Systemic Lupus Erythematosus
10 Things We Hate About Lupus
An Educational Program for Community Rheumatologists
Michelle Petri MD MPH
Johns Hopkins University School of Medicine

Learning Objectives
- Describe the pathophysiology and immunology of systemic lupus erythematosus (SLE)
- Demonstrate the ability to use current options for assessing outcomes and measuring disease activity in SLE
- Assess and compare the risks and benefits of immunosuppressive drugs, hydroxychloroquine, and biologics used in the management of mild-to-moderate SLE and lupus nephritis
- Identify opportunities to reduce organ damage in SLE patients

Top 10 Reasons We Hate Lupus

1. Lupus is a mystery disease
2. Lupus may be difficult to diagnose
3. Lupus disease activity is difficult to measure
4. Patients complain of pain and fatigue
5. Too much prednisone
6. Which immunomodulator &/or immunosuppressant should I use?
7. Activity of lupus nephritis is difficult to monitor
8. My patients are more likely to die from atherosclerosis
9. My patients forget what I tell them!
10. Thrombosis is common

With these challenges, how do we treat lupus to target?

Immunology of SLE

SLE is 2/3 Genetics!

<table>
<thead>
<tr>
<th>Gene</th>
<th>Chromosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSP1</td>
<td>6</td>
</tr>
<tr>
<td>FHL1</td>
<td>1</td>
</tr>
<tr>
<td>HLA-DR</td>
<td>6</td>
</tr>
<tr>
<td>MICA</td>
<td>20</td>
</tr>
<tr>
<td>MICA</td>
<td>X</td>
</tr>
<tr>
<td>MICA</td>
<td>21</td>
</tr>
<tr>
<td>MICA</td>
<td>22</td>
</tr>
</tbody>
</table>

SLE is 1/3 Environmental

- Ultraviolet light
- Drugs/supplements (echinacea, trimethoprim/sulfamethoxazole)
- Smoking
- Infections
- Silica
- Mercury
- Pesticides
Autoantibodies Precede the Diagnosis Of SLE By Years

2. LUPUS MAY BE DIFFICULT TO DIAGNOSE

SLICC* Classification Criteria
At least 1 clinical + at least 1 immunologic criteria (for a total of 4)
OR
Lupus nephritis by biopsy

SLICC Revision of the ACR Classification Criteria

<table>
<thead>
<tr>
<th>Immunologic Criteria</th>
<th>SLE</th>
<th>Other Diseases</th>
<th>Normal Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC4d hat MFI (CI 95%)</td>
<td>17.6 (15.2–20.0)</td>
<td>6.3 (5.7–6.8)</td>
<td>3.3 (4.6–6.1)</td>
</tr>
<tr>
<td>BC4d hat MFI (CI 95%)</td>
<td>110.4 (96.3–124.5)</td>
<td>34.9 (26.1–41.6)</td>
<td>22.5 (21.4–25.8)</td>
</tr>
<tr>
<td>PC4d hat MFI (CI 95%)</td>
<td>16.2 (12.0–20.5)</td>
<td>3.8 (3.0–4.2)</td>
<td>2.0 (1.2–2.8)</td>
</tr>
<tr>
<td>ECR1 hat MFI (CI 95%)</td>
<td>13.3 (12.4–14.1)</td>
<td>16.1 (15.1–17.1)</td>
<td>20.7 (19.6–21.7)</td>
</tr>
</tbody>
</table>

ANA=antinuclear antibodies; BC4d=complement C4d levels on B cells; demoxibeads-esterated; EC4d=complement C4d levels on erythrocytes; ECR1=complement receptor 1 levels on erythrocytes; MVC=mutated citrullinated vimentin antibodies; PC4d=complement C4d levels on platelets; SLE=systemic lupus erythematosus

SLICC Revision of the ACR Classification Criteria

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acute/subacute cutaneous lupus</td>
</tr>
<tr>
<td>2. Chronic cutaneous lupus</td>
</tr>
<tr>
<td>3. Oral/Nasal ulcers</td>
</tr>
<tr>
<td>4. Nonscarring alopecia</td>
</tr>
<tr>
<td>5. Inflammatory synovitis with physician-observed swelling of two or more joints OR tender joints with morning stiffness</td>
</tr>
<tr>
<td>6. Serositis</td>
</tr>
<tr>
<td>7. Renal: Urine protein/creatinine (or 24 hr urine protein) representing at least 500 mg of protein/24 hr or red blood cell casts</td>
</tr>
<tr>
<td>8. Neurologic: seizures, psychosis, mononeuritis multiplex, myelitis, peripheral or cranial neuropathy, cerebritis (acute confusional state)</td>
</tr>
<tr>
<td>9. Hemolytic anemia</td>
</tr>
<tr>
<td>10. Leukopenia (&lt;4000/mm³ at least once) OR Lymphopenia (&lt;1000/mm³ at least once)</td>
</tr>
<tr>
<td>11. Thrombocytopenia (&lt;100,000/mm³) at least once</td>
</tr>
</tbody>
</table>

Complement Split Products Bound to RBCs May Help in Diagnosis of SLE

Anti-C1q Is Associated with Renal Lupus

<table>
<thead>
<tr>
<th>Variable</th>
<th>Renal Lupus (%)</th>
<th>No Renal Lupus (%)</th>
<th>Association with Renal Flare (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-C1q</td>
<td>45.5</td>
<td>19.3</td>
<td>0.006</td>
</tr>
<tr>
<td>Anti-dsDNA</td>
<td>80.2</td>
<td>44.4</td>
<td>0.61-1.0**</td>
</tr>
<tr>
<td>Anti-Sm</td>
<td>29.7</td>
<td>15.0</td>
<td>NA</td>
</tr>
<tr>
<td>Low complement</td>
<td>78.2</td>
<td>50.2</td>
<td>C3: 0.079</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>C4: 0.77</td>
</tr>
</tbody>
</table>

C1q=complement 1 subcomponent Q; dsDNA=double-stranded DNA; Sm-Smith


3. DISEASE ACTIVITY IS DIFFICULT TO MEASURE

Detection of New Clinical Activity in SLE

<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=127)</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>Serum creatinine</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

Key point: Patients should be followed with clinical and laboratory measures every 3 months


Disease Activity Tools: Which One?

"The lack of a gold standard to measure SLE disease activity or a surrogate marker endorsed by international rheumatology societies or national health authorities has impeded the development of SLE therapies."


Physician’s Global Assessment (PGA)

- Used to assess the patient’s overall condition
- A visual analogue scale (10cm) ranging from 0–3 points (no activity to severe life-threatening activity)
- ≥0.3-point increase (10%) = clinically-relevant worsening
- Correlates with other disease activity indices

‘Severe’ means the worst in the universe of lupus, not the worst for an individual patient


SELENA-SLEDAI

- Safety of Estrogens in Lupus Erythematosus National Assessment - SLE Disease Activity Index
- A validated disease activity index that evaluates 24 lupus manifestations
- Parameters are scored if present and attributed to active lupus
- Items are weighted with scores ranging from 1-8
  - maximum score 105;
    - 6–12 is moderate
    - 13-20 is severe
    - >20 is very severe (and rare)
- Score reduction requires complete elimination of disease manifestation or resolution of laboratory abnormality
- ≥ 3-7 point reduction = clinically meaningful improvement

SELENA-SLEDAI

<table>
<thead>
<tr>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannot measure partial improvement of an individual parameter</td>
</tr>
<tr>
<td>Cannot measure worsening of an existing abnormality</td>
</tr>
<tr>
<td>Some items “unfairly” scored (e.g., thrombocytopenia)</td>
</tr>
<tr>
<td>A composite score has limitations</td>
</tr>
<tr>
<td>- cannot distinguish patients with multiple mild manifestations from those with fewer more severe features</td>
</tr>
<tr>
<td>- improvement in one organ may be offset by new involvement in another organ</td>
</tr>
</tbody>
</table>

SRI Used in Belimumab Phase III Trials

- Assesses 24 weighted variables to indicate overall disease severity
- Measures flare activity and severity across 8 organ domains
- No new BILAG A or 2 new BILAG B organ domain scores
- No worsening in PGA
- An overall assessment of changes in patient condition and disease severity

SRI Responders vs Nonresponders

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SRI Resp ( (n=781) )</th>
<th>SRI Nonresp ( (n=923) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-point reduction</td>
<td>40.3%</td>
<td>1.3%</td>
</tr>
<tr>
<td>% organ domains improved (BILAG/SS)</td>
<td>1.45/2.00</td>
<td>0.40/0.39</td>
</tr>
<tr>
<td>% Change in PGA</td>
<td>-58.3%</td>
<td>-34.9%</td>
</tr>
<tr>
<td>Severe flare rate (SLE Flare Index) at wk 52</td>
<td>6.2%</td>
<td>29.1%</td>
</tr>
<tr>
<td>Reduction in prednisone to &lt;7.5 mg/d</td>
<td>25.5%</td>
<td>16.4%</td>
</tr>
<tr>
<td>Increase in prednisone to &gt;7.5 mg/d</td>
<td>4%</td>
<td>22%</td>
</tr>
<tr>
<td>Changes in DNA/C3/C4</td>
<td>-34%/14%/40%</td>
<td>-26%/9%/29%</td>
</tr>
<tr>
<td>SF-36: PCS/MCS (MCID=2.5)</td>
<td>4.94/4.4</td>
<td>2.8/1.7</td>
</tr>
<tr>
<td>Fatigue (FACIT/SF-36 Vitality; MCID=4/5)</td>
<td>5.2/10.4</td>
<td>3/6.5</td>
</tr>
</tbody>
</table>

Don’t Blame EVERYTHING on SLE!

- Hair Loss
- Joint Pains
- Very Tired

WENDY ABEY 36
Could I have Lupus?
Get the whole story.

4. PATIENTS ALWAYS COMPLAIN OF PAIN AND FATIGUE
Health-Related Quality of Life (HRQoL) in SLE

- HRQoL reduction in SLE = that experienced by patients with AIDS, congestive heart failure, post-myocardial infarction\(^1\)

- Not well correlated with disease activity or damage cross-sectionally\(^4\)

- Age, disease duration, fatigue, and psychosocial components correlate with HRQoL\(^4\)

Fatigue

- Among most common complaints in lupus patients (50-80% of patients)\(^1\)

- Chronic fatigue does not correlate with disease activity\(^2\)

- Highly correlated with fibromyalgia, pain, depression, sleep abnormalities, poor quality of life\(^2,5\)

- Associated with reduced physical fitness\(^6\)

Treating Pain and Fatigue: Tai Chi

[Fig showing improvement in FIQ scores over 12 weeks between Tai Chi and control groups]

Treating Fatigue: Belimumab

[Fig showing improvement in fatigue scores between Belimumab responders and non-responders]

Exercise for SLE-related Fatigue

<table>
<thead>
<tr>
<th>Clinical global impression change score</th>
<th>No (%) in exercise group (n=33)</th>
<th>No (%) in relaxation group (n=28)</th>
<th>No (%) in control group (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very much better</td>
<td>3 (9)</td>
<td>4 (14)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Much better</td>
<td>13 (40)</td>
<td>4 (14)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>A little better</td>
<td>5 (15)</td>
<td>4 (14)</td>
<td>3 (9)</td>
</tr>
<tr>
<td>No change</td>
<td>6 (18)</td>
<td>10 (36)</td>
<td>14 (41)</td>
</tr>
<tr>
<td>A little worse</td>
<td>4 (12)</td>
<td>4 (14)</td>
<td>10 (31)</td>
</tr>
<tr>
<td>Much worse</td>
<td>2 (6)</td>
<td>2 (7)</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Very much worse</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Treating Fatigue: Belimumab


5. TOO MUCH PREDNISONE

“The “P” in Prednisone Stands for Poison”

--- Michelle Petri, MD MPH
“High-Dose” Prednisone Should Be Redefined as > 6 mg Daily

<table>
<thead>
<tr>
<th>Average Dose Prednisone</th>
<th>Hazard Ratio* for Organ Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;6-12 mg/day</td>
<td>1.50</td>
</tr>
<tr>
<td>&gt;12-18 mg/day</td>
<td>1.64</td>
</tr>
<tr>
<td>&gt;18 mg/day</td>
<td>2.51</td>
</tr>
</tbody>
</table>

High dose (organ damage) = ≥6 mg/day

*Adjusted for confounding by indication due to SLE disease activity

Mild-to-Moderate Flares Do Not Always Require Maintenance Steroids

Flares in Lupus: Outcome Assessment Trial (FLOAT): Oral methylprednisolone vs IM triamcinolone

No statistically significant difference in “any response” or in “complete response” (except in triamcinolone group at week 2); SF-36 = SF-36 Medical Outcomes Study Short Form–36

The Placebo Group had More Increased Steroid Use Over Time than Belimumab

The Belimumab Group Was More Likely to Reduce Prednisone Over Time Than Placebo
6. WHICH IMMUNOMODULATOR AND/OR IMMUNOSUPPRESSIVE DRUG SHOULD I PICK?

- Reduces flares
- Reduces organ damage
- Reduces lipids
- Reduces thrombosis
- Triples mycophenolate response in lupus membranous nephritis
- Improves survival


Criteria of Low and Higher Risk for Developing Retinopathy

<table>
<thead>
<tr>
<th></th>
<th>Low Risk</th>
<th>Higher Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage</td>
<td>&lt; 6.5 mg/kg hydroxychloroquine</td>
<td>&gt; 6.5 mg/kg hydroxychloroquine</td>
</tr>
<tr>
<td>Duration of use</td>
<td>&lt; 5 years</td>
<td>&gt; 5 years</td>
</tr>
<tr>
<td>Habitus</td>
<td>Lean or average fat</td>
<td>High fat level (unless dosage is appropriately low)</td>
</tr>
<tr>
<td>Renal/liver disease</td>
<td>None</td>
<td>Present</td>
</tr>
<tr>
<td>Concomitant retinal disease</td>
<td>None</td>
<td>Present</td>
</tr>
<tr>
<td>Age</td>
<td>&lt; 60 years</td>
<td>&gt; 60 years</td>
</tr>
</tbody>
</table>


Only SLE Patients with Visual Symptoms Need High Tech hsUHR-OCT or mfERG

High-Speed Ultra–High-Resolution Optical Coherence Tomography Findings in Hydroxychloroquine Retinopathy

- Question: are early toxic effects from hydroxychloroquine (HCQ) detectable by hsUHR-OCT before clinical signs or symptoms
- Fifteen patients referred for evaluation of HCQ maculopathy were studied.
- Six age-matched patients with normal visual function were studied with hsUHR-OCT
- hsUHR-OCT abnormality severity of maculopathy seemed to correlate with severity of mfERG and visual field testing
- Unable to find an asymptomatic patient with evidence of definite damage on hsUHR-OCT


Lupus Nephritis Induction Therapy: MMF = IV Cyclophosphamide Therapy

- In non-Caucasians, MMF is superior
- In renal transplant literature:
  - African-Americans: 3 grams
  - Caucasians: 2 grams
- New issue: MMF interferes with oral contraceptive dosing
  "It is recommended that oral contraceptives are coadministered with CellCept with caution and additional birth control methods be considered" 

Lupus Nephritis Maintenance Therapy: MMF is Superior to Azathioprine

**Figures:**
- Time to treatment failure
- Time to renal flare

Lupus Nephritis: Other Options

- **Belimumab**
  - Not studied specifically in SLE patients with active nephritis
  
- **Leflunomide**
  - For mild-to-moderate SLE disease
  - Induction therapy for renal flare

- **Tacrolimus**
  - Consider in MMF-resistant or partial response patients, alone or in combination
  - Approved for treatment of LN in Japan
  - For severe nephritis (Class IV/V)

- **Rituximab**
  - LUNAR trial was negative

Mycophenolate Use Beyond Nephritis

- **Joints**
  - Did NOT work in RA

- **Cutaneous**

- **CNS-SLE**

- **Reduces extra-renal flares**

Belimumab Multivariate Analysis

- **Characteristics associated with greater treatment effect (p<0.1)**
  - SELENA SLEDAI score: ≥10 (vs ≤9)
  - Complement: low C3/C4 (vs normal)
  - Steroid use: greater (vs no/less)

- **Characteristics not associated with treatment effect (p>0.1)**
  - Study
  - Region
  - Race

SRI 6 Over Time

**Figures:**
- SRI response rate over 52 weeks
- Comparison of Belimumab 10 mg/kg vs placebo

Low C/Anti-dsDNA + Subgroup: SRI Response Rate over 52 Weeks

**Figures:**
- Comparison of Belimumab 10 mg/kg vs placebo
- Overall percent improvement

References:
**7. ACTIVITY OF LUPUS NEPHRITIS IS DIFFICULT TO MONITOR**

- Biopsy all untreated patients with clinical evidence of active LN
- Therapies for all patients with LN:
  - Hydroxychloroquine
  - Angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) for patients with proteinuria ≥0.5 g/24 hours or equivalent protein/creatinine ratio
  - Maintain blood pressure ≤130/80
  - Statins for LDL >100 mg/dl
  - Pregnancy counseling for fertile women
- Treat to target with MMF or CYC (MMF preferred in African Americans and Hispanics)
- Track patients with protein/creatinine ratio, not urine dipstick

**Urine Protein/Creatinine Ratio**

- Gold standard is urine protein/creatinine ratio on a 24 hour collection
- Urine protein/creatinine timed collections (there is a circadian rhythm)
- Spot urine protein/creatinine quantifies proteinuria (as opposed to dipstick)

**Blood Pressure is Associated with Progression of CKD**

Jafar et al, Ann Intern Med 2003;139:244-252

Slide Courtesy of Elizabeth Lighthoon
8. PATIENTS DIE FROM ATHEROSCLEROSIS

Coronary Artery Disease in SLE

- Substantial increased risk that cannot be completely explained by traditional Framingham risk factors
- Hospitalization for acute myocardial infarction (AMI) 2.3 times higher in SLE
- Risk of cardiovascular events is 1.6 times higher in SLE vs Framingham cohort

Can We Reduce Cardiovascular Risk?

- Assess traditional cardiovascular risk factors and treat to target
  - Hypertension
  - Obesity
  - Hyperlipidemia
  - Smoking
  - Sedentary Lifestyle
- Mycophenolate: slowed progression in mice and transplant patients
- Prednisone > 10 mg increases CV event risk


Cognitive Impairment in SLE

- Cognitive dysfunction assessed using diagnostic evaluation suggested by American College of Rheumatology Ad Hoc Committee (N = 67)

<table>
<thead>
<tr>
<th>Score</th>
<th>Percentage</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>14 (21%)</td>
<td></td>
</tr>
<tr>
<td>Mild impairment</td>
<td>29 (43%)</td>
<td></td>
</tr>
<tr>
<td>Moderate impairment</td>
<td>20 (30%)</td>
<td></td>
</tr>
<tr>
<td>Severe impairment</td>
<td>4 (6%)</td>
<td></td>
</tr>
</tbody>
</table>

COGNITIVE IMPAIRMENT

- BAD NEWS—Frequently present at diagnosis
- GOOD NEWS—It remains stable

ANAM* Throughput Scores for Newly Diagnosed SLE Patients and Normal Controls

<table>
<thead>
<tr>
<th>Demographic/ANAM Subtests</th>
<th>SLE Patients</th>
<th>Normal Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous performance</td>
<td>78.4</td>
<td>84.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Matching to sample</td>
<td>23.8</td>
<td>26.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Simple reaction time</td>
<td>187.6</td>
<td>202.0</td>
<td>0.09</td>
</tr>
<tr>
<td>Simultaneous spatial processing</td>
<td>18.8</td>
<td>20.1</td>
<td>0.15</td>
</tr>
<tr>
<td>Sternberg</td>
<td>64.0</td>
<td>71.0</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

*Automated Neuropsychological Assessment Metrics (ANAM)


Anti-NR2

- An advance in the understanding of cognitive impairment in murine SLE has been the recognition of a subset of anti-DNA antibodies that cross-react with the anti-NR2 glutamic receptor.
- At low concentration, the antibodies are positive modulators of receptor function (by increasing excitatory postsynaptic potentials), and at high concentration, they promote excitotoxicity through enhanced mitochondrial permeability transition.
- These antibodies mediate apoptotic cell death of neurons.


Anti-NR2 Murine Model

- Anti-NR2 antibodies plus a break in blood brain barrier can cause CNS changes in a murine model
- Anti-NR2 antibodies not associated with cognitive impairment in humans


10. HOW DO I PREVENT THROMBOSIS?

Venous Thrombosis in SLE

Kaplan-Meier Estimates for Development of Deep Venous Thrombosis by Lupus Anticoagulant, adjusted for Anti-Cardiolipin Antibody

Lupus Anticoagulant Is More Highly Associated With Thrombosis Risk


Aspirin Insufficient for APS Prophylaxis

- Aspirin has NOT been proven effective to reduce thrombosis from antiphospholipid antibodies


Aspirin Resistance More Prevalent in Patients With Lupus

- 15% of patients with lupus have impaired antithrombotic response to aspirin
- Associated with features of metabolic syndrome
  - Higher body mass index (P=0.05)
  - Higher serum CRP concentrations (P=0.018)
  - More likely to be obese (P=0.018)
  - More likely to have diabetes (P=0.034)
- Likely related to inflammation, increased oxidative risk

Hydroxychloroquine Prevents Thrombosis in SLE

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wallace et al, 1987</td>
<td>retrospective</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Petri et al, 1994</td>
<td>prospective cohort</td>
<td>OR 0.3</td>
</tr>
<tr>
<td>Ruiz-Irastorza et al, 2006</td>
<td>prospective cohort</td>
<td>HR 0.28</td>
</tr>
<tr>
<td>Tektonidou et al, 2009</td>
<td>case-control</td>
<td>HR 0.99</td>
</tr>
<tr>
<td>Jung et al, 2010</td>
<td>nested case-control</td>
<td>OR 0.31</td>
</tr>
</tbody>
</table>

CONCLUSIONS

1) SLE is a complex disease with predisposing genetic and environmental factors.
2) SLE is difficult to diagnose.
3) SLE is not a pain disease.
4) Limit the use of Prednisone.
5) Selecting treatment can be difficult, but data are emerging that can help.
6) Follow renal disease with urine protein/creatinine ratio
7) Risk of coronary heart disease greatly increased in patients with SLE.
8) There are many things to hate about SLE, but we love hydroxychloroquine
9) We have a lot of work to do: pt dx’ed at age 20 has 1/6 chance of dying by age 35