EULAR recommendations for the management of systemic lupus erythematosus. Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics


ABSTRACT

Objective: Systemic lupus erythematosus (SLE) is a complex disease with variable presentations, course and prognosis. We sought to develop evidence-based recommendations addressing the major issues in the management of SLE.

Methods: The EULAR Task Force on SLE comprised 19 specialists and a clinical epidemiologist. Key questions for the management of SLE were compiled using the Delphi technique. A systematic search of PubMed and Cochrane Library Reports was performed using McMaster/Hedges clinical queries' strategies for questions related to the diagnosis, prognosis, monitoring and treatment of SLE. For neuropsychiatric, pregnancy and antiphospholipid syndrome questions, the search was conducted using an array of relevant terms. Evidence was categorised based on sample size and type of design, and the categories of available evidence were identified for each recommendation. The strength of recommendation was assessed based on the category of available evidence, and agreement on the statements was measured across the 19 specialists.

Results: Twelve questions were generated regarding the prognosis, diagnosis, monitoring and treatment of SLE, including neuropsychiatric SLE, pregnancy, the antiphospholipid syndrome and lupus nephritis. The evidence to support each proposition was evaluated and scored. After discussion and votes, the final recommendations were presented using brief statements. The average agreement among experts was 8.8 out of 10.

Conclusion: Recommendations for the management of SLE were developed using an evidence-based approach followed by expert consensus with high level of agreement among the experts.

Approximately half a million people in Europe and a quarter of a million people in the USA (projections based on prevalence rates of 30–50 per 100 000) have systemic lupus erythematosus (SLE). The great majority of these patients are women in their childbearing years. SLE is a complex disease with variable presentations, course and prognosis characterised by remissions and flares. Because of the systemic nature of the disease, multiple medical specialties are involved in the care of these patients. To avoid fragmentation and optimise management, there is a presently unmet need to establish an integrated approach based on widely accepted principles and evidence-based recommendations.

Recommendations and/or guidelines represent a popular way of integrating evidence-based medicine to clinical practice. These are systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances. To this end and under the auspices of EULAR, we undertook the task of developing guidelines for the management of various aspects of SLE. To ensure a high level of intrinsic quality and comparability of this approach, we used the EULAR standard operating procedures. We present here 12 key recommendations, selected from a panel of experts, for the management (diagnosis, treatment, monitoring) of SLE using a combination of research-based evidence and expert consensus.

METHODS

The EULAR standardised operating procedures suggest a discussion among experts in the field about the focus, the target population and an operational definition of the term ‘management’, followed by consensus building based on the currently available literature (evidence-based), combined with expert opinion, as needed, to arrive at consensus for a set of recommendations. The expert committee agreed on 12 topics, including general management of SLE (5 questions), neuropsychiatric lupus (2 questions), pregnancy in lupus (1 question), antiphospholipid syndrome (1 question) and lupus nephritis (3 questions). A systematic search of PubMed the Cochrane library was performed, and retrieved items were screened for eligibility based on their title, abstract and/or full content. Evidence was categorised according to study design using a traditional rating scale, and the strength of the evidence was graded combining information on the design and validity of the available data (see the full-text version for more details). The results of the literature search were summarised, aggregated and distributed to the expert committee. Following discussion, voting and adjusting the formulation, the expert committee arrived at 12 final recommendations for the management of SLE (table 1).
Further, the expert committee proposed topics for a Research Agenda.

RESULTS (TABLES 1 AND 2)

Prognosis

SLE runs a highly variable clinical course, and determination of prognosis together with the development of reliable indicators of active disease, disease severity and damage accrual is important. Several clinical manifestations (discoid lesions, arthritis, serositis, renal involvement, psychosis or seizures), laboratory tests (anaemia, thrombocytopenia, leucopenia, serum creatinine), immunological tests (anti-dsDNA, anti-C1q, antiphospholipid, anti-Ro/SSA, anti-La/SSB, antiphospholipid, anti-RNP), may provide prognostic information for the outcome in general and involvement of major organs, and thus should be considered in the evaluation of these patients. Confirmation by imaging (brain MRI), and pathology (renal biopsy) may add prognostic information and should be considered in selected patients.

Co-morbidities

SLE patients are at increased risk for certain co-morbidities, due to the disease and/or its treatment. These co-morbidities include infections (urinary-tract infections, other infections), atherosclerosis, hypertension, dyslipidaemias, diabetes, osteoporosis, avascular necrosis, malignancies (especially non-Hodgkin’s lymphoma). Minimisation of risk factors together with a high-index of suspicion, prompt evaluation, and diligent follow-up of these patients is recommended.

Treatment

In the treatment of SLE without major organ manifestations, antimalarials and/or glucocorticoids are of benefit and may be used. NSAIDs may be used judiciously for limited periods of time at patients at low risk for their complications. In non-responding patients or patients not being able to reduce steroids below doses acceptable for chronic use, immunosuppressive agents such as azathioprine, mycophenolate mofetil and methotrexate should also be considered.

Adjunct therapy

Photo-protection may be beneficial in patients with skin manifestations and should be considered. Lifestyle modifications (smoking cessation, weight control, exercise) are likely to be beneficial for patient outcomes and should be encouraged. Depending on the individual medication and the clinical situation, other agents (low-dose aspirin, calcium/vitamin D, bisphosphonates, statins, antitypertensives (including angiotensin converting enzyme inhibitors)) should be considered. Oestrogens (oral contraceptives, hormone-replacement therapy) may be used, but accompanying risks should be assessed.

Neuropsychiatric lupus

Diagnosis

In SLE patients, the diagnostic work-up (clinical, laboratory, neuropsychological, and imaging tests) of neuropsychiatric manifestations should be similar to that in the general population presenting with the same neuropsychiatric manifestations.

Treatment

SLE patients with major neuropsychiatric manifestations considered to be of inflammatory origin (optic neuritis, acute confusional state/coma, cranial or peripheral neuropathy, psychosis, and transverse myelitis/myelopathy) may benefit from immunosuppressive therapy.

Pregnancy in lupus

Pregnancy affects mothers with SLE and their offspring in several ways.

(a) Mother. There is no significant difference in fertility in lupus patients. Pregnancy may increase lupus disease activity, but these flares are usually mild. Patients with lupus nephritis and antiphospholipid antibodies are more at risk of developing pre-eclampsia and should be monitored more closely.

(b) Fetus. SLE may affect the fetus in several ways, especially if the mother has a history of lupus nephritis, antiphospholipid, anti-Ro and/or anti-La antibodies. These conditions are associated with an increase in the rate of miscarriage, stillbirth, premature delivery, intrauterine growth restriction and fetal congenital heart block. Prednisolone, azathioprine, hydroxychloroquine and low-dose aspirin may be used in lupus pregnancies. At present, evidence suggests that mycophenolate mofetil, cyclophosphamide and methotrexate should be avoided.

Antiphospholipid syndrome

In patients with SLE and antiphospholipid antibodies, low-dose aspirin may be considered for primary prevention of thrombosis and pregnancy loss. Other risk factors for thrombosis should also be assessed. Oestrogen-containing drugs increase the risk for thrombosis. In non-pregnant patients with SLE and APS-associated thrombosis, long-term anticoagulation with oral anticoagulants is effective for secondary prevention of thrombosis. In pregnant patients with SLE and antiphospholipid syndrome combined unfractonated or LMW heparin and aspirin reduce pregnancy loss and thrombosis and should be considered.

Lupus nephritis

Monitoring

Renal biopsy, urine sediment analysis, proteinuria, and kidney function may have independent predictive ability for clinical outcome in therapy of lupus nephritis but need to be interpreted in conjunction. Changes in immunological tests (anti-dsDNA, serum C3) have only limited ability to predict the response to treatment and may be used only as supplemental information.

Treatment

In patients with proliferative lupus nephritis, glucocorticoids in combination with immunosuppressive agents are effective against progression to end-stage renal disease. Long-term efficacy has been demonstrated only for cyclophosphamide-based regimen, which are however associated with considerable adverse effects. In short- and medium-term trials, mycophenolate mofetil has demonstrated at least similar efficacy compared with pulse cyclophosphamide and a more favourable toxicity profile: failure to respond by 8 months should evoke discussions for intensification of therapy. Flares following remission are not uncommon and require diligent follow-up.

End-stage renal disease

Dialysis and transplantation in SLE have rates for long-term patient and graft-survival comparable with those observed in non-diabetic non-SLE patients, with transplantation being the method of choice.
Table 2  Category of evidence and strength of statements

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<td><strong>Nephritis: monitoring</strong></td>
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<td>Serum creatinine</td>
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<tr>
<td>Anti-dsDNA</td>
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<td><strong>Nephritis: treatment</strong></td>
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<td>Combined glucocorticoids and immunosuppressants are effective against ESRD</td>
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<td>MMF has similar efficacy to pulse CY in short-/medium-term trials</td>
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<td>CY efficacy in long-term trials</td>
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<td><strong>End-stage renal disease in SLE</strong></td>
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<td>Transplantation is safe in SLE</td>
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<td>5</td>
<td>C</td>
<td>9.4</td>
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*Mean level of agreement of the Task Force members on each sub-item/statement; \( \text{in elderly SLE patients, low-dose aspirin is associated with improved cognitive function (4/B);} \)
\( ^\dagger \text{this refers to the statement that “in SLE patients, the diagnostic work-up (clinical, laboratory, neuropsychological and imaging tests) of neuropsychiatric manifestations should be similar to that in the general population presenting with the same neuropsychiatric manifestations”;} \)
\( ^\circ \text{non-SLE studies.} \)
patients in various clinical settings or backgrounds. Most importantly, perhaps, no single predicting factor has emerged that could accurately predict the outcome. Thus, the various prognostic factors in a single patient need to be evaluated in conjunction. In general, involvement of major organs denotes a worse prognosis.

Monitoring
SLE is often complicated by exacerbations and flares of varying severity. Several global and organ-specific activity indices are used in the evaluation of SLE patients in routine clinical practice and in clinical trials. More commonly used are the British Isles Lupus Assessment Group Scale (BILAG), European Consensus Lupus Activity Measure (ECLAM), and the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). These indices have been developed in the context of long-term observational studies, are good predictors of damage and mortality, and reflect changes in disease activity. The committee encourages the use of at least one of these indices for the monitoring of disease activity. In addition, new clinical manifestations (skin lesions, anaemia, lymphopenia, or thrombocytopenia), low serum C3 and/or C4 concentrations, anti-dsDNA titres and anti-C1q titres correlate with disease severity and can predict future flares.

While these indices and diagnostic tests may have some diagnostic ability for monitoring disease, none of them has been evaluated in randomised trials for the ability to alter management and patient outcome. The level of changes that should trigger changes in management is also unknown. For example, intensification of therapy based on serological activity alone, especially a rise in anti-dsDNA titres, runs a risk of overtreating patients, although it has been shown to prevent relapses in a randomized clinical trial (RCT). In these cases, most experts advise a closer follow-up for clinical disease activity.

Co-morbidities
SLE patients may be at increased risk for several co-morbidities, and treatment-related morbidity may not be easily separable from disease-related morbidity, thus raising the issue of whether the two may have an additive or synergistic effect. Patients with SLE have an almost 5-fold increased risk of death compared with the general population. Several observational cohorts and case-control studies have identified infections, hypertension, dyslipidaemia, diabetes mellitus, atherosclerosis, coronary heart disease, osteoporosis, avascular bone necrosis and certain types of cancer (non-Hodgkin’s lymphoma, lung cancer, hepatobiliary cancer) as a common cause of morbidity and mortality in SLE patients. However, no randomised trials exist to suggest that intensified screening for these comorbidities would improve outcome. Moreover, many of these data originate from tertiary referral centres that usually provide care to the most severe cases of lupus raising the possibility of spectrum of disease bias. Suboptimal selection of controls may also inflate the reported strength of some of these associations. Nevertheless, clinical experience and available data suggest that comorbidities are a major component of the disease. The committee therefore recommends a high index of suspicion and diligent follow-up.

Treatment of non-major organ involvement
Glucocorticoids, antimalarials, non-steroid anti-inflammatory drugs (NSAIDs) and, in severe, refractory cases, immunosuppressive agents are used in the treatment of SLE patients without major-organ involvement. Despite their widespread use, there are only a few RCTs with variable outcome criteria demonstrating their efficacy in SLE. Moreover, while most studies have shown improvement, it is not apparent whether patients were left with residual disease activity and its extent. The evidence is typically limited to small sample sizes, even when randomisation has been used. The committee recommends judicious use of these agents, taking into consideration the potential harms associated with each of these drugs.

Adjunct-therapy
In a double-blind, intra-individual comparative study, the use of sunscreens could prevent the development of skin lesions following photoprovocation. Although no data are available in SLE specifically, the committee felt that low-dose aspirin may be considered in adult lupus patients receiving corticosteroids, in those with antiphospholipid antibodies and in those with at least one traditional risk factor for atherosclerotic disease.

In patients receiving long-term glucocorticoid therapy, calcium and vitamin D may protect from bone mass loss. Two other studies have demonstrated beneficial effects of bisphosphonates in mixed population of patients with SLE and other inflammatory diseases. Pregnancy should be postponed for 6 months after withdrawal of bisphosphonates. Although oestrogen use has been associated with increased risk for developing SLE, two RCTs have concluded that oral oestrogen contraceptives do not increase the risk for flare in stable disease. Hormone-replacement therapy results in a significantly better change in bone mass density compared with placebo or calcitriol, without increasing the risk for flares. These results may not be generalised to patients with increased risk for thrombo-occlusive incidents, and accompanying risks should be assessed before oestrogen therapy is prescribed.

Despite the lack of SLE-specific literature, weight control, physical exercise and smoking cessation are recommended, especially for SLE patients with increased CVD risk. Statins and antihypertensives (ACE inhibitors) should also be considered in selected patients.

Diagnosis of neuropsychiatric lupus
Neurological and/or psychiatric manifestations occur often in SLE patients and may be directly related to disease itself (primary neuropsychiatric lupus) or to complications of the disease or its treatment (secondary neuropsychiatric lupus). There are several clinical, laboratory/immunological, neuropsychological and imaging tests which have been used in SLE patients presenting with neuropsychiatric manifestations. Altogether, these studies suggest that no single clinical, laboratory, neuropsychological and imaging test can be used to differentiate neuropsychiatric systemic lupus erythematosus (NPSLE) from non-NPSLE patients with similar neuropsychiatric manifestations. A combination of the aforementioned tests may provide useful information in assessment of selected SLE patients presenting with neuropsychiatric symptoms. The diagnostic evaluation should be similar to what the evaluation would be in patients without SLE who exhibit the same neuropsychiatric manifestations.

Treatment of severe, inflammatory neuropsychiatric lupus
Primary neuropsychiatric lupus occurs in the setting of lupus activity in other organs and involves a variety of pathogenic...
mechanisms including immune-mediated neuronal excitation/injury/death or demyelination (which is usually managed with immunosuppressive therapy) and/or ischaemic injury due to impaired perfusion (due to microangiopathy, thrombosis or emboli) commonly associated with the antiphospholipid antibodies which may require anticoagulation.2

We found a single RCT conducted in 32 SLE patients presenting with active NPSLE manifestations such as peripheral/cranial neuropathy, optic neuritis, transverse myelitis, brainstem disease or coma.94 Induction therapy with intravenous methylprednisolone (MP) was followed by either intravenous monthly cyclophosphamide (CY) versus intravenous MP every 4 months for 1 year and then intravenous CY or intravenous MP every 3 months for another year. Eighteen out of 19 patients receiving CY versus 7/13 patients receiving MP (p = 0.03) responded to treatment. Beneficial effects of CY in treatment of severe NPSLE have also been suggested in non-randomised controlled studies.89-91

Pregnancy in lupus

The management of a pregnant SLE patient has always been a challenge for the practising physician, since lupus may affect pregnancy and vice versa. There is not enough evidence to support a deleterious effect of SLE on fertility.82-84 Pregnancy may increase lupus disease activity and cause mild-to-moderate flares, involving mostly skin, joints and blood.85-87

Lupus nephritis98-99 and antiphospholipid antibodies96-97 have been identified as a risk factor for hypertensive complications and pre-eclampsia. SLE patients—especially those with nephritis or antiphospholipid antibodies—are at risk for adverse pregnancy outcomes, including miscarriage, stillbirth and premature delivery (relative risks ranging from 2.2 to 5.8).87 92-94 Pregnancy may increase lupus disease activity and cause mild-to-moderate flares, involving mostly skin, joints and blood.85-87

Lupus nephritis98-99 and antiphospholipid antibodies96-97 have been identified as a risk factor for hypertensive complications and pregnancy.82-84 Lupus nephritis and antiphospholipid antibodies are associated with low birth weight and intra-uterine growth restriction.96-97 Fetal congenital heart block is another complication of SLE pregnancies (2-4.5%),95 99 and it is associated with anti-Ro/SSA or anti-La/SSB autoantibodies.

Prednisolone and other non-fluorinated glucocorticoids, azathioprine, ciclosporin A and low-dose aspirin have been used in lupus pregnancy, but their efficacy and safety have not been demonstrated in randomised trials. The efficacy and safety of hydroxychloroquine in lupus pregnancy have been evaluated in one RCT.100 These recommendations may differ from the ratings of the United States Food & Drug Administration which, in their current form, are often not helpful for the clinician treating patients with chronic disease during pregnancy and lactation.101 There is no evidence to support the use of mycophenolate mofetil or CY, and methotrexate and these agents must be avoided during pregnancy.101-102

Antiphospholipid syndrome in lupus

Antiphospholipid antibodies are commonly encountered in SLE patients and are associated with increased risk for thrombo-occlusive incidents. In such patients, primary and/or secondary prevention of thrombosis is warranted, but the clinical decision is often hampered by accompanying risks for treatment-related adverse effects (ie, major bleeding). Despite the lack of evidence for primary prevention of thrombosis and pregnancy loss, the expert committee recommends the use of low-dose aspirin in SLE patients with antiphospholipid antibodies, especially when other risk factors for thrombosis coexist.

The effectiveness of oral anticoagulation over aspirin alone in prevention of thrombosis in (non-pregnant) SLE patients with antiphospholipid antibodies and thrombosis has been established in retrospective controlled studies.103-106 Two RCTs107-108 have demonstrated no superiority of high-intensity (target INR 3.1-4.0) over moderate-intensity warfarin (INR 2.0-3.0) for secondary prevention, and increased risk for minor bleeding in the high-intensity arm (28% vs 11%).109 Their results, however, are limited in that most patients (>70%) had history of venous—rather than arterial—thrombosis, and that patients who had already had recurrent events on oral anticoagulation were excluded. Conversely, retrospective studies including more patients with previous arterial thrombosis or stroke have concluded that high-intensity warfarin is more efficacious in secondary prevention of thrombosis without increasing the risk for major bleeding.105-108 109 110 The committee proposes that in patients with APS and a first event of venous thrombosis, oral anticoagulation should target INR 2.0-3.0. In the case of arterial or recurrent thrombosis, high-intensity anticoagulation (target INR 3.0-4.0) is warranted.

As for pregnant SLE patients with APS, a recent Cochrane Review concluded that combined unfractionated heparin and aspirin may reduce the risk for pregnancy loss (RR 0.46, 95% CI: 0.29 to 0.71).111 The combination of low-molecular-weight heparin and aspirin also seems to be effective (RR 0.78, 95% CI: 0.59 to 1.57). There are no randomised trials assessing the usefulness of anticoagulation in prevention of recurrent thrombosis during pregnancy. The committee recommends the use of aspirin and heparin for the prevention of APS-related thrombosis during pregnancy.

Lupus nephritis: diagnosis and monitoring

In patients with suspected lupus nephritis, renal biopsy may be used to confirm the diagnosis, evaluate disease activity, chronicity/damage, and determine prognosis and appropriate therapy. The predictive value of second renal biopsy (ie, after treatment initiation) has been assessed in one prospective112 and a few retrospective studies.113 114 It was found that some pathology findings were associated with clinical response and outcome in lupus nephritis. Nevertheless, repeat renal biopsies pose a risk to the patient and may not be feasible for all patients. There is some evidence to support the predictive ability of urine sediment analysis in monitoring lupus nephritis therapy.115-118 Changes in proteinuria,117 serum creatinine,114 116 117 anti-dsDNA and serum C3 concentrations114 118 correlate with renal flares and outcome. It should be emphasised, however, that these studies were not specifically designed to evaluate the efficacy of various tests in monitoring response to therapy of lupus nephritis. There are no randomised trials evaluating the benefits from various monitoring strategies.

Lupus nephritis: treatment

The treatment of lupus nephritis often consists of a period of intensive immunosuppressive therapy (induction therapy) followed by a longer period of less intensive maintenance therapy. In a recent Cochrane Review, CY plus steroids reduced the risk for doubling of serum creatinine level compared with steroids alone (RR = 0.6), but had no impact on overall mortality.110 111 Azathioprine plus steroids reduced the risk for all-cause mortality compared with steroids alone (RR = 0.6), but had no effect on renal outcomes. CY was superior to azathioprine and/or corticosteroids with high-dose, intermittent administration of CY (pulse therapy) demonstrating a more favourable efficacy-to-toxicity ratio than oral CY.112 In a long-term follow-up (median 11 years) of an RCT combination
therapy with glucocorticoids and CY demonstrated efficacy (83% preserved renal function), without substantially increasing the risk for adverse effects. Ovarian failure after CY therapy remains a considerable problem and is both dose- and age-dependent. Gonadal protection may be feasible with the use of GnRH analogues, a finding that requires further confirmation.

The efficacy of MMF as induction therapy has been assessed in 4 RCTs, which concluded that MMF was associated with a reduced risk for treatment failure (RR = 0.7) and for the composite end point of death or ESRD (RR = 0.4) compared with CY. The usefulness of MMF as a maintenance agent has been assessed in a single RCT of 59 patients who received induction therapy with boluses of IV-CY and glucocorticoids and then were randomly assigned to IV-CY, oral azathioprine or oral MMF for 1–3 years. The event-free survival rate for the composite end point of death or ESRD was higher in the AZA and MMF groups than in the CY group. There was a significantly higher incidence of sustained amenorrhoea in the CY group.

The committee recommends that physicians use MMF as induction therapy for selected patients under close observation; failure to achieve a significant response by 6 months at the latest (defined as improvement of serum creatinine and reduction of proteinuria to <1 g/day) should evoke discussions for intensification of therapy. For maintenance therapy, MMF can be used in patients unable to tolerate azathioprine or whose symptoms flare up while on treatment. Although data with MMF are encouraging, in the opinion of the committee the drug cannot replace at present the combination of intravenous CY with intravenous MP as the treatment of choice for severe lupus nephritis. Small, non-controlled trials with short follow-up suggest that up to 50% of refractory patients to CY may have a clinically significant response to rituximab, a monoclonal antibody directed against B cells.

Table 3: Research agenda

<table>
<thead>
<tr>
<th>Epidemiology</th>
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<tr>
<td>Relative importance of environmental factors (exposure to sun, smoking, diet) in the pathogenesis of SLE</td>
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<tr>
<td>Incidence, prevalence, and severity of SLE in various European populations? Is there a north-to-south gradient?</td>
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Pathogenesis

- Genetic factors for disease susceptibility and severity
- Effector mechanisms and repair of tissue injury

Early diagnosis—primary prevention

- Identification of patients at higher risk for SLE
- Feasibility of primary prevention
- Primary prevention of cardiovascular disease in high-risk patients (eg, aspirin, statins, others)

Initial diagnostic work-up and monitoring

- Minimum diagnostic work-up for suspected SLE
- Work-up for disease limited to a single organ (eg, skin, blood, others)

Diagnosis—prognosis

- Diagnostic criteria with improved sensitivity and specificity
- Classification criteria to identify subpopulations of SLE with distinct pathogenetic, clinical, and laboratory features and response to therapy
- Diagnostic algorithms for neuropsychiatric lupus

Treatment

- Indications and optimal targets for autologous stem-cell therapy in SLE
- Major indications for biological therapies in SLE (B cell depletion, inhibition of B cell differentiation, costimulation blockade, toleragens)
- Optimum management of membranous nephropathy
- Options for resistant disease involving major and non-major organs
- Indications, efficacy, toxicity of combined immunosuppressive and anticoagulant therapy for patients with antiphospholipid syndrome and SLE

Flares

- Mechanisms of flare: residual vs sub-clinical disease vs de novo flare
- Biomarkers for residual disease and for early relapse
- Optimal management of flares

Comorbidities

- Primary prevention of cardiovascular disease
- Primary prevention and screening for osteoporosis
- Strategies to increase compliance with therapy and preventive medicine
- Strategies to decrease morbidity and mortality from infection
- Validation of the Charlson Comorbidity score in SLE trials for optimal patient stratification

Neonatal lupus

- Epidemiology, risk factors and management

Pregnancy

- Impact of assisted fertilisation on disease activity
- Effect of maternal immunosuppressive treatment on offspring long-term outcome

Antiphospholipid antibodies

- Determine whether individuals with persistently positive antiphospholipid antibodies should receive prophylaxis (and type of) for thrombosis or pregnancy-related type morbidity
- Recommended treatment for pregnant patients with APS who had pregnancy loss on low-dose aspirin and heparin

Paediatric and adolescent SLE

- Epidemiology, optimal management and long-term outcome

Geriatric lupus

- Epidemiology, optimal management and long-term outcome
Modern immunosuppressive therapies are effective, but none of them cures lupus with approximately one-third of them flaring after remission. Initial management of moderate to severe flare requires induction therapy with immunosuppressive agents, which usually prevent the loss of renal function.\(^{144-145}\)

End-stage renal disease

Despite recent advances in therapy of lupus nephritis, a number of patients may eventually progress to ESRD and will require dialysis treatment or even kidney transplantation. Both dialysis and transplantation in SLE have rates for long-term patient or graft survival comparable with those in non-diabetic/non-SLE patients.\(^{106-142}\) Antiphospholipid antibodies are associated with increased risk for thrombotic events, graft loss and poor transplantation outcome.\(^{106, 141-144}\) There is no evidence from SLE-specific studies to support the superiority of either treatment option. Nonetheless, two retrospective studies including large numbers of patients with ESRD, have demonstrated superiority of renal transplantation over dialysis in terms of long-term patient survival (relative risk 0.19–0.32 at 12–18 months post-transplant).\(^{145, 146}\)

**REFERENCES**


IOF-Servier 2008 Young Investigator Research Award

The IOF-Servier Young Investigator Research Award, presented every two years to an osteoporosis researcher under the age of 40, aims to encourage young scientists to carry out high quality research. The Award is supported by the Servier Research group in partnership with IOF, and awards 40 000 Euros towards original research of significant value and international relevance in the field of osteoporosis. The project must contribute to ensuring that people with osteoporosis receive the best care possible.

Applications for the IOF-Servier 2008 Young Investigator Research Award are being accepted until 3 March 2008. The next grant will be presented at the IOF World Congress on Osteoporosis in December 2008.

http://www.iofbonehealth.org/health-professionals/iof-grants-awards.html