, and design prevention trials with hydroxychloroquine in secondary thrombosis and pregnancy morbidity;
- To determine surrogate markers to select patients for statin trials;
- To design controlled studies with rituximab, belimumab and other anti-B-cell agents;
- To design studies with eculizumab and other complement inhibitors;

to research chemically modified peptide therapy to improve the half-life and minimize immunogenicity.<sup>7</sup>

As an alternative to the current APS treatment, and its unmet needs, we envisage a shift from targeting the coagulation cascade to a mechanistic therapy, targeting the aPL immunological pathogenic mechanism.

## Learning Objectives

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

- Appreciate the APS Classification criteria, risk stratification, treatment indications and current treatment unmet needs.
- Evaluate the treatment strategies in high-risk situations.
- Comment on how to improve treatment compliance.
- Understand the recommendations of the recent 14th APLA Task Force on the use of:
  - New oral anticoagulants (factor X and thrombin inhibitors).
  - Data generated by ongoing international registries.
  - Hydroxychloroquine in primary and secondary prevention.
  - Statins and the use of surrogate markers to evaluate its role.
  - Anti-B-cell agents (rituximab and belimumab).
  - Anti-complement agents (eculizumab and others).
  - Chemically modified peptide therapy.

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## Abstracts

**Plenary IV: Management of SLE and APS:**  
Today and Tomorrow

**Moderators:** Professor Gianfranco Ferraccioli (Italy) &  
Professor Sandra V. Navarra (Philippines)



**Professor Ricard Cervera, MD, PhD, FRCP**  
Hospital Clinic, Barcelona, Catalonia, Spain

## Plasma exchange and IVIG in SLE and APS

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Therapeutic plasma exchange (TPE) is an extracorporeal blood purification technique designed for the removal of large molecular weight substances from the plasma and replacement by either fresh-frozen or stored plasma. The basic premise of TPE is that removal of large molecular weight substances will reduce further damage and may permit reversal of the pathologic process. Examples of these substances include autoantibodies, immune complexes, cryoglobulins, myeloma light chains, endotoxins and cholesterol-containing lipoproteins. Infusion of normal plasma may itself have beneficial effects, independent of removal of abnormal circulating factors. Indeed, there is compelling evidence that replacement of a deficient plasma component contributes too, and that this may be the principal mechanism of action in some entities. Since its clinical availability in the late seventies, TPE has been used in a variety of diseases, such as systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS), the pathogenesis of which may be influenced by humoral factors.<sup>1</sup>

Intravenous immunoglobulins (IVIG) are a highly purified IgG preparation made from pooled human plasma from 3,000 to 10,000 healthy blood donors and typically contain more than 95% unmodified IgG, which has functionally intact Fc-dependent effector functions and only trace amounts of IgA, IgM, soluble CD4+, CD8+, HLA molecules and certain cytokines. They were initially used for the treatment of primary immunodeficiency syndromes. However, more recently IVIG have proven useful for the treatment of a wide variety of other clinical conditions such as infectious processes, neuroimmunological diseases and different systemic autoimmune diseases, including SLE and APS.<sup>2</sup>

### Learning Objectives

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

- Understand the rationale and mechanisms of action of therapeutic plasma exchange (PE) and intravenous immunoglobulins (IVIG) in SLE and APS.
- Outline the clinical indications of these therapeutic procedures in SLE and APS.
- Recognize their potential side effects.
- Review the current treatment recommendations and preview the trends of these procedures in SLE and APS therapy.



## Abstracts

**Plenary IV: Management of SLE and APS:**  
Today and Tomorrow

**Moderators:** Professor Gianfranco Ferraccioli (Italy) &  
Professor Sandra V. Navarra (Philippines)



### **Professor Richard A. Furie, MD**

Hofstra North Shore-LIJ School of Medicine, New York, USA

## Managing SLE Today and in 2025

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The lupus community witnessed major treatment breakthroughs in nearly every decade over the last 70 years. In the late 1940s the discovery of compound E, cortisone, revolutionised the treatment of patients not only with lupus but across all inflammatory diseases. During the 1950s, azathioprine was introduced as a chemotherapeutic agent, but it was adopted soon thereafter as a drug for patients with rheumatic diseases. The antimalarial quinacrine was also first used in the early 1950s. Subsequently, cyclophosphamide became the eighth cytotoxic anticancer drug approved by the Food and Drug Administration (FDA). Its application to patients with severe forms of lupus remains to this day. In the late part of the twentieth century, mycophenolate mofetil received approval to combat acute kidney transplant rejection, and in the early part of the twenty-first century it was

adopted as a rival to cyclophosphamide for lupus nephritis (although it is not FDA-approved for this condition). The twentieth century closed with a foray into clinical trials in an effort to discover safer and more efficacious drugs for our lupus patients. While the outcomes of such efforts have been largely unsuccessful, two positive Phase 3 studies with belimumab led to its approval in 2011.<sup>1-3</sup> Along the way, experience with other biologics, such as rituximab<sup>4</sup> and abatacept,<sup>5</sup> was gained, and while these drugs are not approved for lupus, they are used by many physicians to treat their lupus patients. What will the next decade bring? There is currently unprecedented activity in the area of drug development in patients with lupus.<sup>6-11</sup> Although the obstacles to drug development are many, there is no doubt that by the year 2025, rheumatologists will have an expanded treatment armamentarium.

### Learning Objectives

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

- Recognise unmet needs in the treatment of patients with lupus.
- Understand issues related to clinical trial design.
- Be familiar with strategies for drug development in lupus.
- Know which clinical trial efforts are currently underway.



## Notes

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