Abstract Book

Fira Palace Hotel, Barcelona, Spain 16–18 March 2012





Continuing Medical Education



The 'European CME Forum' is accredited by the European Accreditation Council for Continuing Medical Education (EACCME) to provide the following CME activity for medical specialists: 'Inaugural Meeting of the Lupus Academy'. The EACCME is an institution of the European Union of Medical Specialists (UEMS) www.uems.net. The 'Inaugural Meeting of the Lupus Academy' is designated for a maximum of 9 hours of European external CME credits. Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity. Through an agreement between the UEMS and the American Medical Association, physicians may convert EACCME credits to an equivalent number of AMA PRA Category 1 Credits™. Information on the conversion process can be found at www.ama-assn.org/go/internationalcme. Live educational activities occurring outside of Canada recognised by the

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HUMAN GENOME SCIENCES



Welcome

Dear Friends and Colleagues,

We are delighted to welcome you to the 2012 Inaugural Meeting of the Lupus Academy, which we anticipate to be one of the most refreshing and informative meetings on the Lupus calendar.

This continuing medical education (CME) accredited meeting aims to provide valuable insights into advances in global research and clinical practice in Lupus and allied diseases. The scientific programme, developed by our Steering Committee of six international experts in Lupus, is designed to create a highly interactive forum through which we can exchange information and experiences about the management of Lupus across Europe. It will give you the opportunity to meet world-leading clinicians and scientists, exchange information and personal experiences, and further develop your knowledge in this high-profile therapeutic area.

We sincerely hope that the meeting will provide you with new ideas and enhanced enthusiasm for future interaction and discussion with your colleagues in Lupus.

With kind regards,

The Lupus Academy Steering Committee

Professor Roger A. LevyProgramme Director, Co-Chairman

Professor Ricard CerveraMeeting Course Director, Co-Chairman

Professor David A. Isenberg Professor Munther A. Khamashta Professor Sandra V. Navarra Professor Ronald F. van Vollenhoven

Mission Statement

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

Programme

Friday 16 March		Page	
19:00	Opening Address	David A. Isenberg & Ricard Cervera	
Keynote Presentation Moderator: David A. Isenberg			
19:10	Re-classifying lupus: can we improve the ACR revised criteria and is this a single disease anyway?	Michelle Petri	16
19:40	Welcome Dinner, Fira Palace Hotel		

Saturday	17 March		Page
07:00-08:15	Breakfast, Fira Palace Hotel		
Plenary I: Pa	thogenesis and Biomarkers	Moderator: Ricard Cervera	
08:30	B cells in the pathogenesis of lupus: a surprising twist	Claudia Mauri	18
08:50	New biomarkers in lupus: what's looking really good?	Matthias Schneider	20
Roundtable:	The Kidney	Moderator: David P. D'Cruz	
09:10	Can we avoid end-stage disease in all patients?	Liz Lightstone	22
09:30	How to recognise and manage membranous lupus nephropathy	Chi Chiu Mok	24
09:50	Renal microangiopathy related to APS in lupus: how important is it?	Maria G. Tektonidou	26
10:10	Questions and answers		
10:40	Coffee		
Case Study	Workshops		
11:00	Moderator: Chi Chiu Mok Kidney disease: when to biopsy? how to approach?	Presenters: Liz Lightstone & Maria G. Tektonidou	30
11:00	Moderator: David P. D'Cruz CNS and CV diseases: can we predict? how to avoid?	Presenters: John G. Hanly & Ian N. Bruce	32
11:00	Moderator: Munther A. Khamashta Pregnancy, contraception and APS: counselling and approach	Presenters: Imad Uthman & Roger A. Levy	34
11:00	Moderator: David A. Isenberg Metrics: outcome measures in clinical practice	Presenters: Sandra V. Navarra & Matthias Schneider	36
12:30	Lunch		
Plenary II: Antiphospholipid Syndrome Moderator: Roger A. Levy			
14:00	The challenge of antiphospholipid syndrome	Munther A. Khamashta	40



Programme

Saturday 17 March		Page	
Roundtable:	CV, CNS and Pregnancy	Moderator: Munther A. Khamashta	
14:20	How to assess CV morbidity in SLE	lan N. Bruce	42
14:40	Instruments to measure outcomes of neuropsychiatric manifestations	John G. Hanly	44
15:00	The paradigm of pregnancy in SLE revisited	Roger A. Levy	46
15:20	Questions and answers		
Case Study	Workshops (with Coffee)		
16:00	Moderator: Chi Chiu Mok Kidney disease: when to biopsy? how to approach?	Presenters: Liz Lightstone & Maria G. Tektonidou	30
16:00	Moderator: David P. D'Cruz CNS and CV diseases: can we predict? how to avoid?	Presenters: John G. Hanly & lan N. Bruce	32
16:00	Moderator: Munther A. Khamashta Pregnancy, contraception and APS: counselling and approach	Presenters: Imad Uthman & Roger A. Levy	34
16:00	Moderator: David A. Isenberg Metrics: outcome measures in clinical practice	Presenters: Sandra V. Navarra & Matthias Schneider	36
17:30 Close of Day 1			
19:00 Meet in the hotel lobby for transport to dinner at La Dama del Paraigua			

Sunday 18 March		Page	
07:00-08:15	Breakfast, Fira Palace Hotel		
Roundtable:	Treatment I	Moderator: David A. Isenberg	
08:30	What trials of new biologic therapies have taught us: success arises from failure	Richard A. Furie	48
08:50	Differential drug effects in various ethnic groups: what are the data?	Sandra V. Navarra	50
09:10	The pros and cons of hydroxychloroquine	Guillermo Ruiz-Irastorza	52
09:30	09:30 Questions and answers		
10:00 Coffee			
Roundtable:	Roundtable: Treatment II Moderator: Sandra V. Navarra		
10:30	Classic and modern immunosuppressive drugs: from the NIH to the Euro-lupus regimen	Ricard Cervera	54
10:50	Should lupus be treated early and aggressively or not?	David P. D'Cruz	56
11:10	Biologic therapies for lupus – new and shiny, but are they effective? David A. Isenberg		58
11:30 Questions and answers			
12:00	Closing remarks	Ricard Cervera & Roger A. Levy	

Biographies



Professor Ian N. Bruce, MD, FRCPUniversity of Manchester *UK*

lan Bruce is Professor of Rheumatology at the Arthritis Research UK Epidemiology Unit, School of Translational Medicine, University of Manchester. He is co-Chair of the Inflammatory Musculoskeletal Conditions Division, and lead for the Cardiovascular Research Group. He qualified in medicine from Queen's University Belfast in 1988 and gained his MRCP in 1991. He trained in medicine and rheumatology in Northern Ireland and completed his MD thesis on the pathogenesis of systemic vasculitis in 1995. He was the Geoff Carr Lupus Fellow at the University of Toronto, before moving to Manchester in 1998 as an NHS consultant, transferring to the University in 2003.

Professor Bruce is on the Editorial Board of the journal *Rheumatology.* He is a member of the Systemic Lupus International Collaborating Clinics (SLICC)

and the British Isles Lupus Assessment Group, and participates in a number of national and international multicentre studies that are seeking to refine our understanding of SLE. He leads the Cardiovascular Group within the Arthritis Research UK Epidemiology Unit and is joint Principal Investigator on the Norfolk Arthritis Registry (NOAR), Cardiovascular Substudy. He is involved in the Wellcome Trust Case Control Consortium and the British Society for Rheumatology Biologics Registry Control Consortium.

Professor Bruce's major research focus is on the association between inflammatory rheumatic diseases and premature atherosclerosis/coronary heart disease. In particular, his focus is on systemic lupus erythematosus and rheumatoid arthritis. He has published 100 papers in his field.

Disclosures

Spain

Grants/Research: UCB, GlaxoSmithKline & Roche.

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Speakers' Bureau: Human Genome Sciences, Bristol-Myers Squibb & Pfizer.



Professor Ricard Cervera, MD, PhD, FRCP Hospital Clínic, Barcelona

Ricard Cervera is Head of the Department of Autoimmune Diseases (which he co-founded in 1995), at Hospital Clínic, Barcelona. He is also Director of the Research Group on Systemic Autoimmune Diseases at the Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS). 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 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, Chairman of the Medical Advisory Board of the Catalan Association of Lupus Patients, and Medical Advisor to Lupus Europe. He chaired the 6th 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 systemic lupus erythematosus and the antiphospholipid syndrome, with special focus on its 'catastrophic' variant. He has presented over 300 invited lectures and published more than 800 scientific papers, including original articles in the New England Journal of Medicine, The Lancet, Annals of Rheumatic Diseases, Arthritis and Rheumatism, American Journal of Medicine, and Medicine (Baltimore). He is co-editor of 20 books, including 'The Antiphospholipid Syndrome', 'Vascular Manifestations of Systemic Autoimmune Diseases', and 'Diagnostic Criteria in Autoimmune Diseases'.

Disclosures

Consultant/Advisor: GlaxoSmithKline, Human Genome Sciences, Roche, Medimmune, UCB, Cephalon, Inova, Werfen Group & Menarini Diagnostics.

Professor Cervera is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the inaugural meeting programme and materials.





Dr David P. D'Cruz, MD, FRCPSt Thomas' Hospital, London *UK*

David D'Cruz is Consultant Rheumatologist and Clinical Team Lead at the Louise Coote Lupus Unit, St Thomas' Hospital, London. He is also George Koukis Reader in Vascular Rheumatology at Kings College School of Medicine, London. He graduated from St Mary's Hospital Medical School, London in 1983 and undertook Senior House Officer and Registrar rotations at University College and the Royal London Hospitals. He was a Registrar and held an Arthritis Research Campaign Clinical Research Fellowship at St Thomas' Hospital, London, and then became Senior Lecturer in Rheumatology at St Bartholomew's and The Royal London Hospitals, a post he held until 2000.

Dr D'Cruz is one of the Managing Editors of the journal *Lupus* and was Editor-in-Chief of the *Journal of Autoimmune Diseases* from its launch in 2004 until 2009. He was President of the Rheumatology Section of the Royal Society of Medicine from 2008–2009.

Dr D'Cruz's major clinical and research interests are systemic lupus erythematosus (SLE)— particularly lupus nephritis treatment and outcome, antiphospholipid syndrome, and systemic vasculitis. He is actively involved in clinical research projects including new therapies for SLE and vasculitis and has published over 130 peer-reviewed papers, 60 editorials and reviews, and 15 book chapters.

Disclosures

Grants/Research: Aspreva Pharmaceuticals. Consultant/Advisor: GlaxoSmithKline. Speakers' Bureau: GlaxoSmithKline.



Professor Richard A. Furie, MD Hofstra North Shore-LIJ School of Medicine, New York USA

Richard Furie is Chief of the Division of Rheumatology and Allergy-Clinical Immunology at North Shore-Long Island Jewish Health System, New York and Professor of Medicine at the Hofstra North Shore-LIJ School of Medicine. He directs the Program in Novel Therapeutics, the health system's clinical research programme in musculoskeletal disease. He also directs the hospital's Systemic Lupus Erythematosus (SLE) and Autoimmune Disease Treatment Center, which has become nationally recognised for its role in the development of new therapies for SLE.

Professor Furie is on the Editorial Board of the Lupus Foundation of America Lupus News. He is regarded as one of the senior rheumatologists in the New York metropolitan area, and has been on the Boards of Directors of the local chapters of the Arthritis Foundation and the Lupus Alliance of America. He is a member of the Lupus Foundation of America's Medical-Scientific Advisory Council and of the Medical and Scientific Advisory Board of the SLE Foundation. Professor Furie served as the American College of Rheumatology's Chair of the Annual Scientific Meeting for 3 years, and currently chairs the Committee on Education.

Professor Furie is a rheumatologist whose interests lie in the management of patients with lupus and antiphospholipid antibody syndrome. He is particularly active in clinical research aimed at advancing new therapies for patients with rheumatic diseases.

Disclosures

Grants/Research: GlaxoSmithKline, Human Genome Sciences, Bristol-Myers Squibb, Genentech, Roche, Biogen Idec & UCB. Consultant/Advisor: GlaxoSmithKline, Human Genome Sciences, Bristol-Myers Squibb, Genentech, Roche, Biogen Idec & UCB. Speakers' Bureau: GlaxoSmithKline & Human Genome Sciences.

Biographies



Professor John G. Hanly, MD, MRCPI, FRCP Dalhousie University, Nova Scotia Canada

John Hanly is Professor of Medicine and Pathology at Dalhousie University and attending staff physician in Capital Health, Halifax, Nova Scotia, Canada. He is the Director of the Dalhousie University Lupus Clinic in Halifax, Nova Scotia. Professor Hanly obtained his medical degree from the National University of Ireland in 1978 and trained in general internal medicine and clinical rheumatology in Ireland prior to relocating to Canada in 1984. He undertook clinical fellowships in rheumatology and immunology at the University of Toronto and McMaster University before joining the Faculty of Medicine at Dalhousie University in 1987.

Professor Hanly is on the Editorial Boards of the *Journal of Rheumatology* and *Lupus*. He is a

member of several national and international research networks involved in clinical studies of systemic lupus erythematosus (SLE). He is the Chair of the Systemic Lupus International Collaborating Clinics (SLICC), a research network comprising 37 lupus investigators in 30 academic centres in 11 countries. He has published extensively and has received awards in recognition of his achievements in clinical research in lupus.

Professor Hanly's major research focus is the study of pathogenic mechanisms and clinical outcomes in SLE, with a particular emphasis on ways in which lupus may affect the brain and other parts of the nervous system. He also conducts clinical trials in patients with SLE and rheumatoid arthritis.

Disclosures

None.



Professor David A. Isenberg, MD, FRCP, FAMSUniversity College London UK

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 Arthritis Research Campaign Diamond Jubilee Chair of Rheumatology at UCL in 1996. He has Fellowships from 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

and was Chair of the Systemic Lupus International Collaborating Clinics (SLICC) group. During the past 20 years, Professor Isenberg has undertaken many roles at Arthritis Research UK, for whom he currently chairs the autoimmune rheumatic disease clinical trials sub-committee. He is past President of the British Society for Rheumatology (2004–2006) and has chaired the Society's Biologics Register Committee for the past 5 years (2006–2011). Professor Isenberg is the 2010 recipient of the Evelyn Hess Prize from the Lupus Foundation of America for his contribution to lupus research and treatment.

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 (SLE), Sjögren's syndrome, myositis, and antiphospholipid antibody syndrome.

Disclosures

Consultant/Advisor: Roche, GlaxoSmithKline, Merck Serono, Teva, Celltech & Human Genome Sciences. 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 inaugural meeting programme and materials.





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

Munther Khamashta is Reader/Consultant Physician and Director of The Lupus Research Unit at St Thomas' Hospital, London, and 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 UK.

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 Erythmatosus. 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 500 original papers, and 750 abstracts presented at national and international meetings. He has also published several books.

Disclosures

Consultant/Advisor: GlaxoSmithKline, Human Genome Sciences & Medimmune.

Professor Khamashta is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the inaugural meeting programme and materials.



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

Roger Levy is Adjunct Professor of Rheumatology at The State University of Rio de Janeiro, Brazil. Graduating from medical school at the 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.

Professor Levy holds positions on a number of Editorial Boards including the Journal of Clinical Rheumatology, Lupus, 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 was President of the Rio de Janeiro Rheumatology Society (2007–2008). He is currently coordinating the vasculopathy committee of the Brazilian Society of Rheumatology and will chair the XIV International Antiphospholipid Congress (APLA) and the Latin American Congress of Autoimmunity (LACA) in Rio de Janeiro in 2013.

Professor Levy's research is based around the clinical and immunological aspects of systemic lupus erythematosus, antiphospholipid syndrome, Sjögren's syndrome, and pregnancy in rheumatic patients. He has published over 80 articles in medical journals, over 100 abstracts, and over 20 book chapters, and has lectured in many countries.

Disclosures

Grants/Research: Actelion, Anthera, Biogen Idec, Bio-Rad, Celltrion, GlaxoSmithKline, Human Genome Sciences & Pfizer. Consultant/Advisor: Abbott, Bristol-Myers Squibb, Janssen, Fourteen22, GlaxoSmithKline & Human Genome Sciences. Speakers' Bureau: Abbott, Bristol-Myers Squibb, Janssen, GlaxoSmithKline, Human Genome Sciences, Pfizer & Roche. Professor Levy is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the inaugural meeting programme and materials.

Biographies



Dr Liz Lightstone, PhD, FRCPImperial College London *UK*

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

Dr Lightstone has major roles in undergraduate and postgraduate medicine at Imperial College, in particular in her role as Director of the North West Thames Foundation School. She is a member of the LUPUS UK Peer Review Panel. She is an elected member of the UK Renal Association Executive and is active in the Renal Association Clinical Affairs Board, the Education and Training and the Equal Opportunities Committees.

Dr Lightstone's research is now focused on lupus nephritis and renal disease in ethnic communities. Together with colleagues in the ICHNT RTC, she has pioneered the use of steroid-minimising regimens in lupus nephritis. She is working on identifying urine biomarkers that better predict the outcome of lupus nephritis. She is joint Principal Investigator on a study, funded by Kidney Research UK, to identify the incidence and progression of chronic kidney disease in the Indian Asian community in West London. Her main clinical interests are in lupus nephritis and the management of women with kidney disease in pregnancy.

Disclosures

Consultant/Advisor: GlaxoSmithKline, Roche, Aspreva Pharmaceuticals, Biogen Idec, Vifor & Genentech.



Professor Claudia Mauri, PhDUniversity College London *UK*

Claudia Mauri is Professor of Immunology at University College London (UCL). She received her PhD in 1984 from University La Sapienza in Rome, Italy, and performed postdoctoral work in London at The Kennedy Institute of Rheumatology, Imperial College London. She moved to UCL in 2002 where she established her group, which was amongst the first to identify a novel subset of B cells with a powerful immunosuppressive capacity. Her work was seminal in the identification of CD40 activation for the regulatory B cell activation and how the adoptive transfer of this B cell subset can efficiently prevent disease development and ameliorate established arthritis. Her group has also phenotypically identified regulatory B cells and demonstrated that they are contained within the immature transitional 2 B cell subset (T2-Breg), demonstrating that this immature subset of B cells has a striking and previously unrecognised immunoregulatory potential.

Professor Mauri's research interests lie in understanding the mechanisms driving autoimmunity, and in understanding the function of regulatory B cells in experimental models of rheumatic disease and in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis. Her group has recently translated the results obtained from experimental models to both healthy individuals and patients with rheumatoid arthritis and SLE. In a recent publication her group described the existence of human regulatory B cells and showed how they achieve suppression. Professor Mauri's laboratory has also demonstrated that regulatory B cells isolated from patients with SLE are functionally defective. She is author of over 60 papers.

Disclosures

None.





Dr Chi Chiu Mok, MD, FRCPTuen Mun Hospital
Hong Kong

Chi Chiu Mok is Chief of Rheumatology at Tuen Mun Hospital, Hong Kong. He is also the founder and Director of the Center for Treatment of Rheumatic Diseases at Pok Oi Hospital, Hong Kong. Dr Mok is the Secretary of the Accreditation Board of Rheumatology of the Hong Kong College of Physicians and is an Honorary Teaching Professor of the Chinese University of Hong Kong. He is the Principal Investigator of a number of clinical trials of novel biological agents in systemic lupus erythematosus (SLE), rheumatoid arthritis, and glucocorticoid-induced osteoporosis.

Dr Mok is on the Editorial Boards of a number of leading journals, including the *International Journal of Rheumatic Diseases*, *Current Rheumatology Review*, *Immunology* and *Immunogenetics Insights*, and *The Open Rheumatology Journal*. He is an *ad hoc*

reviewer for more than 50 rheumatology and medical journals. He is President of The Hong Kong Society of Rheumatology, and was on the organising panel for Ten Topics in Lupus, 2010, in Hong Kong.

Dr Mok's main research interest is SLE in which he has published more than 140 first-author papers in various international peer-reviewed journals and presented more than 165 abstracts at major international meetings. Up until November 2011, he had reviewed more than 300 papers and six research grants. In addition, he was lead author of the 'Management of Rheumatoid Arthritis: Consensus Recommendations from the Hong Kong Society of Rheumatology' published in 2011.

Disclosures

Consultant/Advisor: Pfizer.



Professor Sandra V. Navarra, MD, FPCP, FPRAUniversity of Santo Tomas, Manila *Philippines*

Sandra Navarra is Professor and Head of Rheumatology at University of Santo Tomas, Manila, 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 a former President of the Philippine Rheumatology Association. She founded the Arthritis Care and Research Foundation of the Philippines where she is currently the Scientific Programmes Director, and the Lupus Foundation of the Philippines where she served as Medical Director. Currently President and CEO of the Rheumatology Educational Trust Foundation Inc. (RETFI), she is the prime mover of Lupus Inspired Advocacy (LUISA) Project for lupus education and research, and the

People Empowerment for Arthritis and Lupus (PEARL) Movement for lay education programmes.

Professor Navarra is a Senior Associate Editor of the *International Journal of Rheumatic Diseases*, 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 education and research.

Professor Navarra has organised several national and regional educational meetings including the Ten Topics in Rheumatology (Asia, 2009) and currently chairs the organising committee for the Asian Lupus Summit to be held in Manila, Philippines in 2012.

Disclosures

Speakers' Bureau: Roche, GlaxoSmithKline, Pfizer & Merck Sharp & Dohme.

Professor Navarra is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the inaugural meeting programme and materials.

Biographies



Professor Michelle Petri, MD, MPHJohns Hopkins University School of Medicine, Baltimore *USA*

Michelle Petri is a Professor of Medicine and Director of the Lupus Center at the Johns Hopkins University School of Medicine, Baltimore, USA. She attended medical school at Harvard University and fulfilled her internal medicine residency at the Massachusetts General Hospital. She then completed two fellowship programs at the University of California, San Francisco in allergy and immunology, and rheumatology. She received her MPH from Johns Hopkins University School of Hygiene and Public Health and Epidemiology. She is the Director of the Hopkins Lupus Cohort, a longitudinal study of morbidity and mortality in systemic lupus erythematosus (SLE), and co-Director of the Hopkins Lupus Pregnancy Center.

Professor Petri is on the Editorial Boards of *The Journal of Rheumatology* and *Arthritis and Rheumatism*. She is a member of the Lupus Foundation of America's Education Committee (1992–present), and the American College of

Rheumatology's Council on Research Sub-committees for Clinical Trials (1993–present) and Medical Student Recruitment (1993–present). She was Chair of the FDA Arthritis Advisory Committee from 1997–1998 and is a Fellow of the American College of Rheumatology.

Professor Petri's main research interest is SLE, including the longitudinal study of outcomes (demographic disease activity, treatment, and laboratory tests), lupus in pregnancy and pregnancy outcomes, prevention of atherosclerosis in lupus patients, and research into brain changes during disease progression. She is also involved with longitudinal studies on the 'interferon signature' genes, which are biomarkers for SLE, and on genotype-phenotype comparisons in SLE, with initial focus on Fc gamma receptor alleles.

Disclosures

Grants/Research: Human Genome Sciences, Medimmune, UCB, Teva & Anthera. Consultant/Advisor: Human Genome Sciences, GlaxoSmithKline, Medimmune, UCB, Pfizer & Anthera.



Professor Guillermo Ruiz-Irastorza, MD, PhD Hospital Universitario Cruces, Bizkaia Spain

Guillermo Ruiz-Irastorza is Head of the Autoimmune Research Unit at the Hospital Universitario Cruces, Bizkaia, Spain. He received his MD from Universidad Autónoma de Madrid, Spain in 1990 and became a specialist in internal medicine in 1996. Following his PhD from the University of the Basque Country, Spain, in 1999, Professor Ruiz-Irastorza spent a year as a Research Fellow at the Lupus Research Unit, St Thomas' Hospital, UK, before returning to the Hospital Universitario Cruces to take up the position of Consultant Physician in Internal Medicine. In 2004, he received his title of Professor of Medicine from the University of the Basque Country, Spain.

Professor Ruiz-Irastorza is a member of the Editorial Board of *Lupus*, and a reviewer of several journals in the fields of rheumatology and autoimmune diseases.

He is a member of the board of the Grupo de Estudio de las Enfermedades Autoinmunes Sistémicas (GEAS), which coordinates the first Spanish national lupus inception cohort study (RELES). He has also been a full member of the Systemic Lupus International Collaborating Clinics (SLICC) since 2008.

Professor Ruiz-Irastorza's research interests focus on systemic lupus erythematosus, antiphospholipid syndrome, and pregnancy and autoimmune diseases. He is author of over 90 publications and 15 book chapters.

Disclosures

None.





Professor Dr Matthias Schneider, MD, PhD Heinrich-Heine-University, Düsseldorf Germany

Matthias Schneider is Head of Rheumatology in the Clinic for Endocrinology, Diabetology, and Rheumatology at Heinrich-Heine-University in Düsseldorf, where he has been a Professor since 1994. He received his MD after training at the Westphalian-Wilhelms-University in Münster. He has qualifications in internal medicine, rheumatology, physical therapy, and endocrinology.

Professor Schneider is Medical Advisor to the Board of the German Lupus Erythematosus Self Help Group. From 1999–2003, he was co-Chairman of the ACR Committee 'Lupus Response'. He has also served as Chairman of the German Cooperation Multipurpose Arthritis Centres (2002–2010), as a Board Member of the German Society of Rheumatology (since 2005),

and as a Committee member for 'The (European League Against Rheumatism) EULAR Lupus Guideline' (since 2005). He is also Head of the Advisory Panel and Medical Advisor to Lupus Europe.

Professor Schneider's main research interests are systemic lupus erythematosus (SLE), rheumatology, and rheumatic diseases. He has a particular interest in early diagnosis, and the validity of different imaging techniques for identifying and monitoring disease progression. He also studies gender-specific consequences for patients with rheumatoid arthritis or SLE in the work place. He has published over 99 papers in rheumatology and lupus.

Disclosures

Grants/Research: GlaxoSmithKline & UCB.

Consultant/Advisor: GlaxoSmithKline, UCB & Suppremol GmbH.

Speakers' Bureau: GlaxoSmithKline & UCB.



Dr Maria G. Tektonidou, MD, PhDUniversity of Athens *Greece*

Maria Tektonidou is Lecturer in Rheumatology at the University of Athens School of Medicine, Greece, and Head of the Rheumatology Unit of the First Department of Internal Medicine at Laikon Hospital, Athens. She received her medical degree and her PhD on antiphospholipid syndrome from the University of Athens. From 2008 to 2011, she worked as a guest researcher at the NIAMS/NIH, Bethesda, USA on outcome measures, health quality, and validation of new biomarkers in patients with systemic autoimmune diseases.

Dr Tektonidou serves as a reviewer for 15 international journals. She is a member of The European League Against Rheumatism (EULAR) Task Force on systemic lupus erythematosus (SLE) and the European Forum on Antiphospholipid Antibodies, and is co-investigator in international clinical trials. She is co-author of recent evidence-based recommendations for the management of SLE with

neuropsychiatric manifestations and for the prevention and management of thrombosis in antiphospholipid antibody-positive patients. She was also a member of the Task Force on Catastrophic Antiphospholipid Syndrome (APS) and Non-criteria APS Manifestations set up to assess the clinical utility of the international consensus statement on classification criteria and treatment guidelines for catastrophic APS.

Dr Tektonidou's major research interests include epidemiology, clinical manifestations, management and outcomes of patients with systemic autoimmune diseases, especially antiphospholipid syndrome and SLE. She has also published on the validation of promising new biomarkers for diagnosis, disease activity assessment and prognosis in patients with systemic autoimmune diseases. She has over 60 peer-reviewed publications in international journals and book chapters.

Disclosures

None.

Biographies



Professor Imad Uthman, MD, MPH, FRCP American University of Beirut Lebanon

Imad Uthman is Professor of Clinical Medicine and Head of the Division of Rheumatology, at the Faculty of Medicine and Medical Centre of the American University of Beirut, Lebanon. He received his MD from the American University of Beirut in 1988, before qualifying in internal medicine and then specialising in rheumatology. He also spent time as a Rheumatology Fellow at Notre Dame Hospital, Montreal, Canada, returning to his alma mater in 1995.

Professor Uthman is on the Editorial Boards of Rheumatology and of Letter to Editor: Rheumatology. He is President of the Lebanese Society of Rheumatology, and sits on his institution's Biomedical Review Board. Professor Uthman's major research interests include the study of antiphospholipid syndrome, systemic lupus erythematosus (SLE), biologic therapies in rheumatic diseases, vasculitis, paediatric rheumatology, and the clinical characteristics of rheumatic diseases in Lebanon. His broader interests include work on the human leukocyte antigen profile of patients with Behcet's Disease, and establishment of a serum bank for patients with connective tissue diseases. His clinical interests revolve around personalised healthcare and predicting which patients may benefit from certain treatments to avoid them having to try several therapies before finding one that works for them. He is the author of over 80 publications on various aspects of SLE, lupus, and the rheumatic diseases in leading international rheumatology journals.

Disclosures

Sweden

Grants/Research: Roche & MSD.

Speakers' Bureau: Roche, Jansen Cilag & Abbott.



Professor Ronald F. van Vollenhoven, MD, PhD Karolinska University Hospital

Ronald van Vollenhoven is Chief of the Unit for Clinical Therapy Research, Inflammatory Diseases at the Karolinska Institute and Chief of the Clinical Trials Unit in Rheumatology at Karolinska University Hospital, Sweden. He received his MD and PhD from the University of Leiden, The Netherlands. After graduating in 1984, he pursued immunology research at Cornell Medical College, New York, followed by specialty training in internal medicine at the State University of New York. He did a fellowship in rheumatology at Stanford University, California, and received American Board of Internal Medicine certification in both internal medicine and rheumatology. He was Assistant Professor of Medicine, then Medical Services Chief and Fellowship Director, in the Division of Immunology and Rheumatology at Stanford University. In 1998 he moved to Sweden and became Senior Physician and Chief of the Clinical Trials Unit in the Department of Rheumatology at the Karolinska University Hospital; he was appointed to his current position in 2010.

Professor van Vollenhoven is on several Editorial Boards, including *Annals of the Rheumatic Diseases*. He is on The European League Against Rheumatism (EULAR) scientific programme committee, and is Chair of the Swedish health economics working group, HeraS. He is co-founder of the International Registry for Biologics In Systemic lupus erythematosus (IRBIS) and of the NORD-STAR collaboration for Nordic trials in the rheumatic diseases.

Professor van Vollenhoven's research interests focus on the development and systematic evaluation of biological and immunomodulatory treatments for rheumatic diseases, including clinical efficacy, pharmacology, outcomes, and pharmacoeconomics. He has been Principal Investigator in many clinical trials of novel therapies in rheumatic diseases. He has published over 150 original papers, book chapters and reviews, and is editor of the textbook 'Targeted Treatment of the Rheumatic Diseases'.

Disclosures

Grants/Research: Abbott, GlaxoSmithKline, Merck Sharp & Dohme, Pfizer, Roche & UCB. Consultant/Advisor: Abbott, GlaxoSmithKline, Merck Sharp & Dohme, Pfizer, Roche & UCB.

Professor van Vollenhoven is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the inaugural meeting programme and materials.

Unfortunately, Professor van Vollenhoven will not be attending the Inaugural Meeting of the Lupus Academy in 2012.



Notes	



Keynote Presentation

Moderator: Professor David A. Isenberg

Professor Michelle Petri, MD, MPH

Johns Hopkins University School of Medicine, Baltimore *USA*

Re-classifying lupus: can we improve the ACR revised criteria and is this a single disease anyway?

The American College of Rheumatology (ACR) Systemic Lupus Erythematosus (SLE) classification criteria have recently been revised by the Systemic Lupus International Collaborating Clinics (SLICC). The new criteria were validated in order to meet new methodology requirements, improve their clinical relevance, and to incorporate the immunological developments in SLE since the criteria were first written in 1982.

A set of 702 expert-rated patient scenarios formed the basis of the new classification criteria. An initial rule was developed using recursive partitioning and logistic regression, which was then simplified and refined based on a consensus from SLICC physicians. A new sample of 690 SLE patients and controls was then used to validate the SLICC classification rule.

Classification of SLE using the SLICC criteria rule requires: a) Four separate criteria, of which at least one should be a clinical criterion *and* one an immunological criterion; or b) Lupus nephritis alone

in the presence of antinuclear antibodies or anti-dsDNA antibodies. The SLICC classification rule resulted in fewer misclassifications in the derivation set than the current ACR classification rule (49 *versus* 70, p=0.0082), had greater sensitivity (94% *versus* 86%, p<0.0001) and showed equal specificity (92% *versus* 93%, p=0.39). The SLICC classification rule resulted in fewer misclassifications in the validation set (66 *versus* 74, p=0.43) and had greater sensitivity (97% *versus* 83%, p<0.0001), but the specificity was lower (84% *versus* 96%, p<0.0001).

A large set of patient scenarios was rated by experts, who found that the new SLICC classification criteria were robust. More inclusive and updated definitions for each criterion were available, which, crucially, required that at least one each of both clinical and immunologic criteria were required to make a classification of SLE. However, lupus nephritis by biopsy alone (in the presence of SLE autoantibodies) is sufficient for classification under the new SLICC classification.

Learning Objectives

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

- Discuss the subdivision of SLE based on gene expression, ethnicity and presence of autoantibodies.
- Understand the new SLICC classification criteria for SLE.

Acknowledgement

Abstract adapted from reference 1.

References

1. Petri M, Orbai A, Alarcon G, Gordon C, Merrill J, Fortin P. Derivation and validation of systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2011;63:A1708.



Notes	



Plenary I: Pathogenesis and Biomarkers

Moderator: Professor Ricard Cervera

Professor Claudia Mauri, PhDUniversity College London
UK

B cells in the pathogenesis of lupus: a surprising twist

B cells have taken a centre stage in autoimmunity through the remarkable success of rituximab. With other B cell-targeting therapies in the pipeline, it has become imperative to distinguish B cells capable of suppressing disease from those causing it. Studies in a number of murine models of autoimmunity published over the last decade have provided compelling evidence that, in addition to producing antibodies, B cells also release cytokines.^{1,2} Thus, researchers have shown that B cells producing interleukin-10, namely regulatory B cells (Bregs), possess a powerful suppressive capacity and have the ability to interfere and dampen down excessive inflammatory responses.3 By taking advantage of experimental models of inflammation we have shown that Bregs are important in the maintenance of regulatory T cells (Tregs) and the suppression of pro-inflammatory responses.4 Mice specifically lacking Bregs developed devastating inflammation and displayed reduced numbers of other suppressor

cells.⁵ We have translated our results to healthy individuals and patients with systemic lupus erythematosus (SLE) and have shown that in patients with SLE, Bregs fail to exert their suppressive effect and to convey suppression to other regulatory cells. These results suggest that Bregs might play a critical role in controlling inflammatory responses and preventing SLE. Interestingly, SLE patients responding to rituximab have a higher number of functionally suppressive Bregs than those not responding to rituximab treatment.

Little is known about the biology of Bregs and why they stop working in patients with SLE. B cell-depletion therapy indiscriminately kills all B cells, good and bad. Thus, being able to distinguish suppressive from pathogenic B cells could have very important implications, since specific targeting of harmful B cells and better selection of patients most likely to benefit from these therapies would improve patient care.

Learning Objectives

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

- Understand the importance of the existence of one more B cells subset.
- Understand that B cells, in addition to producing antibodies, play a pleiotropic role including suppression
 of other immune cells.
- Gain more understanding into B cell-targeted therapies.

Acknowledgement

This work was supported by the Nuffield Foundation Oliver Bird Rheumatism Programme, Arthritis Research UK and Lupus UK.

- 1. Mauri C, Blair PA. Regulatory B cells in autoimmunity: developments and controversies. *Nat Rev Rheumatol* 2010;6:636–43.
- 2. Blair PA, Norena LY, Flores-Borja F, et al. CD19(+)CD24(hi)CD38(hi) B cells exhibit regulatory capacity in healthy individuals but are functionally impaired in systemic lupus erythematosus patients. *Immunity* 2010;32:129–40.
- 3. Mauri C. Regulation of immunity and autoimmunity by B cells. Curr Opin Immunol 2010;22:761-7.
- 4. Evans JG, Chavez-Rueda KA, Eddaoudi A, et al. Novel suppressive function of transitional 2 B cells in experimental arthritis. *J Immunol* 2007;178:7868–78.
- Carter NA, Vasconcellos R, Rosser EC, et al. Mice lacking endogenous IL-10-producing regulatory B cells develop exacerbated disease and present with an increased frequency of Th1/Th17 but a decrease in regulatory T cells. J Immunol 2011;186:5569–79.



Notes	



Plenary I: Pathogenesis and Biomarkers

Moderator: Professor Ricard Cervera

Professor Dr Matthias Schneider, MD, PhD Heinrich-Heine-University, Düsseldorf *Germany*

New biomarkers in lupus: what's looking really good?

In a heterogeneous disease like systemic lupus erythematosus (SLE), physicians wish to have markers that enhance diagnostic accuracy, assess disease activity, and improve treatment efficacy and prognosis.

Based on the known pathophysiological processes in SLE, autoantibodies, complement components, different types of toll-like receptors (TLRs), various immune cells, cytokines, chemokines, transcription factors or consequences of repair mechanisms may be tested as candidate biomarkers in SLE. In addition, markers that separate disease activity from infectious complication are needed urgently.

The translation of these candidate biomarkers into clinically useful biomarkers is complicated by the genetic heterogeneity, complexity of disease expression, variations in individual treatments, and the lack of standardized documentation of patients with lupus. When trying to determine disease course and prognosis, this multifaceted situation is further complicated by the fact that we do not understand the time-dependent effect of these biomarkers on predicting the clinical manifestation of SLE.

This is best shown by antinuclear antibodies (ANA), which obviously have some diagnostic importance for SLE, but are also found in up to 25% in the normal population. These antibodies could serve as prognostic markers as ANAs are present in approximately 50% of patients up to 5 years before disease manifestation,² but there are no published data to identify and differentiate possible SLE patients from the normal population. Moreover, these data can only be obtained by screening the entire population. Other antibodies, such as anti-phospholipid antibodies, define a subpopulation at risk for thromboembolic events, but their predictive value is not high enough to be used as preventive therapy; they can only be used in response to a clinical event.3 Even the best biomarker for predicting disease activity, C3 complement, is just a conceptual predictor of disease outcome;4 therefore, all biomarkers can be viewed as minor parts of a diagnostic picture that supports the physician's clinical judgement.

Learning Objectives

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

- Understand the complexity of biomarkers in SLE.
- Know that biomarkers are valid only in combination with clinical manifestations.
- Recognise that careful clinical investigation is the best 'biomarker' in SLE.

- 1. Li QZ, Karp DR, Quan J, et al. Risk factors for ANA positivity in healthy persons. Arthritis Res Ther 2011;13:R38.
- 2. Arbuckle MR, McClain MT, Rubertone MV, et al. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. N Engl J Med 2003;349:1526–33.
- 3. Miyakis S, Lockshin MD, Atsumi T, *et al.* International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006;4:295–306.
- 4. Mosca M, Tani C, Aringer M, *et al.* European League Against Rheumatism recommendations for monitoring patients with systemic lupus erythematosus in clinical practice and in observational studies. *Ann Rheum Dis* 2010:69:1269–74.



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Roundtable: The Kidney Moderator: Professor Dr David P. D'Cruz

Dr Liz Lightstone, PhD, FRCPImperial College London

Can we avoid end-stage disease in all patients?

Lupus nephritis remains a common complication of systemic lupus erythematosus (SLE) and is much more common in patients of non-Northern European descent. End-stage renal failure (ESRF), secondary to lupus nephritis, was common prior to the introduction of the use of cyclophosphamide. ESRF is now a relatively rare event but is much more common among those patients of Black or Asian origin.¹⁻⁴

Prevention of ESRF is possible if the following criteria are met:

- International Society of Nephrology/Renal Pathology Society (ISN/RPS) class III/IV or V nephritis is diagnosed early and treated promptly with more than just steroids.
- 2. Flares of nephritis are diagnosed early and treated promptly.
- 3. Chronic tubulointerstitial damage is avoided.
- 4. Proteinuria is controlled not only by control of nephritis but control of blood pressure and use of renin–angiotensin blockade.
- 5. Blood pressure is meticulously controlled.

However, some patients will progress to ESRF regardless of best efforts. This is largely due to the following:

- Presentation with aggressive, rapidly progressive, nephritis — a rapidly progressive glomerulonephritis picture.
- 2. Presentation with poor prognostic lesions, such as crescents and fibrinoid necrosis.
- 3. Childhood onset of lupus nephritis.
- 4. Recurrent flares and acquisition of chronic tubulointerstitial and glomerular scarring.
- Treatment-resistant forms of nephritis and failure to change medications prior to accrual of damage, failure of current therapeutic regimens, and genetic factors, e.g. ethnic predisposition to worse renal outcomes.
- 6. Non-adherence to medication.

Learning Objectives

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

- Describe the histological and clinical characteristics of poor prognostic lupus nephritis.
- Understand the importance of early diagnosis and treatment.
- Understand the rationale for treatment regimens.
- Understand the need for meticulous blood pressure control.
- Identify high-risk groups and strategies to reduce ESRF.

- 1. Costenbader KH, Desai A, Alarcon GS, et al. Trends in the incidence, demographics, and outcomes of end-stage renal disease due to lupus nephritis in the US from 1995 to 2006. Arthritis Rheum 2011;63:1681–8.
- 2. Hiraki LT, Lu B, Alexander SR, et al. End-stage renal disease due to lupus nephritis among children in the US, 1995–2006. Arthritis Rheum 2011;63:1988–97.
- 3. Lightstone L. Lupus nephritis: where are we now? Curr Opin Rheumatol 2010;22:252-6.
- 4. Patel M, Clarke AM, Bruce IN, Symmons DP. The prevalence and incidence of biopsy-proven lupus nephritis in the UK: Evidence of an ethnic gradient. *Arthritis Rheum* 2006;54:2963–9.



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Roundtable: The Kidney Moderator: Dr David P. D'Cruz

Dr Chi Chiu Mok, MD, FRCP Tuen Mun Hospital Hong Kong

How to recognise and manage membranous lupus nephropathy

Renal disease carries substantial morbidity and mortality in patients with systemic lupus erythematosus (SLE). In some ethnic groups, the incidence of renal disease is up to 60% within the first 5 years following onset of SLE.1 Among the histological classes of lupus nephritis, membranous nephropathy comprises one-fifth of all cases. Membranous lupus nephropathy (MLN) is characterised histologically by the presence of global or segmental continuous granular subepithelial immune deposits, often associated with concomitant mesangial immune deposits and hypercellularity.² According to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification, diffuse membranous glomerulonephritis refers to pure MLN lesions. When concomitant proliferative lesions are present, both diagnoses will be reported (for instance V+III or V+IVG/S).3 Compared with proliferative lupus nephritis, MLN often presents with a higher degree of proteinuria, but better renal function, and less commonly with concomitant active lupus serology or extra-renal SLE activity. Patient survival and renal survival rates of MLN vary considerably, because

of the heterogeneity among the published studies. The risk of progression from MLN to renal failure is generally reduced in the absence of proliferative lesions, but patients are more prone to arterial or venous thromboembolic complications. The optimal therapy for MLN is unclear because of the paucity of controlled trials. Cardiovascular protection and blockade of the renin-angiotensin system should be instituted early. Mixed membranous and proliferative lupus nephritis should be treated in the same way as pure proliferative lupus nephritis. When pure MLN is associated with clinically relevant proteinuria, renal insufficiency or failure to respond to supportive therapies, immunosuppressive treatment is indicated. Treatment options include glucocorticoids combined with azathioprine, mycophenolate mofetil, calcineurin inhibitors or alkylating agents.4 For refractory disease, a combination of different immunosuppressive agents or with the biological agents can be considered.5 Experimental modalities, such as rituximab, sirolimus and infliximab should be explored in future studies.

Learning Objectives

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

- Know the prevalence of MLN among biopsy-confirmed lupus nephritis patients.
- Recognise the differences in clinical presentation and histological features of MLN in comparison to proliferative nephritis in SLE.
- Recognise patient survival and renal survival rates in MLN.
- Understand evidence-based treatment for MLN.
- Identify complications of MLN.

- 1. Mok CC, Tang SK. Incidence and predictors of renal disease in Chinese patients with systemic lupus erythematosus. *Am J Med* 2004;117:791–5.
- 2. Mok CC. Membranous nephropathy in systemic lupus erythematosus: a therapeutic enigma. *Nat Rev Nephrol* 2009;5:212–20.
- 3. Weening JJ, D'Agati VD, Schwartz MM, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. *Kidney Int* 2004;65:521–30.
- 4. Kasitanon N, Petri M, Haas M, *et al.* Mycophenolate mofetil as the primary treatment of membranous lupus nephritis with and without concurrent proliferative disease: a retrospective study of 29 cases. *Lupus* 2008;17:40–5.
- 5. Mok CC. Therapeutic options for resistant lupus nephritis. Semin Arthritis Rheum 2006;36:71–81.



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Roundtable: The Kidney Moderator: Dr David P. D'Cruz

Dr Maria G. Tektonidou, MD, PhD

University of Athens *Greece*

Renal microangiopathy related to APS in lupus: how important is it?

Antiphospholipid syndrome (APS)-associated nephropathy, first described in primary APS, is characterised by acute thrombotic lesions in alomeruli or arterioles (thrombotic microangiopathy). chronic vascular lesions such as fibrous intimal hyperplasia, organised thrombi with or without recanalisation, fibrous arterial and arteriolar occlusions and focal cortical atrophy. APS-associated nephropathy has also been detected in patients with systemic lupus erythematosus (SLE)-related APS and in SLE/non-APS patients with positive antiphospholipid antibodies (aPL), in addition to but independently of lupus nephritis.^{2,3} Hypertension is recognised as the predominant clinical manifestation of APS-associated nephropathy, followed by haematuria, proteinuria (mild to nephrotic range) and renal insufficiency. Arterial thromboses (especially stroke), pulmonary embolism, livedo reticularis, anticardiolipin antibodies and a positive lupus anticoagulant have been

associated with APS nephropathy. Antiphospholipid syndrome nephropathy occurs more frequently in patients with positive aPL (with or without APS) than those without aPL and also among patients with APS (primary or SLE-related) than in SLE/aPL/non-APS patients. During the follow-up period, manifestations of APS (especially arterial thromboses) develop more frequently in SLE/non-APS patients with APS nephropathy than in those without. Based on these observations, it has been suggested that APS-associated nephropathy be included in the classification criteria for APS. Currently, there is no consensus on its management; however, antiplatelet treatment with, or without, an anticoagulant should be considered.4 Multicentre studies are needed to examine the full-spectrum of clinical and histological characteristics, long-term renal outcome, and the management of APS-associated nephropathy.

Learning Objectives

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

- Describe the histological and clinical characteristics of APS-associated nephropathy.
- Have awareness of the existence of APS-associated nephropathy among patients with systemic lupus erythematosus.
- Identify conditions associated with renal thrombotic microangiopathy.
- Understand the therapeutic management of APS-associated nephropathy.

- 1. Nochy D, Daugas E, Droz D, *et al.* The intrarenal vascular lesions associated with primary antiphospholipid syndrome. *J Am Soc Nephrol* 1999;10:507–18.
- 2. Daugas E, Nochy D, Huong DL, et al. Antiphospholipid syndrome nephropathy in systemic lupus erythematosus. *J Am Soc Nephrol* 2002;13:42–52.
- 3. Tektonidou MG, Sotsiou F, Nakopoulou L, Vlachoyiannopoulos PG, Moutsopoulos HM. Antiphospholipid syndrome nephropathy in patients with systemic lupus erythematosus and antiphospholipid antibodies: prevalence, clinical associations, and long-term outcome. *Arthritis Rheum* 2004;50:2569–79.
- Cervera R, Tektonidou MG, Espinosa G, et al. Task Force on Catastrophic Antiphospholipid Syndrome (APS) and Non-criteria APS Manifestations (I): catastrophic APS, APS nephropathy and heart valve lesions. Lupus 2011:20:165–73.



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Case Study Workshops

Saturday 17 March	
Morning (11:00) & Afternoon (16:00) Case Study Workshops	
Moderator: Chi Chiu Mok Kidney disease: when to biopsy? how to approach?	Presenters: Liz Lightstone & Maria G. Tektonidou
Moderator: David P. D'Cruz CNS and CV diseases: can we predict? how to avoid?	Presenters: John G. Hanly & lan N. Bruce
Moderator: Munther A. Khamashta Pregnancy, contraception and APS: counselling and approach	Presenters: Imad Uthman & Roger A. Levy
Moderator: David A. Isenberg Metrics: outcome measures in clinical practice	Presenters: Sandra V. Navarra & Matthias Schneider

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 16:00 hours.

Case Study Workshop

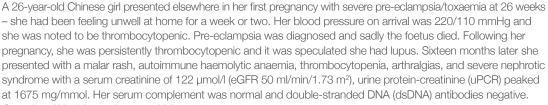




Moderator: Dr Chi Chiu Mok Presenters: Dr Liz Lightstone & Dr Maria G. Tektonidou

Kidney disease: when to biopsy? how to approach?

Dr Liz Lightstone, PhD, FRCP



Question: Would you do a renal biopsy? Question: What would it show? Question: How would you treat her?

Following our treatment regimen her PCR was <50 mg/mmol at 9 months after the start of treatment and there was no proteinuria (PCR <20 mg/mmol) 18 months after treatment.

Question: How long should she stay on maintenance treatment?

Question: What would you advise if she wishes to get pregnant - and, if she becomes pregnant, what treatment should she receive and which drugs should she be on or not be on?



A 30-year-old Portuguese woman attends for preconception counselling. She had class V lupus nephritis diagnosed and treated in Portugal 9 years earlier. She was treated with high-dose oral prednisolone for 9 months and went into complete sustained remission. She had been treatment-free for several years. At her first appointment for preconception advice, it transpired that she was 10 weeks pregnant! Additionally, she had positive dsDNA antibodies, normal complement, low serum albumin, normal serum creatinine and uPCR of 769 mg/mmol.

Question: Would you biopsy her? Question: What would it show? Question: How would you treat her?

Using our treatment regimen she improved throughout pregnancy and within a few weeks postpartum she was

in complete renal remission. She expresses her intent to become pregnant again.

Question: When would you advise her to get pregnant?

Question: What drugs would you change?

Case 3

A 45-year-old Indian Asian woman presents with severe lupus. She is anaemic, thrombocytopenic, severely hypertensive, has creatinine of 110 mmol/l (eGFR 46/min/1.73 m²), is nephrotic with uPCR 1237 mg/mmol and albumin of 19 g/l and has a dsDNA antibody titre of 2053, low C3, low C4.

Question: Would you biopsy her? Question: What would it show? Question: How would you treat her?

Using our standard treatment regimen she achieved partial remission with a creatinine of 55 (eGFR >90 mls/min/1.73 m²), and uPCR down to 150 mg/mmol by 6 months post treatment. However, she was intolerant of the medication and stopped adhering. She believed the treatment was making her worse and that she would simply go away and die. Her proteinuria started to rise and she became nephrotic again. Her mother had died and she went to India to scatter her ashes. She returned to clinic very unwell with a significant relapse with a uPCR now of 2120 mg/mmol, creatinine rising to 135 mmol/l (eGFR of 36 mls/min/1.73 m²) and serum albumin of 9 g/l, and she declined further treatment.

Question: Would you biopsy her now? Question: What would it show? Question: How would you treat her?



Dr Maria G Tektonidou, MD, PhD

Case 4

In January 2003, a 15-year-old female presented with fever, butterfly rash, arthritis, lymphadenopathy, Raynaud's phenomenon, purpuric rash of the lower extremities, leukopenia, anaemia, thrombocytopenia, positive anti-nuclear antibody (ANA), high anti-DNA levels, positive cryoglobulins and low levels of complement proteins C3 and C4. The diagnosis of systemic lupus erythematosus (SLE) was made and treatment with prednisolone (15 mg) and azathioprine (150 mg/d) gradually improved the patient's symptoms and laboratory results. Nine months later the patient developed proteinuria (600 mg/24h) and microscopic haematuria (RBC: 30–40/hpf) with normal serum creatinine levels, whereas the renal biopsy showed class Illb lupus nephritis (according to the WHO classification). Treatment according to the Euro Lupus protocol was started comprising six fortnightly intravenous-cyclophosphamide (IV-CY) pulses of 500 mg, and renal response was achieved at the end of the induction therapy. Maintenance treatment with mycophenolate mofetil 2 g/d was introduced, which subsequently decreased to 1 g/d due to neutropenia. Four years later, the patient presented with fever, lymphadenopathy, arthritis, mouth ulcers, vasculitic rash, leukopenia, anaemia, high erythrocyte sedimentation rate (ESR), increase of anti-DNA and decrease of complement levels, proteinuria (1.2 g/24h), haematuria (red blood cell: 20–30/high power field) with normal serum creatinine levels/glomerular filtration rate (GFR). Mycophenolate mofetil was discontinued and the patient received prednisolone 0.5 mg/kg and six monthly pulses of IV-CY (750 mg/m²), followed with azathioprine 150 mg/d. The patient remained in complete remission until January 2010, when she developed proteinuria 2–3 g/24h with normal renal function and no nephritic urinary sediment. Renal biopsy showed membranous lupus nephritis and therapy with rituximab (two fortnightly pulses of 1g) was administered alongside azathioprine with a gradual improvement in the degree of proteinuria to less than 1 g/

Learning Objectives

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

- Understand the indications for renal biopsy in lupus nephritis.
- Describe the recommended induction treatment in class III/IV lupus nephritis.
- Describe the recommended maintenance treatment in III/IV lupus nephritis.
- Understand the definition and management of a renal flare.
- Understand the management of membranous lupus nephritis.
- Understand how to approach a flare of lupus nephritis in pregnancy.

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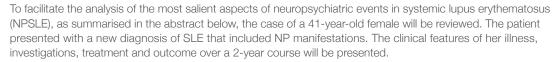
Case Study Workshop

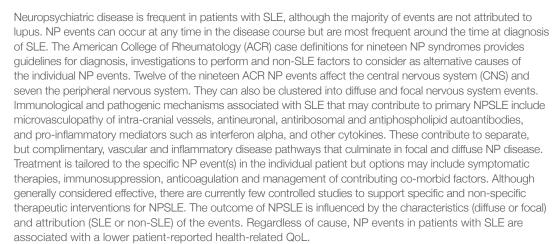


Moderator: Dr David P. D'Cruz Presenters: Professor John G. Hanly & Professor Ian N. Bruce

Workshop: CNS and CV diseases: can we predict? how to avoid?

Professor John G. Hanly, MD, MRCPI, FRCP









Professor Ian N. Bruce, MD, FRCP

Several cases of patients with SLE who have presented at various ages and after a variable time to diagnosis will be presented and discussed. This workshop will also consider patients from different ethnic backgrounds and with a variety of clinical manifestations, including patients with background lupus nephritis.

These cases will help us to understand how certain aspects of SLE may help identify patients at particular risk of cardiovascular (CV) complications, including myocardial infarction (MI) and stroke. We will discuss how CV risk factor profiles may change over time according to the stage of disease and how the level of intervention the patient requires can fluctuate over time.

We will consider the justification behind current proposed guidelines for the assessment and management of risk factors in patients with SLE and discuss the limitations of the evidence available to date. We will also discuss different approaches and settings in which risk factor assessment may occur and will illustrate one example of a nurse-led risk factor screening programme and how this can compliment the day-to-day management of the manifestations in a busy clinical setting.



Learning Objectives

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

- Appreciate the frequency and clinical diversity of NPSLE.
- Consider an approach for determining cause of NP events in SLE.
- Review the immunology and pathogenesis of primary NPSLE.
- Examine therapeutic options for patients with NPSLE.
- Assess the outcome of NP events and their impact on quality of life (QoL).
- Identify and understand the profiles of patients with SLE who are at particular risk of developing CV disease.
- Discuss the practical issues around assessing and screening for risk factors.
- Consider different screening approaches and strengths and weaknesses of these, in patients with SLE.
- Consider how screening for risk factors can be integrated into routine clinical practice.

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Case Study Workshop



Moderator: Professor Munther A. Khamashta Presenters: Professor Imad Uthman & Professor Roger A. Levy

Pregnancy, contraception and APS: counselling and approach

Professor Imad Uthman, MD, MPH, FRCP

Case

A 35-year-old female sustained a stroke 2 years ago and is on warfarin. Her laboratory profile shows IgG ACA: 85 GPL (high) and IgG Anti-β2 GPI: 75 (high). She has been married for 10 years and she wishes to conceive. She seeks advice for the management of her anticoagulation therapy should she become pregnant.

Case 2

A 29-year-old female married for 7 years has had no successful pregnancies. Her laboratory profile revealed IgG ACA: 90 GPL (high), IgM ACA: 75 MPL (high), and positive lupus anticoagulant (LAC). This patient is planning for *in vitro* fertilisation (IVF) and has read extensively about antiphospholipid syndrome (APS), she is therefore seeking advice on the best approach to prevent complications secondary to APS should her pregnancy be successful. She is also questioning whether or not she should receive anticoagulation during her IVF cycle.

Case 3

A 24-year-old female has systemic lupus erythematosus (SLE) with positive LAC, IgG ACA: 29 GPL (moderate) and IgM ACA: 35 MPL (moderate). Her medical history reveals one pregnancy loss secondary to intrauterine foetal demise during the second trimester. Her lupus is well controlled and she wishes to become pregnant. She is seeking advice on the best medical approach for management during her pregnancy.

Professor Roger A. Levy, MD, PhD

Case 4

A 38-year-old patient of mixed ethnicity has cutaneous-articular SLE and is 6 weeks pregnant, with a history of four second-trimester foetal losses — she had used low-dose aspirin during her fourth pregnancy. Her LAC is positive (60 GPL, 44 MPL).

Case 5

A 31-year-old patient with isolated APS is 20 weeks pregnant and taking prednisone 10 mg/d, but tapering dose because her platelet count was 86,000/µl on 20 December 2011 compared with 30,000/µl on 19 January 2011. Her previous pregnancy, 2 years ago, was complicated with massive proteinuria and thrombocytopenia (lowest 5,000 platelets), for which she was treated with pulse methylprednisolone and intravenous immunoglobulin.

Case 6

A 25-year-old patient with SLE, and two previous uneventful pregnancies, had negative tests for antiphospholipid antibodies and anti-dsDNA, and no protein in her urine. She is not planning to conceive in the next 2–3 years and asks for advice about contraception.

Learning Objectives

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

- Offer the most appropriate contraceptive scheme for individual SLE patients.
- Understand how to manage a pregnant woman with positive anti-Ro/SS-A antibodies.
- Diagnose and manage antiphospholipid syndrome (APS) during pregnancy.
- Differentiate between pre-eclampsia, lupus nephritis and APS microangiopathy, and treat accordingly.



References (further reading)

- 1. Clowse ME, Magder LS, Petri M. The clinical utility of measuring complement and anti-dsDNA antibodies during pregnancy in patients with systemic lupus erythematosus. *J Rheumatol* 2011;38:1012–6.
- 2. Yazdany J, Trupin L, Kaiser R, et al. Contraceptive counseling and use among women with systemic lupus erythematosus: a gap in health care quality? Arthritis Care Res (Hoboken) 2011;63:358–65.
- 3. Culwell KR, Curtis KM, del Carmen Cravioto M. Safety of contraceptive method use among women with systemic lupus erythematosus: a systematic review. *Obstetrics Gynecol* 2009;114:341–53.
- 4. Petri M, Kim MY, Kalunian KC, et al. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med 2005;353:2550-8.
- 5. Chabbert-Buffet N, Amoura Z, Scarabin PY, et al. Pregnane progestin contraception in systemic lupus erythematosus: a longitudinal study of 187 patients. Contraception 2011;83:229–37.

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Case Study Workshop



Moderator: Professor David A. Isenberg Presenters: Professor Sandra V. Navarra & Professor Dr Matthias Schneider

Metrics: outcome measures in clinical practice

Professor Sandra V. Navarra, MD, FPCP, FPRA

Case :



A 29-year-old female has had stable SLE on hydroxychloroquine 200 mg twice daily and prednisone 10 mg/day until a week ago when she developed fever, hair loss, and pruritic rashes, accompanied by malaise and joint pains. Physical examination showed temperature 38.5C, diffuse alopecia, cervical lymph nodes, tender proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints without swelling nor erythema, and scattered maculopapular rashes on the trunk and extremities.

Question: What is her SELENA*-SLEDAI score?

Blood counts, urinalysis and serum complement were normal. She improved on paracetamol and anti-histamine. *Question: Is there a mild/moderate SELENA flare?*

*Safety of Estrogen in Lupus Erythematosus National Assessment

Case 2



A 19-year-old female has been doing well on hydroxychloroquine 200 mg/day until a month ago when she was hospitalised for a haematological flare with platelet count of 10,000 and fever to 39C. Infection was ruled out, and she received IV methylprednisolone 1000 mg daily for 3 days and was discharged with a platelet count of 160,000. Prednisone 40 mg/day was tapered over the next 3 weeks to 10 mg/day; hydroxychloroquine was continued. *Question: The SELENA SLEDAI score at hospitalisation is?*

Case 3

A 32-year-old female has stable nephritis on prednisone 5 mg/day and mycophenolate mofetil 2 g/day. Three weeks ago, she started to complain of malaise, visual disturbance and difficulty with thought processes. A few hours ago, she was brought to the emergency department because of severe migraine headaches unrelieved by paracetamol; brain MRI showed several small white matter lesions. After extensive evaluation, a diagnosis of CNS involvement secondary to SLE was made. The patient was started on prednisone 40 mg/day to which she responded quickly and was discharged from hospital improved the following day. *Question: Name the correct BILAG index category grading for the nephritis and CNS involvement?*

A year later, she develops bilateral cataracts and begins to complain of pain on both hips. Hip radiographs showed evidence of osteonecrosis.

Question: Can baseline SLE disease activity indices accurately predict subsequent damage and other outcomes?

Professor Dr Matthias Schneider, MD, PhD

Question: How do you score SELENA flare and BILAG?

Case 4

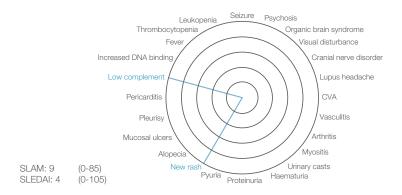
A 50-year-old white woman has had SLE for 20 years. She was originally diagnosed on the basis of a malar rash, arthritis, leukopenia, photosensitivity, pericarditis and oral ulcers. Following her diagnosis she also developed a seizure disorder, which is now treated, and a self-limited course of frank psychosis that required brief hospitalisation. Her disease course has been complicated by bilateral avascular necrosis of her hips. She underwent arthroplasty of her left hip 5 years ago and a core decompression of her right hip 1 year ago with moderate success in relieving her pain. She has also experienced significant remote alopecia in association with scalp inflammation that has left some appreciable scarring.

She presents now with a 14-day history of mild fatigue in association with a new malar rash, mild shortness of breath and cough on exertion, and symptoms suggesting Raynaud's phenomenon. She has pain in her right hip when she walks, in addition to a swollen and tender right wrist. She denies any seizures in the last 6 months, her thought processes are regular and she does not feel depressed or anxious. Examination reveals an erythematous and maculopapular rash to both cheeks, but her head and neck exam is otherwise normal. Her lung and cardiovascular examination is normal, but musculoskeletal examination reveals a tender and swollen right



wrist. Passive and active motion about her right hip is constrained at extremes of motion secondary to pain. No other joints are tender or swollen.

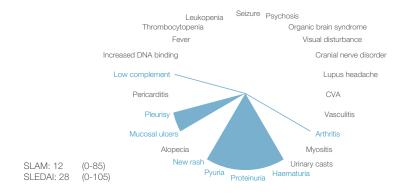
Haematological findings include: white count 3.1 (lymph 1600), haemoglobin 103, haematocrit 0.31, platelets 169, ESR 33, complement down. Urine normal.



Case 5

A 44-year-old white woman, G5, P2, A3 has had lupus for 10 years and was initially diagnosed on the basis of a malar rash, photosensitivity, mouth ulcers, arthritis, pleuropericarditis and renal abnormalities. She has a 3-week history of new mouth ulcers and a malar rash. She complains of mild shortness of breath on extreme exertion. She also complains of pain and swelling of both knees and ankles in addition to occasional gastrointestinal pain without a change in her bowel habits. Examination reveals a BP of 180/100. Head and neck examination confirms the presence of multiple mouth ulcers and a malar rash. Respiratory, cardiovascular and CNS examinations are normal. Her musculoskeletal examination reveals joint effusions and pain in both knees. She also has a swollen and tender left ankle and left wrist.

Haematological findings include: white count 9.1, lymph 7.0, haemoglobin 118, haematocrit 0.34, platelets 345, ESR 20, creatinine 142, creatinine clearance 80 ml/min (70% normal). DNA binding negative. Complement down. Urinanalysis: 24 hour protein 6.2 g/l, >30 RBC/hpf, >30 WBC/hpf. One red blood cast. Chest X-ray shows small bilateral pleural effusions.



Learning Objectives

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

- Provide an overview of the main activity measures in systemic lupus erythematosus (SLE):
 - SLEDAI: Systemic Lupus Erythematosus Disease Activity Index
 - BILAG: British Isles Lupus Assessment Group index
 - ECLAM: European Consensus Lupus Activity Measurement
 - SLAM: Systemic Lupus Activity Measure.
- Describe the clinical implications of the Systemic Lupus International Collaborative Clinics/American College of Rheumatology (SLICC/ACR) Damage Index.
- Apply disease activity measures to specific clinical situations and state how these may influence clinical decision-making.

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Plenary II: Antiphospholipid Syndrome

Moderator: Professor Roger A. Levy

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

The challenge of antiphospholipid syndrome

Antiphospholipid syndrome (APS), first described almost 30 years ago,¹ is now recognised as a major cause of deep vein thrombosis (DVT), stroke and heart attacks in young people (under 45 years of age). It is also the most common treatable cause of recurrent miscarriages and a major cause of late foetal death.² Other clinical manifestations include cardiac valvular disease, livedo reticularis, renal thrombotic microangiopathy, thrombocytopenia, haemolytic anaemia, epilepsy and cognitive impairment. The presence of antiphospholipid antibodies (aPL) has been closely related to the development of thrombosis and complications in pregnancy. However, not all patients with aPL will develop the clinical features. Lupus anticoagulant is generally thought to be

more strongly associated with the risk of clinical manifestations of APS than anticardiolipin and anti-β²-glycoprotein-I antibodies.³ The exact pathogenic mechanisms leading to thrombosis and/or pregnancy morbidity are poorly understood. Treatment of thrombosis is based on long-term oral anticoagulation and patients with arterial events should be treated aggressively.⁴ Obstetric care is based on combined medical–obstetric high-risk management and treatment with aspirin and heparin. Hydroxychloroquine is a potential additional treatment for this syndrome. Possible future therapies for non-pregnant patients with APS include statins, rituximab and new anticoagulant drugs (dabigatran and rivaroxaban).⁵

Learning Objectives

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

- Review the clinical and laboratory criteria for the classification of APS.
- Assess the risk of thrombosis and pregnancy complications in individuals that test positive for antiphospholipid antibodies.
- Describe the obstetric and thrombotic manifestations of APS.
- Discuss the evidence and best data supporting treatment decisions in APS.

- 1. Hughes GR. Thrombosis, abortion, cerebral disease, and the lupus anticoagulant. *Br Med J (Clin Res Ed)* 1983;287:1088–9.
- 2. Ruiz-Irastorza G, Khamashta MA. Lupus and pregnancy: integrating clues from the bench and bedside. Eur J Clin Invest 2011;41:672–8.
- 3. Pengo V, Ruffatti A, Legnani C, et al. Incidence of a first thromboembolic event in asymptomatic carriers of high-risk antiphospholipid antibody profile: a multicenter prospective study. *Blood* 2011;118:4714–8.
- 4. Ruiz-Irastorza G, Cuadrado MJ, Ruiz-Arruza I, et al. Evidence-based recommendations for the prevention and long-term management of thrombosis in antiphospholipid antibody-positive patients: report of a task force at the 13th International Congress on antiphospholipid antibodies. Lupus 2011;20:206–18.
- 5. Ruiz-Irastorza G, Crowther M, Branch W, Khamashta MA. Antiphospholipid syndrome. Lancet 2010;376:1498–509.



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Roundtable: CV, CNS and Pregnancy

Moderator: Professor Munther A. Khamashta

Professor Ian N. Bruce, MD, FRCPUniversity of Manchester
UK

How to assess CV morbidity in SLE

Patients with systemic lupus erythematosus (SLE) are now recognised to have a significantly increased risk of developing cardiovascular disease (CVD) including premature coronary heart disease (CHD) and early onset stroke. The overall risk of CVD in lupus is increased by a factor of 5–10 fold. In addition to clinical CHD, subclinical atherosclerosis is also noted in a high proportion of SLE patients. Atherosclerosis also begins at an early age and is a major driver of the clinical events observed.¹

A number of studies over the last 30 years have identified risk factors for cardiovascular events in SLE. These include certain classic risk factors, particularly hypertension and hyperlipidaemia. In addition, lupus patients tend to be more prone to developing aspects of the metabolic syndrome, which may also contribute to cardiovascular risk.² Exposure to chronic inflammation, the hallmark of SLE, also seems to drive atherogenesis and patients with renal involvement

and/or previous inflammatory cardiac disease may be particularly prone to atherosclerosis. Antiphospholipid antibodies are also likely to contribute either to the atherosclerotic process itself or to precipitation of clinical events. A number of drug therapies used in lupus, particularly corticosteroids, contribute to risk while antimalarial drugs may offer a protective effect.^{3,4}

There are no clinical trials to guide preventative management; however a proactive approach to screening and targeted reduction of classic risk factors seems to be important.⁵ In addition, careful control of disease activity, with the use of the minimal amount of steroid, whilst ensuring the patient takes antimalarial drugs, are also generally recommended. Whether novel biological therapies will contribute a protective effect remains to be demonstrated. Large-scale clinical trials will be needed to test a number of these hypotheses and allow translation to widespread clinical guidelines.

Learning Objectives

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

- Cardiovascular risk is increased in patients with lupus.
- Atherosclerotic manifestations can occur at an early age.
- Careful assessment of classic risk factors should be an integral part of lupus management.
- A targeted approach to risk factor modulation is recommended.
- Minimising steroid use and using antimalarial drugs where possible may have atheroprotective effects.

- 1. Urowitz MB, Gladman D, Ibanez D, et al. Atherosclerotic vascular events in a multinational inception cohort of systemic lupus erythematosus. *Arthritis Care Res (Hoboken)* 2010;62:881–7.
- 2. Parker B, Bruce IN. The metabolic syndrome in systemic lupus erythematosus. *Rheum Dis Clin North Am* 2010;36:81–97, viii.
- 3. Bruce IN, Gladman DD, Urowitz MB. Detection and modification of risk factors for coronary artery disease in patients with systemic lupus erythematosus: a quality improvement study. Clin Exp Rheumatol 1998;16:435–40.
- 4. Nikpour M, Urowitz MB, Gladman DD. Epidemiology of atherosclerosis in systemic lupus erythematosus. *Curr Rheumatol Rep* 2009;11:248–54.
- 5. Al-Herz A, Ensworth S, Shojania K, Esdaile JM. Cardiovascular risk factor screening in systemic lupus erythematosus. *J Rheumatol* 2003;30:493–6.



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Roundtable: CV, CNS and Pregnancy

Moderator: Professor Munther A. Khamashta

Professor John G. Hanly, MD, MRCPI, FRCP

Dalhousie University, Nova Scotia Canada

Instruments to measure outcomes of neuropsychiatric manifestations

Neuropsychiatric (NP) disease is frequent in patients with systemic lupus erythematosus (SLE). The American College of Rheumatology (ACR) case definitions for 19 NP syndromes provide auidelines for diagnosis. investigations to perform and non-SLE factors to consider as alternative causes of the individual NP events. 1 The majority of events are not attributed to lupus.² Twelve of the 19 ACR NP events affect the central nervous system and seven affect the peripheral nervous system. These can also be clustered into diffuse and focal nervous system events. In individual patients with NP manifestations, it is important to distinguish between a reversible clinical event mediated by an autoimmune/inflammatory pathogenic mechanism and an irreversible event due to organ damage. Within validated instruments for the assessment of global SLE disease activity and cumulative organ damage, there are variables that capture some of the individual NP manifestations in

the ACR case definitions of NP events:3 these may be used to document specific NP events and change over time. In addition, the SF-36 questionnaire has been validated as a generic outcome measure for groups of NP events clustered on the basis of their characteristics and attribution.4 Treatment is tailored to the specific NP event(s) in individual patients but the options include symptomatic therapies, immunosuppression, anticoagulation and management of contributing co-morbid factors. Although generally considered effective, there is currently a paucity of controlled studies to support specific and non-specific therapeutic interventions for NPSLE. The outcome of NPSLE is influenced by the characteristics (diffuse or focal) and attribution (SLE or non-SLE) of the events.5 Regardless of attribution, NP events in SLE patients are associated with a lower patient self-reported health-related quality of life.

Learning Objectives

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

- Appreciate the clinical diversity and attribution of NPSLE.
- Examine the difference between NP events as a consequence of disease activity vs. organ damage.
- Review the outcome measurements available for individual NP events.
- Review the outcome measurements available for global NP events.
- Assess the outcome of NP events and their impact on quality of life.

- 1. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum 1999;42:599–608.
- 2. Hanly JG, Urowitz MB, Sanchez-Guerrero J, et al. Neuropsychiatric events at the time of diagnosis of systemic lupus erythematosus: an international inception cohort study. Arthritis Rheum 2007;56:265–73.
- 3. Strand V, Gladman D, Isenberg D, Petri M, Smolen J, Tugwell P. Outcome measures to be used in clinical trials in systemic lupus erythematosus. *J Rheumatol* 1999;26:490–7.
- 4. Hanly JG, Urowitz MB, Jackson D, et al. SF-36 summary and subscale scores are reliable outcomes of neuropsychiatric events in systemic lupus erythematosus. *Ann Rheum Dis* 2011;70:961–7.
- 5. Hanly JG, Urowitz MB, Su L, et al. Short-term outcome of neuropsychiatric events in systemic lupus erythematosus upon enrollment into an international inception cohort study. *Arthritis Rheum* 2008;59:721–9.



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Roundtable: CV, CNS and Pregnancy

Moderator: Professor Munther A. Khamashta

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

The paradigm of pregnancy in SLE revisited

It used to be common knowledge that pregnancy was detrimental for lupus patients, and that lupus compromised pregnancy outcome. Improvement in diagnostic tools and disease control, identification of biomarkers, better understanding of the efficacy and safety of drugs used during planned pre-conception, as well as during pregnancy and lactation, has contributed to more frequent and better-managed pregnancies in patients with lupus.

Clear communication between rheumatology and obstetric teams is crucial for successful outcomes and disease control. Pre-conception counselling is essential, and drugs that interfere with conception (eg. cyclophosphamide, NSAIDs) or with the forming foetus (eg. methotrexate, leflunomide) should be withdrawn or substituted, and certain drugs (eg. bisphosphonates, thalidomide) should not be used in women who plan to conceive. Physiological alterations that occur during pregnancy, in addition to the pregnancy-related 'problems', should not be confused with lupus flare. Anaemia, knee pain, low back pain, chloasma, carpal tunnel syndrome and dyspnoea can occur in any pregnant women, whereas haemolysis, polyarthritis, rash, mucosal ulcers and vasculitis are most certainly related to lupus flare.

Hydroxychloroquine is recommended during pregnancy and lactation with no risk for the infant; prednisone and prednisolone can be used, but conservatively when needed: and azathioprine is generally well tolerated by the infant during pregnancy and lactation. 1-3 Anti-Ro/SS-A may induce heart block and foetal echocardiograms should be performed routinely.4 Treatment for antiphospholipid syndrome (APS) should be adapted; and warfarin replaced by low molecular weight heparin (LMWH) combined with low-dose aspirin (LDA).1 When an antiphospholipid antibody is found without a thrombotic history, LDA is given; if this treatment fails, LMWH plus LDA should be tried for subsequent pregnancies. Hypertension, proteinuria and oedema may be due to pre-eclampsia as well as lupus nephritis, or to APS microangiopathy, Notably, while pre-eclampsia occurs after 20 weeks, lupus nephritis and APS microangiopathy can occur at any time. The differentiation of these situations is fundamental for ideal care; indeed, only in lupus nephritis there is complement consumption, anti-dsDNA antibodies, and urinary red blood cell casts. Importantly, treatment decisions should balance foetal and maternal risks of the flare feature and the treatment options, for each individual situation 5

Learning Objectives

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

- Counsel women with lupus, on the ideal timing and adaptation of their medication regimen, to help them to experience an uneventful pregnancy.
- Differentiate the common features and complications of normal pregnancy from true lupus flare during pregnancy.
- Understand how to approach a pregnant woman with anti-Ro/SS-A antibodies.
- Diagnose and manage APS during pregnancy.
- Differentiate between pre-eclampsia, lupus nephritis and APS microangiopathy and treat accordingly.

- 1. Baer AN, Witter FR, Petri M. Lupus and pregnancy. Obstet Gynecol Surv 2011;66:639-53.
- 2. Levy RA, Vilela VS, Cataldo MJ, et al. Hydroxychloroquine (HCQ) in lupus pregnancy: double-blind and placebo-controlled study. Lupus 2001;10:401–4.
- 3. Ostensen M, Khamashta M, Lockshin M, et al. Anti-inflammatory and immunosuppressive drugs and reproduction. Arthritis Res Ther 2006;8:209.
- 4. Pisoni CN, Brucato A, Ruffatti A, et al. Failure of intravenous immunoglobulin to prevent congenital heart block: Findings of a multicenter, prospective, observational study. *Arthritis Rheum* 2010;62:1147–52.
- 5. Bramham K, Hunt BJ, Bewley S, *et al.* Pregnancy outcomes in systemic lupus erythematosus with and without previous nephritis. *J Rheumatol* 2011;38:1906–13.



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Roundtable: Treatment I Moderator: Professor David A. Isenberg

Professor Richard A. Furie, MD

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

What trials of new biologic therapies in SLE have taught us: success arises from failure

The first trials of novel therapies for systemic lupus erythematosus (SLE) were conducted in the early 1990s. Despite valiant efforts to develop abetimus sodium (LJP-394) and dehydroepiandrosterone (DHEA), neither drug was proven to be efficacious. However, this early foray into drug development in SLE not only demonstrated that large clinical trials could be performed in SLE and lupus nephritis, it also displayed commitment from both the lupus community and industry to bring safer and more effective therapies to patients. An explosion in SLE clinical trials activities ensued, but progress was thwarted by repeatedly negative outcomes. To facilitate SLE drug development, the United States Food and Drug Administration (FDA) released a guidance document

in 2005 entitled 'Draft Guidance for Industry on Systemic Lupus Erythematosus – Developing Drugs for Treatment.' While the reasons for failure were multifactorial, ineffective trial design, confounding background therapies, and inadequate response endpoints contributed to the negative outcomes; but, success arises from failure. Building on lessons learned from phase I and II trials, two global phase III trials with belimumab were successfully executed leading to the drug's approval by several regulatory agencies. Not only have valuable lessons been learned over time, the accrued knowledge, which will be reviewed in this presentation, has been and will continue to be incorporated into trials of the future. 1–5

Learning Objectives

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

- Describe challenges facing SLE clinical trial design.
- Discuss how obstacles to clinical trials in SLE have been addressed.
- Identify opportunities to improve SLE trial design and outcomes.

- 1. Appel GB, Contreras G, Dooley MA, et al. Mycophenolate mofetil versus cyclophosphamide for induction treatment of lupus nephritis. J Am Soc Nephrol 2009;20:1103–12.
- 2. Bruce IN, Gordon C, Merrill JT, Isenberg D. Clinical trials in lupus: what have we learned so far? Rheumatology (Oxford) 2010;49:1025–7.
- 3. Furie RA, Petri MA, Wallace DJ, et al. Novel evidence-based systemic lupus erythematosus responder index. Arthritis Rheum 2009;61:1143–51.
- 4. Kalunian K, Kim M, Hanrahan L, *et al.* Initial results for the LFA Collective Data Analysis Initiative (LFA CDAI): How do subjects from lupus clinical trials randomized to standard of care respond over time? *Arthritis Rheum* (Abstract): 2011.
- 5. Merrill JT, Neuwelt CM, Wallace DJ, et al. Efficacy and safety of rituximab in moderately-to-severely active systemic lupus erythematosus: the randomized, double-blind, phase II/III systemic lupus erythematosus evaluation of rituximab trial. Arthritis Rheum 2009;62:222–33.



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Roundtable: Treatment I Moderator: Professor David A. Isenberg

Professor Sandra V. Navarra, MD, FPCP, FPRA

University of Santo Tomas, Manila *Philippines*

Differential drug effects in various ethnic groups: what are the data?

Since the seminal paper establishing the role of cyclophosphamide pulse therapy in treating lupus nephritis.1 there has been a relative lull in the development of new therapies – until the past decade when there was a surge in the number of randomised controlled trials in systemic lupus erythematosus (SLE).2 Mycophenolate mofetil (MMF) has been one of the most extensively studied treatments for lupus nephritis. Although the key Aspreva Lupus Management Study (ALMS) trial failed to meet its primary endpoint, showing MMF to be superior to intravenous cyclophosphamide (IVC),3 further analysis demonstrated a significant influence of race and geographical region on response to therapy, with a higher proportion of responders to MMF in the non-white, Blacks and Hispanics, and Latin American cohorts. Additionally, black patients were more likely to have adverse events with IVC whereas Asian patients were more likely to withdraw from MMF due to adverse events. These findings are congruent with those from an earlier MMF trial, in which the majority of patients were black, and MMF was more effective at inducing remission than IVC.

The Exploratory Phase II/III SLE Evaluation of Rituximab (EXPLORER) trial, which tested the efficacy and safety of rituximab (RTX) in patients with moderately-to-severely active extrarenal SLE, did not show any difference between placebo and RTX in primary and secondary endpoints.4 However, a beneficial effect of RTX was observed in the African American and Hispanic subgroups. Furthermore, a large number of off-label and open-label studies of RTX for various types of organ involvement show positive results. The combined phase III multicenter trials of BeLimumab In Subjects with Systemic lupus erythematosus (BLISS-52 and BLISS-76) treated 1684 patients with active SLE.5,6 Both trials met the primary composite endpoint of SLE responder index, and there was no significant interaction effect on belimumab treatment among the racial groups. Overall, the varying signals on the effect of race or ethnicity on efficacy and safety of various drugs in major clinical trials underscore the need to individualise therapy for every lupus patient managed in clinical practice.

Learning Objectives

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

- Review the main indications for immunosuppressive drugs and biologic agents in the management of SLE.
- Highlight ethnic or racial differences in treatment effects of drugs for SLE based on clinical trial data.
- Apply relevant clinical trial data onto clinical decision-making for individual patients with SLE.

- 1. Boumpas DT, Austin HA, 3rd, Vaughn EM, et al. Controlled trial of pulse methylprednisolone versus two regimens of pulse cyclophosphamide in severe lupus nephritis. *Lancet* 1992;340:741–5.
- 2. Houssiau FA, Vasconcelos C, D'Cruz D, et al. The 10-year follow-up data of the Euro-Lupus Nephritis Trial comparing low-dose and high-dose intravenous cyclophosphamide. Ann Rheum Dis 2010;69:61–4.
- 3. Isenberg D, Appel GB, Contreras G, et al. Influence of race/ethnicity on response to lupus nephritis treatment: the ALMS study. Rheumatology (Oxford, England) 2010;49:128–40.
- 4. Merrill JT, Neuwelt CM, Wallace DJ, et al. Efficacy and safety of rituximab in moderately-to-severely active systemic lupus erythematosus: the randomized, double-blind, phase II/III systemic lupus erythematosus evaluation of rituximab trial. *Arthritis Rheum* 2010;62:222–33.
- 5. Navarra SV, Guzman RM, Gallacher AE, et al. Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011;377:721–31.
- 6. Furie R, Petri M, Zamani O, et al. A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. *Arthritis Rheum* 2011;63:3918–30.



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Roundtable: Treatment I Moderator: Professor David A. Isenberg

Professor Guillermo Ruiz-Irastorza, MD, PhD

Hospital Universitario Cruces, Bizkaia Spain

The pros and cons of hydroxychloroquine

Antimalarial drugs are among the oldest drugs used to treat rheumatic diseases. The interference of these drugs with lysosomal acidity and the blockade of toll-like receptor 9 signalling prevent processing of low-affinity antigens, resulting in immunomodulation without immunosuppression. 1 In systemic lupus erythematosus (SLE), the role of antimalarial drugs has been traditionally limited to manage constitutional symptoms, musculoskeletal manifestations and skin rashes. However, there is increasing evidence that suggests more widespread effects. Results from the Canadian Hydroxychloroquine Withdrawal Study made it clear that hydroxychloroquine effectively prevents lupus flares.² More recent observational studies suggest some effect of antimalarial drugs in lowering serum lipid levels, decreasing subclinical atherosclerosis, preventing the evolution from SLE-like to full-blown SLE and protecting lupus patients against cancer and major infections. Moreover, antimalarial drugs have antithrombotic effects observed in lupus patients with and without antiphospholipid antibodies.³ Hydroxychloroquine has been shown to prevent damage accrual in lupus patients, especially in those without early damage. The most remarkable data come from

three prospective cohorts in Spain, US and South America. These studies were consistent in showing a statistically significant and clinically important prolonged survival of lupus patients treated with antimalarial drugs. This effect persisted after adjustment for confounding by indication, using propensity score analysis.4 The effects of hydroxychloroquine in pregnant women with SLE are similarly beneficial, with effective protection against disease flares and no harm to the growing foetus being reported. Toxicity of hydroxychloroquine is infrequent, mild and usually reversible. Its safety profile compares favourably with that of chloroquine, especially regarding ocular toxicity. Maculopathy has been calculated to be 25-fold more frequent with chloroquine that with hydroxychloroquine. Recent research shows, however, an increased likelihood of retinal toxicity once a cumulative dose of 1000 g of hydroxychloroguine has been reached. Thus, regular ophthalmological control is warranted in lupus patients taking hydroxychloroquine.5 Given the wide range of beneficial effects and the excellent safety profile, long-term treatment with hydroxychloroquine should be considered in all patients with SLE without contraindications

Learning Objectives

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

- Understand the basic immunomodulatory effects of antimalarial drugs.
- Review the beneficial clinical effects of hydroxychloroquine in lupus.
- Analyse antimalarial side effects to recognise patients at risk for suffering toxicity.

- 1. Ruiz-Irastorza G, Ramos-Casals M, Brito-Zeron P, Khamashta MA. Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus: a systematic review. *Ann Rheum Dis* 2010;69:20–8.
- 2. A randomized study of the effect of withdrawing hydroxychloroquine sulfate in systemic lupus erythematosus. The Canadian Hydroxychloroquine Study Group. *N Engl J Med* 1991;324:150–4.
- 3. Tektonidou MG, Laskari K, Panagiotakos DB, Moutsopoulos HM. Risk factors for thrombosis and primary thrombosis prevention in patients with systemic lupus erythematosus with or without antiphospholipid antibodies. *Arthritis Rheum* 2009;61:29–36.
- 4. Shinjo SK, Bonfa E, Wojdyla D, et al. Antimalarial treatment may have a time-dependent effect on lupus survival: data from a multinational Latin American inception cohort. *Arthritis Rheum* 2010;62:855–62.
- 5. Marmor MF, Kellner U, Lai TY, Lyons JS, Mieler WF. Revised recommendations on screening for chloroquine and hydroxychloroquine retinopathy. *Ophthalmology* 2011;118:415–22.



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Roundtable: Treatment II Moderator: Professor Sandra V. Navarra

Professor Ricard Cervera, MD, PhD, FRCP

Hospital Clínic, Barcelona Spain

Classic and modern immunosuppressive drugs: from the NIH to the Euro-lupus regimen

The multiplicity of clinical presentations seen with systemic lupus erythematosus (SLE) means treatment must be personalised according to individual patient needs, this is particularly true when considering the presence and severity of renal involvement.

Corticosteroids have probably been the most useful treatment to manage SLE, however these should be prescribed at the lowest possible dose and for the shortest period of time in order to minimise their adverse effects. Nevertheless, many patients require low-dose corticosteroids as maintenance treatment for long periods in order to avoid flares.

When high corticosteroid doses are needed, or internal organ involvement (especially renal) is present, other immunosuppressive agents such as azathioprine, cyclophosphamide or mycophenolate mofetil should be introduced. The most important trials that have assessed the safety and efficacy of these immunosuppressive drugs will be discussed, including the National Institutes of Health (NIH) trials, ¹ Euro-lupus, ²⁻⁴ Mycophenolate Mofetil versus Azathioprine for Maintenance Therapy of Lupus Nephritis (MAINTAIN), ⁵ and the Aspreva Lupus Management Study (ALMS). ⁶

Learning Objectives

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

- Understand the most important immunosuppressive regimens that have been used to treat patients with SLE.
- Analyse the most representative trials performed to assess the safety and efficacy of immunosuppressive drugs in SLE.
- Recognise the most representative meta-analyses that compare the main immunosuppressive drugs used in SLE.
- Make more informed treatment decisions when choosing the most appropriate immunosuppressive drugs to treat patients with SLE.

- 1. Boumpas DT, Austin HA, 3rd, Vaughn EM, et al. Controlled trial of pulse methylprednisolone versus two regimens of pulse cyclophosphamide in severe lupus nephritis. *Lancet* 1992;340:741–5.
- 2. Houssiau FA, Vasconcelos C, D'Cruz D, et al. The 10-year follow-up data of the Euro-Lupus Nephritis Trial comparing low-dose and high-dose intravenous cyclophosphamide. *Ann Rheum Dis* 2010;69:61–4.
- 3. Houssiau FA, Vasconcelos C, D'Cruz D, et al. Early response to immunosuppressive therapy predicts good renal outcome in lupus nephritis: lessons from long-term followup of patients in the Euro-Lupus Nephritis Trial.

 Arthritis Rheum 2004;50:3934–40.
- 4. Houssiau FA, Vasconcelos C, D'Cruz D, et al. Immunosuppressive therapy in lupus nephritis: the Euro-Lupus Nephritis Trial, a randomized trial of low-dose versus high-dose intravenous cyclophosphamide. Arthritis Rheum 2002;46:2121–31.
- 5. Houssiau FA, D'Cruz D, Sangle S, et al. Azathioprine versus mycophenolate mofetil for long-term immunosuppression in lupus nephritis: results from the MAINTAIN Nephritis Trial. *Ann Rheum Dis* 2010;69:2083–9.
- 6. Isenberg D, Appel GB, Contreras G, et al. Influence of race/ethnicity on response to lupus nephritis treatment: the ALMS study. *Rheumatology (Oxford, England)* 2010;49:128–40.



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Roundtable: Treatment II Moderator: Professor Sandra V. Navarra

Dr David P. D'Cruz, MD, FRCPSt Thomas' Hospital, London
UK

Should lupus be treated early and aggressively or not?

Systemic lupus erythematosus (SLE) is a multisystem autoimmune rheumatic disorder with a very broad spectrum of clinical presentations. Patients often present with a variety of non-specific symptoms such as arthralgia, oral ulcers, fatigue, and hair loss. Other patients, however, may present acutely with severe multi-organ disease, especially renal involvement. The initial clinical assessment of the patient is therefore critical in planning the therapeutic approach with a view to tailoring therapy to the extent and severity of the disease. When assessing patients, it is important to capture all aspects of the disease. This is conventionally done under three headings: disease activity, damage and quality of life, and there are validated tools to objectively document these disease components.^{2,3} Treatment is primarily aimed at reducing disease activity, preventing damage and permanent organ failure and improving the patient's quality of life. Attention should also be directed at fertility and pregnancy planning and reducing the risks of atherothrombosis in susceptible patients.

All patients should be treated early, yet this depends on early diagnosis and there is often a significant delay in diagnosing patients with SLE because of the presentation of non-specific symptoms. After diagnosis, patient education with information about SLE, counselling on managing debilitating symptoms such as fatigue, and chronic disease management strategies are vital in improving adherence to treatment and outcome.4 A therapeutic triangle is often considered: first-line therapy should be with antimalarial drugs. Depending on the severity and extent of the disease, corticosteroids and immunosuppressive agents may be used, and third-line agents include biologic agents such as rituximab and belimumab.5 The more severe the disease presentation, the more intensive and aggressive the therapy should be, with consequent risks of toxicity. The best example of such a strategy is the management of lupus nephritis. Alongside drug therapies there should be aggressive management of cardiovascular and thrombosis risk factors in all patients.

Learning Objectives

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

- Understand the wide spectrum of clinical presentations of SLE and the need for careful clinical assessment.
- Have an awareness of the need to document disease activity, damage and quality of life measures.
- Be aware of the importance of patient education and non-drug management strategies.
- Understand the need to commence treatment early and to tailor treatment to the individual patient.
- Understand the need for preventing the accumulation of damage in order to reduce morbidity and mortality.

- 1. D'Cruz DP, Khamashta MA, Hughes GR. Systemic lupus erythematosus. Lancet 2007;369:587–96.
- 2. Nossent J, Kiss E, Rozman B, et al. Disease activity and damage accrual during the early disease course in a multinational inception cohort of patients with systemic lupus erythematosus. Lupus 2010;19:949–56.
- 3. McElhone K, Castelino M, Abbott J, et al. The LupusQoL and associations with demographics and clinical measurements in patients with systemic lupus erythematosus. *J Rheumatol* 2010;37:2273–9.
- 4. Davies RJ, Lomer MC, Yeo SI, Avloniti K, Sangle SR, D'Cruz DP. Weight loss and improvements in fatigue in systemic lupus erythematosus: a controlled trial of a low glycaemic index diet versus a calorie restricted diet in patients treated with corticosteroids. *Lupus* 2012.
- 5. Lo MS, Tsokos GC. Treatment of systemic lupus erythematosus: new advances in targeted therapy. Ann N Y Acad Sci 2012;1247:138–52.



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Roundtable: Treatment II Moderator: Professor Sandra V. Navarra

Professor David A. Isenberg, MD, FRCP, FAMS

University College London

Biologic therapies for lupus – new and shiny, but are they effective?

Recent analysis with a 30-year follow-up study in patients with lupus nephritis, from the Centre for Rheumatology, University College London, has indicated very clearly that even optimising the treatment of lupus nephritis with corticosteroids and immunosuppressive drugs is insufficient to prevent a small, but significant, number of patients from going into renal failure and often dying.

It is clear, therefore, that to improve the outcome of patients with severe lupus nephritis, more targeted therapy is important and essential.

Increased understanding of the immune response has allowed us to identify key molecules critically involved in the development of lupus. Unfortunately, some of the earlier trials, for example those using abatacept and abetimus, failed to reach their endpoints. Even rituximab, which over 20 groups around the world² have reported can provide a highly effective treatment of patients with resistant lupus, did not meet its endpoint in two large randomised studies. ^{3,4} The reasons for this have been debated elsewhere² but certainly include an 'over indulgence' in the

amount of concomitant corticosteroids and other immunosuppressive drugs used in these trials.

More encouragingly, two trials using the B-lymphocyte stimulator (BLyS) antibody (belimumab) met their endpoints in two parallel studies involving over 1,600 patients with lupus.⁵ Albeit in a much smaller study, epratuzumab, which blocks the CD22 receptor, was also shown to be effective.⁶ Hopes also remain high for monoclonal antibodies that block interferon alpha.

The optimal use of biologics in patients with systemic lupus erythematosus is far behind their use in rheumatoid arthritis. However, there is now an increasing number of reasons to believe that biologics will, in the next decade, become an established part of the treatment both of 'hard to treat' lupus and, more excitingly, be used at the time of diagnosis. Indeed, there is genuine hope that biologic therapies, given either when immunosuppressive therapies have failed or at the time of diagnosis, will become a standard form of treatment in the next decade.

Learning Objectives

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

- Appreciate that the limits of benefit from conventional immunosuppression in SLE have been reached.
- Describe how a better understanding of the immune response has led to more targeted approaches for lupus therapy.
- Describe the role of B cells in the origins of lupus, and the potential therapeutic benefits achieved by blocking B cells or their products.

- 1. Croca SC, Rodrigues T, Isenberg DA. Assessment of a lupus nephritis cohort over a 30-year period. *Rheumatology (Oxford, England)* 2011;50:1424–30.
- Favas C, Isenberg DA. B-cell-depletion therapy in SLE-what are the current prospects for its acceptance? Nature Reviews 2009;5:711-6.
- 3. Rovin BH, Furie R, Latinis K, et al. Efficacy and safety of rituximab in patients with active proliferative lupus nephritis: The lupus nephritis assessment with rituximab (LUNAR) study. Arthritis Rheum 2012:doi: 10.1002/art.34359. [Epub ahead of print].
- 4. Merrill JT, Neuwelt CM, Wallace DJ, et al. Efficacy and safety of rituximab in moderately-to-severely active systemic lupus erythematosus: the randomized, double-blind, phase II/III systemic lupus erythematosus evaluation of rituximab trial. Arthritis Rheum 2010;62:222–33.
- 5. Navarra SV, Guzman RM, Gallacher AE, et al. Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011;377:721–31.
- Petri M, Pike M, Kelley K, Kilgallen B, Gordon C. Systemic lupus erythematosus responder index assessment of responders in EMBLEM, a phase Ilb study in patients with moderate to severe systemic lupus erythematosus. *Arthritis & Rheumatism* 2011;63:A1378.



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