Systemic Lupus Erythematosus (SLE) in Depth: From Practical to Clinical Considerations

Learning Modules 1-2
Please Select the Learning Module You Would Like to View:

Module 1: Understanding SLE – Practical Tips in Managing Patients

1.1 The Faces of SLE
1.2 What Is the Impact of SLE?
1.3 SLE in the Long Term for Patients
1.4 Optimizing Patient Care

Module 2: The Clinical Impact of SLE – Defining and Achieving Success for your Patients

2.1 The Impact of Disease Activity in SLE
2.2 Treatment Considerations in SLE – Balancing Risk and Benefit
2.3 Treat-to-Target as an Approach to Improved Patient Outcomes
2.4 Key Practice Takeaways
Welcome to Module 1

Module 1 | Understanding SLE – Practical Tips in Managing Patients
In this module, the following topics will be covered:

<table>
<thead>
<tr>
<th>Who</th>
<th>What</th>
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<tbody>
<tr>
<td>is a typical SLE patient?</td>
<td>is the impact of SLE on patients, from a health and QoL perspective?</td>
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<table>
<thead>
<tr>
<th>How</th>
<th>What</th>
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<td>can SLE impact a patient over the long term, and what can be done to mitigate the impact?</td>
<td>steps – from monitoring to communication – can be taken to optimize patient care?</td>
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2.4 Key Practice Takeaways
Who Is the Typical Patient?
More Often Than Not, She Is a Young Female

Prepubertal vs. postpubertal
Prepubertal onset is associated with a greater risk of organ damage\(^1\)

<19 years of age
Greater risk of mortality vs. adult SLE population\(^2\)

Age 15-45
90\% of individuals being diagnosed are women, with most patients developing SLE between the ages of 15 and 45\(^3\)
2-4 times more frequent and more severe among non-white populations\(^4\).

SLE is...

Also, more severe\(^4\) among:
- Males
- Pediatric patients
Certain Ethnic Populations Experience the Disease More Severely

Regardless of age or gender, Hispanic, African American and Asian patients with SLE tend to experience greater disease activity and faster accrual of organ damage:

- Hematological
- Serosal
- Neurological
- Renal
Certain Ethnic Populations

Compared to white patients with SLE:

Accrue more damage over time, at a faster pace\textsuperscript{4}  
More frequently develop specific organ damage (eg, renal and cutaneous)\textsuperscript{4}
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<td>2.4</td>
<td>Key Practice Takeaways</td>
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SLE: Various Symptoms, Various Patient Experiences

• SLE is a chronic, multi-symptom autoimmune disease⁵

• Symptoms are diverse, with inflammation affecting a wide variety of organ systems⁵,⁶

• The course of the disease varies from patient to patient. There are periods of disease inactivity followed by flares (waxing and waning disease)⁵
For the Majority, Physical Manifestations Are Common

- 8 in 10 patients experience skin-related symptoms
- Up to 8 in 10 patients experience cognitive impairment
- 6 in 10 patients develop nephritis within 10 years of diagnosis
- SLE patients are also over 2.5 times more likely to experience a cardiovascular event
SLE impacts patients’:

- Psychosocial wellbeing\textsuperscript{11-16}
- Interpersonal relationships\textsuperscript{11-16}
- Quality of life\textsuperscript{11-16}
- Productivity\textsuperscript{11-16}
- Healthcare utilization\textsuperscript{11-16}
Higher Mortality Rates

Patients with SLE have a higher mortality rate compared to the general population\textsuperscript{17}

Younger patients with SLE (16-24) have much higher rates of mortality compared to their age cohort in the general population\textsuperscript{17}

Most Common Causes of Death\textsuperscript{17} (\(N = 1\,255\))\textsuperscript{*}

- Lupus: 23% (\(N = 291\))
- Heart Disease: 10% (\(N = 126\))
- Malignancy: 9% (\(N = 114\))
- Infection/Pneumonia: 5% (\(N = 64\))
- Renal: 3% (\(N = 34\))
- Stroke: 2% (\(N = 21\))

Adapted from Bernatsky, et al.\textsuperscript{17}

\textsuperscript{*} Cause of death was acquired through probabilistic linkage to vital statistics registries. It is possible that the primary cause of death when identified as lupus was actually another condition (eg, cardiovascular disease or infection) but the patient’s pre-existing diagnosis of SLE may have led to this being listed as the cause of death.

Collaboration of the Systemic Lupus International Collaborating Clinics (SLICC) and the Canadian Network for Improved Outcomes In Systemic Lupus (CaNIOS) investigator groups (US, Canada, England, Scotland, Iceland, Sweden, South Korea). Mortality data were collected for 9,547 patients followed 1958-2001 (76,948 person-years). A total of 1,255 deaths occurred. Specific causes of death were not available from all cohorts. Durations of disease at time of enrolment was < 2 years for most patients and 90% of patients were female. Race/ethnicity was not reported for the entire cohort.
Hospitalizations Are Common

Approximately 20%-25% of patients with SLE are hospitalized annually\textsuperscript{17,18}

1 in 6 patients are readmitted within 30 days\textsuperscript{15}
Nearly all patients (91%) reported a negative effect on their ability to perform at least one valued life activity, such as cooking, family care, and sleeping. 

- Leisure: 42%
- Walking: 44%
- Cooking: 50%
- Family Care: 58%
- Errands: 61%
- Working/School: 73%
- Sleeping: 74%
- Vigorous Activity: 83%

Adapted from Katz, et al. 12
SLE Impacts Patients’ Career Decisions

- 44% Changed their career paths due to the disease
- 63% Retired or quit working earlier than planned
- 67% Reduced their work hours

*Data from the 2011 National Burden of Lupus survey funded and developed by GSK. This survey included 957 people in the lupus community—502 people who reported being diagnosed with SLE, 204 supporters (family members or friends) of people with lupus and 251 rheumatologists.
Meet Christa
The SELENA-SLEDAI, can be used to objectively assess a patient’s overall disease activity. It is included for the purpose of demonstrating how the variables you may already be evaluating in your clinical practice correlate with the SELENA-SLEDAI disease descriptors.

**SELENA-SLEDAI SCORE: 12 points**

Arthritis 4 points, Pleurisy 2 points, Rash 2 points, Elevated anti-dsDNA titer 2 points, Low complement 2 points

---

**Medication History:**

Antimalarial agent since diagnosis; low dose glucocorticoids daily since last flare; intramuscular glucocorticoid injections as needed to control joint pain and stiffness; immunosuppressive agents.

**Lab Values:**

- Hemoglobin (g/dL) ....................... 10.2
- Platelets (x10^9/L) ..................... 170
- WBCs (x10^9/L) .......................... 3.2
- Urinalysis .............................. Normal
- Creatinine (mg/dL) ........................ 1.2
- Anti-dsDNA (IU/mL) ..................... 150
- Complement C3 and C4 (mg/dL) ........ 88 and 9
- Lymphocytes (x10^9/L) .................. 1 100

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The SELENA-SLEDAI, can be used to objectively assess a patient’s overall disease activity. It is included for the purpose of demonstrating how the variables you may already be evaluating in your clinical practice correlate with the SELENA-SLEDAI disease descriptors.

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**Patient Case Study**

**Christa**

Mother of two school-aged children who is mostly confined to home due to fatigue

Taking antimalarials plus low-dose glucocorticoids

Christa is a mother to two active children who often volunteers for school and sporting team events. She has had to reduce her activities and travel because of an increased need to rest.

**History:**

- Diagnosed with SLE 8 years ago
- Had 2 flares in the first year (joint pain in fingers), resulting in higher glucocorticoid doses
- Higher glucocorticoid dosage has led to side effects (weight gain and swelling of the ankles)
- Feels her disease is getting worse

**Clinical Profile:**

- Persistent pain in the proximal interphalangeal joints
- Pleurisy
- Recurrent photosensitive discoid rash
- Constantly tired and aching, and has rashes on her face and ears
Christa: Mother of two school-aged children who is mostly confined to home due to fatigue

"I’ve been able to manage my SLE pretty well for the first few years. The glucocorticoids are helpful but at the same time, the side effects have been more bothersome than I’d like to admit. At some point, I just want to know if I can get better…or if this is the beginning of a permanent downturn. I can’t picture myself watching the kids on the sidelines for good, when a year ago, I was coaching two soccer teams."

Note: This is a hypothetical patient; for illustrative purposes only.
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In Two Studies, Permanent Organ Damage Was Found in 33%-50% of Patients by Year 5\textsuperscript{21,22}

Adapted from Chambers, et al.\textsuperscript{21} Adapted from Urowitz, et al.\textsuperscript{22}

Retrospective analysis of records for patients with ≥ 10 years of consistent follow-up presenting at the University College London Hospital SLE clinic. Year 0 represents time of diagnosis. Mean age at diagnosis was 31.2 years, 95% of patients were female, 72% were white, 14% were black, 10% were Asian (Indian), and 4% were “other.”\textsuperscript{21} Cohort analysis of SLE patients followed for a minimum of 5 years by the Systemic Lupus International Collaborating Clinics International Research Network, comprising 27 centers from 11 countries. Year 0 represents time of enrollment. Mean age at enrollment was 35.3 years, 87% of patients were female, 55% were white, 12% were black, 14% were Asian, 16% were Hispanic and 2% were “other.”\textsuperscript{22}
In the same two studies, SDI scores and organ damage increased year over year:

Patients with damage in selected categories, and overall SDI scores:

<table>
<thead>
<tr>
<th>Damage Category</th>
<th>1 Year</th>
<th>5 Year</th>
<th>10 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropsychiatric Damage</td>
<td>2.6%</td>
<td>11.2%</td>
<td>14.7%</td>
</tr>
<tr>
<td>Musculoskeletal Damage</td>
<td>2.2%</td>
<td>5.6%</td>
<td>12.1%</td>
</tr>
<tr>
<td>Renal Damage</td>
<td>0.4%</td>
<td>6.9%</td>
<td>12.9%</td>
</tr>
</tbody>
</table>

Patients with SDI scores > 0

- 32.2% (N = 298) at 1 year
- 49.7% (N = 298) at 10 years

Patients with organ damage are at risk of more rapid progression to further damage.  

Adapted from Chambers, et al. 21 Urowitz, et al. 22
Did You Know...

The cost per patient\(^*\) for a severe flare is approximately $12,000\(^{23}\).

\(^{*}\)Patients with SLE were extracted from a large Medicaid database 2002-2009, \(n = 14,777\) with 14,262 matched non-SLE patients.
Even With Low Disease Activity, Organ Damage Occurs^{22}

Multiple factors may contribute to damage accrual, including the chronic use of corticosteroids.^{22}

Adapted from Urowitz, et al.^{22}

*The SLEDAI-2K (SLE Disease Activity Index 2000) is a validated measure of global SLE disease activity.

†The SDA (SLICC/ADR Damage Index) is a validated measure of assessing damage in SLE.

Prospective analysis of patients in the SLICC cohort recruited within 15 months of diagnosis and followed annually for ≥ 5 years. Mean age at enrollment: 35.3 years; 87% female; 55% white, 12% black, 14% Asian, 16% Hispanic, 2% “Other”. At enrollment, mean disease duration = 5.5 months; mean SLEDAI-2K score = 5.9.
Organ Damage in SLE as Assessed by the SLICC Damage Index Is Considered to Be Permanent

“...Control of disease activity in patients is thought to be important in reducing permanent organ damage and is likely to impact on the outcome of the patient.”

– Lopez R, et al. 24
Organ Damage Can Go Unnoticed

- Osteonecrosis may be asymptomatic in patients with SLE\textsuperscript{25}

Cardiovascular (CV) disease may be subclinical

- In patients with SLE vs. control group:
  - Prevalence of plaques in internal carotid artery is \textbf{3x} higher\textsuperscript{26}
  - Endothelial dysfunction, an early marker of atherosclerosis, is \textbf{2x} as common\textsuperscript{27}
Risks of coronary heart disease and stroke are significantly higher for patients with SLE compared to general population.

- 2-10X increased risk of CHD\textsuperscript{28}
- 6-8X increased risk of stroke\textsuperscript{10}
### Increased Risk of Myocardial Infarction

#### Incidence Rate of MI per 1,000 Person-Years

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Rate ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>$\infty$</td>
<td>NA</td>
</tr>
<tr>
<td>25-34</td>
<td>$\infty$</td>
<td>NA</td>
</tr>
<tr>
<td>35-44</td>
<td>52.43</td>
<td>21.6, 98.5</td>
</tr>
<tr>
<td>45-54</td>
<td>2.47</td>
<td>0.8, 6.0</td>
</tr>
<tr>
<td>55-64</td>
<td>4.21</td>
<td>1.7, 7.9</td>
</tr>
</tbody>
</table>

For women aged 35-44 the risk is greatest: 50x greater vs. general population.²⁹

Adapted from Manzi, et al.²⁹

Prospective analysis of the incidence of MI in 498 women with SLE. Cardiovascular incidence rates were compared to 2,208 women of similar age participating in the Framingham Offspring Study, a prospective investigation of cardiovascular disease and the children of the 5,209 men and women who participated in the original Framingham Heart Study. A comparison of MI rates was made over the same time period (1980-1993).²⁵
Monitoring for CV Health

• Refer to traditional Framingham risk factors and lupus-associated risk factors such as duration and level of disease activity and homocysteine levels\textsuperscript{29}

• Even in young patients (35-44 years) with SLE, chest pain could be a warning sign of ischemic heart disease\textsuperscript{28,30}

• Evaluate patients at least once yearly\textsuperscript{31}
Bone Health May Be Compromised

- Risk of fracture is estimated to be significantly higher among patients with SLE\(^{32}\)

Patients with SLE: estimated 5x more likely to have bone fracture compared to age-matched controls

18 to 24 year-olds with SLE 12x more likely to have bone fracture vs. general population
Monitoring for Bone Health

- Monitor regularly for the signs of osteoporosis early in disease course, since bone fracture risk associated with SLE disease activity may be independent of glucocorticoid use or menopausal status\(^{33}\)

- Monitor more frequently if patient has additional risk factors (eg, menopause)\(^{34}\)
Nephritis: One of the Most Serious Complications

- Majority of patients will develop renal damage in the course of the disease\(^7\)
- 60% of patients will develop renal abnormalities in the first 10 years after diagnosis\(^9\)
- Renal damage is one of the most important predictors of mortality\(^3^5\)
Monitoring for Kidney Disease

- Assess patient’s history of renal disease
  - Urinalysis should be routinely performed, even in the absence of previously diagnosed nephritis\(^9\)
  - Evaluate associated risk factors and perform diagnostic assessments\(^9\)

- The risk of end stage renal disease is:
  - 11% 5 years after diagnosis\(^{36}\)
  - 22% 15 years after diagnosis\(^{36}\)

- For patients with diagnosed nephritis, monitoring should be performed regularly\(^9\)
Cognitive Impairment Affects Up to 80% of Patients

- Cognitive impairment is the most frequent neurologic damage in SLE\(^{37}\).
- Difficulties in concentration, attention, memory and visual perception are common\(^{38}\).
- Headache, depression and anxiety are also common\(^{8}\).
Monitoring for Cognitive Impairment

- Refer to ACR nomenclature for neuropsychiatric syndromes to aid in diagnosis\(^5\)

- For patients with symptoms of cognitive impairment, monitor their clinical history, and perform standardized neuropsychological testing\(^{39}\)
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As a multi-symptom disease, often unpredictable in its activity, SLE requires expertise from a multi-disciplinary team:

- Rheumatologists
- Dermatologists
- Neurologists/Psychiatrists
- Ophthalmologists
- Cardiologists
- Nephrologists
- Maternal-Fetal Specialists
- Infectious Disease Specialists
- Orthopedic/Musculoskeletal Specialists
- Psychologists
- Social Workers/Counselors
In my clinical practice, I find the multidisciplinary team to be crucial for patient care...in addition to developing a strong partnership with the patient, good communication with other HCPs is critical in the management of SLE...

– Dr. Anca Askanase
52% of patients report that they minimize their symptoms when talking to physicians*\(^{21}\)

72% of physicians are unaware that patients tend to underreport their symptoms*\(^{21}\)

*Data from the 2011 National Burden of Lupus survey was funded and developed by GSK. This survey included 957 people in the lupus community—502 people who reported being diagnosed with SLE, 204 supporters (family members or friends) of people with lupus and 251 rheumatologists.
What Can We Do to Enhance Patient Interactions?

5 Key Actions⁴¹:

- Involve patient in SLE management plan
- Define clear goals
- Be an active listener
- Help patient understand disease
- Encourage patient to ask questions
A Patient’s Perspective

…over the years, I’ve learned the importance of building a strong and open relationship with my doctors. It’s so extremely important.

– Rena, currently living with lupus

Rena is a paid spokesperson for GSK.
In Patients With SLE, Cognitive Impairment May Impact Their Ability to Manage Their Condition

• Many patients exhibit some form of cognitive impairment

“Sorry... I forgot what you told me.”
What tests should be conducted?

Periodic follow-up and laboratory testing, including:

- Complete blood counts with differential
- Creatinine
- Urinalyses

are imperative for detecting signs and symptoms of new organ-system involvement and for monitoring response and adverse reactions to therapies.
How Often Should Patients Be Monitored?

- For patients with very mild stable disease: every 3-6 months\textsuperscript{5}
- Periodic assessment of complement levels and dsDNA titers may be used as adjuncts to clinical evaluation for predicting lupus flares\textsuperscript{43}
Lastly, Be Aware of Treatment-related Complications:

- Opportunistic infections and certain malignancies can develop, most often in patients receiving chronic immunosuppressive therapy\(^4\)\(^3\)

- Chronic corticosteroid use is associated with cataracts, diabetes mellitus, atherosclerotic heart disease, osteoporosis and osteonecrosis, and fluid retention\(^5\)

- Long-term use of NSAIDs is associated with GI bleeding and kidney damage\(^5\)


Welcome to Module 2

Module 2 – The Clinical Impact of SLE – Defining and Achieving Success for your Patients
Module 2 Learning Objectives

In this module, we’ll cover the following topics:

**How**
- How does disease activity affect long-term outlook?

**What**
- What considerations should be taken in balancing risk/benefit in treating SLE?

**What**
- What is Treat-to-Target and can it help improve patient outcomes? Some current thinking on achieving meaningful targets

**How**
- How can we help manage patients to optimize care in the face of an unpredictable, chronic condition?
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Survival rates of SLE patients have improved over the past 5 decades\textsuperscript{1}

However, SLE patients still have a 2.6x higher mortality rate vs. general population\textsuperscript{1}
- Causes of death vary, but majority of deaths are due to CV events, infections or cancer\textsuperscript{2}
- Persistent disease activity is linked to increased organ damage, which in turn is predictive of increased damage and mortality\textsuperscript{2}
Disease Activity Is Linked To Organ Damage Accrual

Adapted from Doria, et al. 2004

Mean SLICC DI

Follow-up, Years

CAD

RRD

CQD

MDA

CAD = chronic active disease; CQD = clinically quiescent disease; MDA = minimal disease activity; RRD = relapsing-remitting disease; SLICC DI = Systematic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.
Persistent Disease Activity: Predictor of Negative Outcomes

Persistent disease activity has long-term consequences for patients:

- Possible predictor of flares, which impacts morbidity and mortality\(^3,4\)
- Lower probability of remission\(^4,5\)
- Higher use of glucocorticoids\(^6,7\)
Hospitalization rates for serious infections in SLE patients were as much as 24 times higher than in the general public.\textsuperscript{8}

*Retrospective analysis using data of the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project, of the Agency for Healthcare Research and Quality from 1996-2011.
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Overview of Mainstay Treatments in SLE

**Less Severe Disease**
- Antimalarials
- NSAIDs
- Low doses of corticosteroids
- Helpful in treatment of mild symptoms such as arthralgias and musculoskeletal cutaneous manifestations

**SLE**

**More Severe Disease**
- Corticosteroids
- Cytotoxic and immunosuppressive agents*
  *In addition to medications for less severe disease.
- Used in patients with significant organ involvement and severe cutaneous manifestations
All drugs have potential side effects, so the balance of risk versus benefit is always at the forefront of a [SLE] treatment regimen.

– Levy, et al.¹⁰
In Addition To Disease Activity, Drug-related Side Effects Can Result In Accrual of Organ Damage

Adapted from Doria, et al. ²
Antimalarials

In the treatment of SLE, the mechanism of action of antimalarials is not fully understood; their anti-inflammatory and immunosuppressive properties may help explain their effectiveness.\(^9\)

- Antimalarials have been associated with reduced disease activity, reduced risk of flares and organ damage, and reduced mortality.\(^{11-15}\)
- Improved ophthalmology screening tools and new knowledge on prevalence of toxicity can help clinicians minimize vision loss.\(^{16}\)
• Most common side effects: gastrointestinal upset, dermatologic reactions, headache, and lightheadedness.

• Rare but serious side effects include psychosis, convulsions, toxic neuropathy, skeletal myopathy, cardiac myopathy, and ophthalmologic toxicity, including vision loss.

• American College of Rheumatology recommends a baseline examination (funduscopy and visual field) prior to initiating antimalarial treatment.

  ▪ Follow up ophthalmologic assessments every 6-12 months.
Immunosuppressants

Immunosuppressant agents are typically reserved for more severe disease, as well as for patients who have active disease despite antimalarials and/or glucocorticoids.

- Used in induction and maintenance of remission and reduction of flares or relapses.
- Can be given in combination with glucocorticoids to control flares, or to lower the dose of each medication; or to reduce incidence of adverse events.
- Some immunosuppressant agents may be used to treat neuropsychiatric symptoms and severe cutaneous manifestations.
Potential adverse events include (varies with specific medications in this class):

- Myelosuppression\textsuperscript{17}
- Hepatotoxicity\textsuperscript{17}
- Renal dysfunction\textsuperscript{17}
- Infertility\textsuperscript{17}
- Increased risk of infection and/or cancer\textsuperscript{17}

Common monitoring parameters:

- Baseline and routine CBC, platelet count, SCr, LFTs, and urinalysis (depending on individual drug)\textsuperscript{17}
Owing to their potent anti-inflammatory effects, glucocorticoids are used to treat a wide number of rheumatic diseases, including SLE:

- Low-to-moderate doses used for mucocutaneous and vasculitic skin lesions (with no organ involvement)\textsuperscript{18}
- Useful for moderate-to-severe polyarthritis\textsuperscript{18}
- High doses used for major organ involvement\textsuperscript{18}

Glucocorticoids are potent, inexpensive, and rapid in onset.\textsuperscript{19} They can be used to treat a range of manifestations at various dosage ranges.\textsuperscript{18}

*In this module, the term ‘glucocorticoids’ also refers to prednisone equivalents.
…Our clinical decision making concerning the use of glucocorticoids in SLE patients is often based on clinical experience, making it more an art than science.

– Luijten, et al.
### Adverse effects of glucocorticoids—time and dose relationship

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Time-dependent</th>
<th>Dose-dependent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis</td>
<td>Yes (early)</td>
<td>Yes (maximum 6 months)</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Yes (early)</td>
<td>Yes</td>
</tr>
<tr>
<td>Cushing Syndrome</td>
<td>Yes (at least 1 month)</td>
<td>Yes</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Increased risk of infections</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cataracts</td>
<td>Yes (delayed)</td>
<td>Yes</td>
</tr>
<tr>
<td>Psychological and behavioral</td>
<td>Yes (early)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Adapted from Ruiz-Irastorra, et al. 21
Please Select the Learning Module You Would Like to View:

**Module 1** | Understanding SLE – Practical Tips in Managing Patients

1.1 | The Faces of SLE

1.2 | What Is the Impact of SLE?

1.3 | SLE in the Long Term for Patients

1.4 | Optimizing Patient Care

**Module 2** | The Clinical Impact of SLE – Defining and Achieving Success for your Patients

2.1 | The Impact of Disease Activity in SLE

2.2 | Treatment Considerations in SLE – Balancing Risk and Benefit

2.3 | Treat-to-Target as an Approach to Improved Patient Outcomes

2.4 | Key Practice Takeaways
Disease Activity in SLE May Appear in Different Patterns*5,22-24

60-85% of SLE patients fall under RR or CA patterns5,22

Adapted from Barr, et al.22

*Data from prospective observational studies of SLE patients with follow-up times of at least 5-year period.5,22-24
Prevention of flares may be a realistic goal\textsuperscript{25}
EULAR has made defining remission in SLE a priority focus, with the establishment of the DORIS (Definition of Remission in SLE) task force.

It is remarkable that while remission has been used to describe a favorable clinical state for [SLE]...there has not yet been an agreed-upon definition of remission in SLE.

— van Vollenhoven, et al.26
Examples of Proposed Stages of SLE Disease

**Lupus Low-disease Activity State**\(^{27}\)

- SLEDAI-2K ≤ 4
- No new signs/symptoms of disease activity since previous assessment
- PGA ≤ 1
- Current glucocorticoid dose ≤ 7.5 mg/day
- Well-tolerated immunosuppressants/biologics

**Serologically Active Clinically Quiescent (SACQ)**\(^{28}\)

- ≥ 2 years without clinical disease activity
- Persistent serologic activity (anti-dsDNA and/or low complement)
- Antimalarials permitted
- No corticosteroids or immunosuppressives

**Remission**\(^{29}\)

- Complete: 5 years without clinical or serologic disease activity (only antimalarials permitted)
- Clinical remission off glucocorticoids: SACQ (antimalarials/immunosuppressants permitted)
- Clinical remission on glucocorticoids: SACQ (glucocorticoids ≤ 5 mg/day, antimalarials, immunosuppressants permitted)
Systemic rheumatic diseases such as SLE do not have a single measurement that accurately depicts disease course and patient outcome. Knowing this, the idea of broadening treatment goals and success may prove to be more useful and achievable. Treat-to-Target is a therapeutic strategy with the view to improve disease outcomes.
Implementing Treat-to-Target in Practice

Recommendations for improving SLE management using a Treat-to-Target approach were developed by a multidisciplinary, multinational task force.

A selection of the recommendations are as follows...

Adapted from Doria, et al.
The treatment target of SLE should be remission of systemic symptoms, organ manifestations or, where remission cannot be reached, the lowest possible disease activity, measured by a validated lupus activity index and/or organ-specific monitors\textsuperscript{25}

Adapted from Doria, et al.\textsuperscript{30}
Preventing Flares Is a Realistic Goal\textsuperscript{25}

Prevention of flares (especially severe flares) is a realistic target in SLE and should be a therapeutic goal\textsuperscript{25}
Preventing Damage Accrual Is a Major Goal

Since damage predicts subsequent damage and death, prevention of the damage accrual should be a major therapeutic goal in SLE.
Treat Factors Linked to Poor HRQoL$^{25}$

Factors negatively influencing HRQoL such as fatigue, pain, and depression should be addressed in addition to control of disease activity and prevention of damage$^{25}$.
SLE maintenance treatment should aim for the lowest glucocorticoid dosage needed to control disease, and if possible, glucocorticoids should be withdrawn completely.
Treat-to-Target Can Be Successful if...

1. The appropriate target(s) can be identified\(^25\)
2. Measuring the target is possible\(^25\)
3. Appropriate interventions exist to (attempt to) achieve the target\(^25\)
Patient Case Study

Meet Alicia
The SELENA-SLEDAI, can be used to objectively assess a patient’s overall disease activity. It is included for the purpose of demonstrating how the variables you may already be evaluating in your clinical practice correlate with the SELENA-SLEDAI disease descriptors.

**SELENA-SLEDAI SCORE: 6 points**
Rash 2 points, Arthritis 4 points

**Medication History:**
- Moderate dosage of glucocorticoid daily
- Reducing doses of glucocorticoids results in flares

**Lab Values:**
- Hemoglobin (g/dL) .................. 12.2
- Platelets (x10^9/L) ................. 210
- WBCs (x10^9/L) .................... 3.9
- Urinalysis .......................... Normal
- Creatinine (mg/dL) ................. 0.9
- Proteinurin (g/day) ................. 0.1
- Anti-dsDNA (IU/mL) ............... 5
- Complement C3 and C4 (mg/dL) ... 90 and 30
- Lymphocytes (x10^9/L) .......... 1,100

**History:**
- Diagnosed 5 years ago
- Received an antimalarial until intolerable GI upset
- Has occasional pain in her wrists and rashes on the face

**Clinical Profile:**
Chronic fatigue with flares of malar rash and polyarthritis in the wrists.

Note: This is a hypothetical patient; for illustrative purposes only.
Getting up in the morning is hard because this is when my arthritis feels the worst. At this age, I should have enough energy to keep up with my children, but I don’t. If there was something I could do to get my energy levels up and the flares down, I’d definitely consider it.
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2.3 Treat-to-Target as an Approach to Improved Patient Outcomes
2.4 Key Practice Takeaways
How Can Current Perspectives Change Current Practices?

A selection of recommendations from various peer-reviewed sources and task forces are presented here...
When Remission Is Not Possible, Consider Alternate Targets

- Complete remission is the goal for patients with SLE\textsuperscript{25}
- Clinical remission (complete or partial) can be an effective target as well\textsuperscript{25}
- Low-disease activity would be a subsequent goal if clinical remission is not achievable\textsuperscript{25}

Adapted from Doria, et al.\textsuperscript{30}
Minimize Disease Activity

- Persistent disease activity can result in ongoing organ damage\textsuperscript{31}
- Disease activity and immunologic factors can predict flares
- Assess disease activity regularly; patient history, physical assessment, and labs can help detect and define disease activity\textsuperscript{32-35}
Monitor For Subclinical Activity

• Regular monitoring should be undertaken to detect “silent variables”\(^{36}\)

• Data support following patients with mild or inactive disease at 3-4 month intervals\(^{36}\)

In a retrospective analysis, 1 in 4 patients seen over 2 years had at least one “solitary silent variable,” detectable only through routine laboratory assessments (\(N = 515\))\(^{36}\):

<table>
<thead>
<tr>
<th>Variable Detected</th>
<th>Number of Visits with New Variable ((N = 173))</th>
<th>Number of Patients with ≥ 1 Visit with New Variable ((N = 126))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cast</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Hematuria</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Pyuria</td>
<td>42</td>
<td>35</td>
</tr>
<tr>
<td>Low complement</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>DNA antibodies</td>
<td>36</td>
<td>32</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Elevated serum creatinine</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Low hemoglobin</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

Frequency of New Silent Variables of Interest in 515 Patients, ≥ 3 Visits, ≥ 18 Months’ Follow-up

Laboratory parameters were the sole manifestation of SLE in 24.7% of patients.
Reduce – As Much As Possible – Glucocorticoid Dosage

- Glucocorticoids are invaluable in the treatment of SLE; however, their chronic use has consistently shown to increase irreversible damage in lupus patients, a major predictor of morbidity and mortality.\(^\text{21}\)
- Use of the lowest effective dose of glucocorticoids can reduce the risk of glucocorticoid-related damage accrual.\(^\text{25,37}\)
- In general, the risk of organ damage increases at a dose of 7.5 mg/day.\(^\text{38}\)

Adapted from Al Sawah, et al.\(^\text{38}\)

*At the time of this analysis, the cohort included 2,265 patients with SLE who were followed over the course of 26 years between 1987 and October 2012, with the average duration of follow-up from cohort entry until lost to follow-up being 6.2 years. Cox proportional hazards models were used to estimate the impact of different levels of exposure to [glucocorticoids] (as defined by [glucocorticoid] cut-off points endorsed in some SLE clinical trials) on the risk of developing any new organ damage or any new organ damage at the individual organ systems over time. Organ damage was measured by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) or by components of the SDI at the individual organ systems level.

Analysis* of data from the Hopkins Lupus Cohort study of 2,265 patients over 26 years, investigating impact of [glucocorticoid] doses on risk of organ damage development.\(^\text{38}\)
Patient Case Study

Meet Brianne
Patient Case Study

Brianne
Full-time professional with worsening symptoms affecting her work life

Taking an antimalarial agent alone but is having flares requiring short-term glucocorticoids

Brianne is a certified accountant working full-time. Over the past 6 months, she’s experienced increasing difficulty in completing tasks on time due to:

- Increased fatigue
- Joint pain in her hands, which are crucial for her ability to do computer work for extended periods of time

History:
- Diagnosed with SLE 2 years ago
- For past 6 months, has experienced:
  - Fatigue
  - Hair loss
  - Increasing pain in her hands and fingers
  - Ulcers on her palate

Medication History:
- Antimalarial for 2 years; moderate dosage of glucocorticoid daily for flares

Lab Values:
- Hemoglobin (g/dL) ..................... 12.2
- Platelets (x10⁹/L) ..................... 260
- WBCs (x10⁹/L) ......................... 3.9
- Urinalysis.......................... Normal
- Creatinine (mg/dL) ..................... 1.2
- Proteinuria (g/day) ................... Normal
- Anti-dsDNA (IU/mL) ...................... 40
- Complement C3 and C4 (mg/dL). . . . 60 and 5
- Lymphocytes (x10⁹/L) ............... 1200

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SELENA-SLEDAI SCORE: 12 points
Arthritis 4 points, Mucosal ulcers 2 points, Alopecia 2 points, Elevated anti-dsDNA 2 points, Low complement 2 points

Note: This is a hypothetical patient; for illustrative purposes only.
Brianne: Full-time professional with worsening symptoms affecting her work life

I started working at a new accounting firm last year and was really keen on taking on bigger projects and clients. But lately it’s been challenging to keep up – and it scares me to think I’ll have to scale back. I’ve worked so hard to get where I am – I just wish to get back to some kind of normal.

Note: This is a hypothetical patient; for illustrative purposes only.


References


