SYSTEMIC LUPUS ERYTHEMATOSUS

GEORGIA LUPUS EMPOWERMENT SUMMIT 2023

Jagindra N. Mangru, M.D.

Cumming Rheumatology and Arthritis, LLC.

3970 Deputy Bill Cantrell Memorial Road, Ste. 203, Cumming, GA 30040

770-887-5159 (P), 770-887-9496 (F)

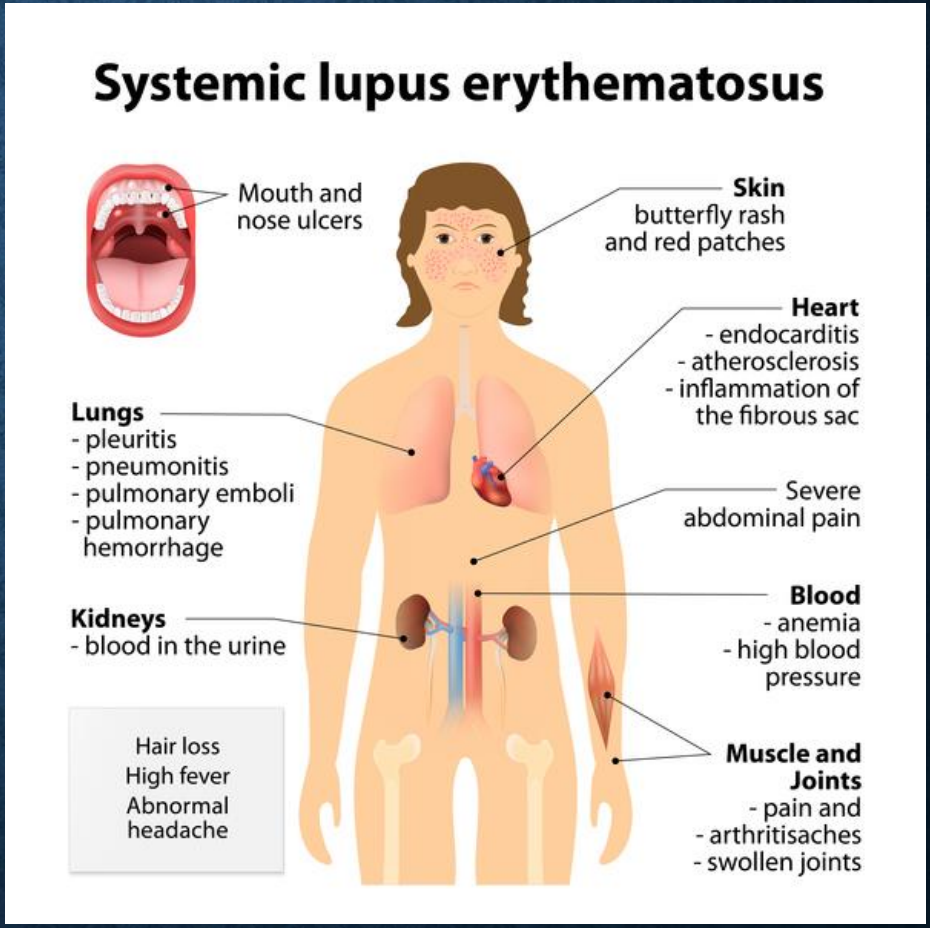
www.cummingrheumatology.com

OBJECTIVES

1. To recognize the burden of Lupus in the general population and its impact on different ethnicities.
2. To understand current concepts in the pathogenesis of Lupus.
3. To identify common manifestations of Lupus.
4. To provide an update on the current FDA approved medications in Lupus.

WHAT IS LUPUS?

Systemic lupus erythematosus (also called SLE or lupus) is a chronic inflammatory or autoimmune disease.



1 in 3 **lupus patients suffer from multiple autoimmune diseases**

The Incidence and Prevalence of Systemic Lupus Erythematosus, 2002–2004 The Georgia Lupus Registry

S. Sam Lim,1 A. Rana Bayakly,2 Charles G. Helmick,3 Caroline Gordon,4 Kirk A. Easley,1 and Cristina Drenkard1

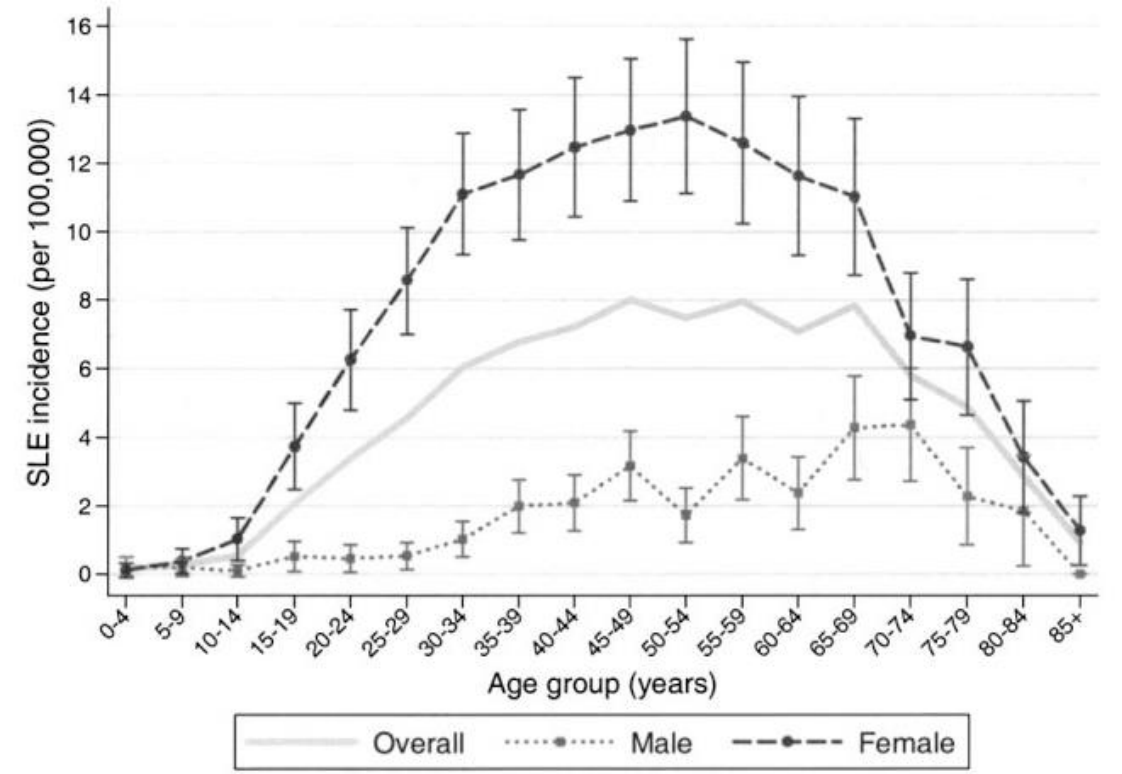


Figure 1. Age- and sex-specific systemic lupus erythematosus

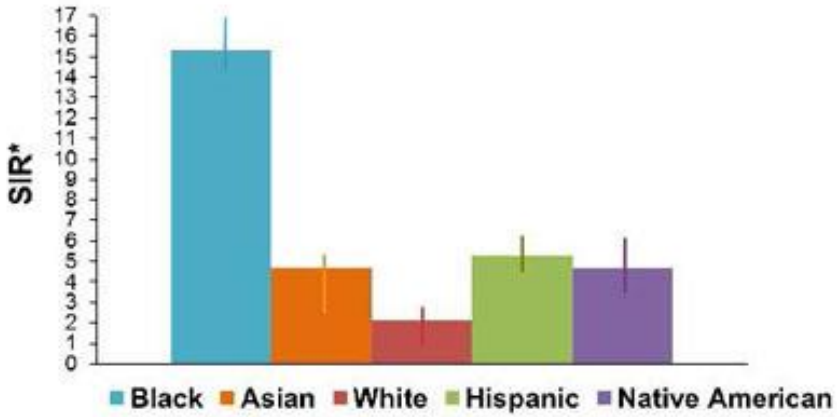
9 out of 10 **adults with lupus are women**

Young women with peak incidence 15-40 years (child bearing)

EPIDEMIOLOGY RENAL

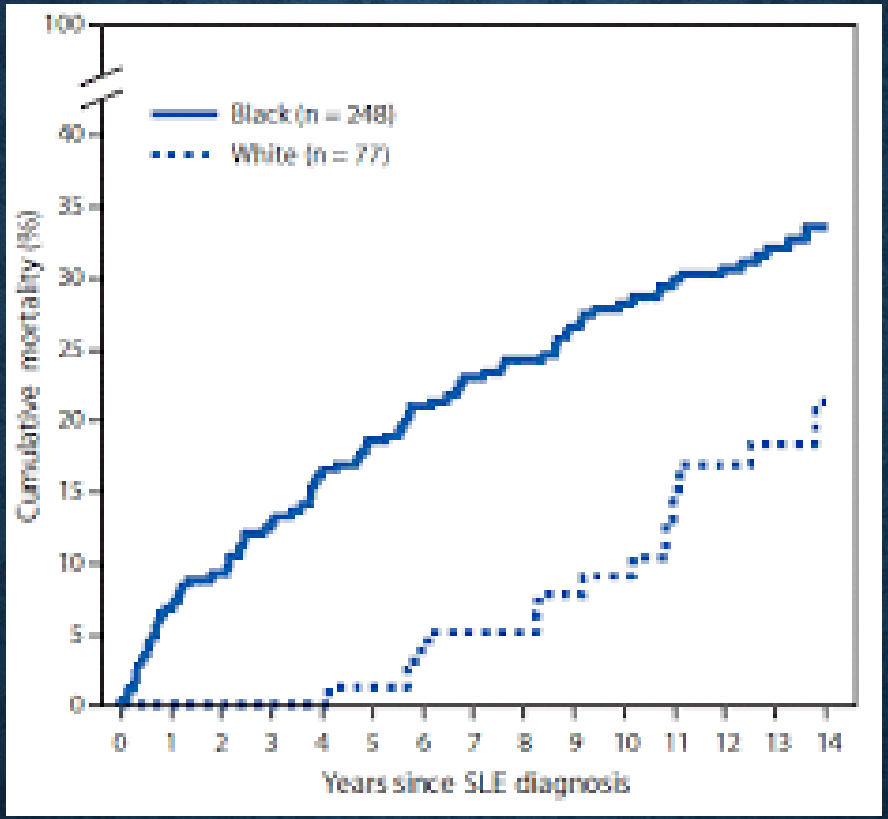
Disparities in Lupus Outcomes—Renal

Standardized Incidence Rates, End-Stage Renal Disease Due to Lupus Nephritis, United States, 2001–2006



* Standardized incidence rate: end-stage renal disease cases/million person-years.

Costenbader KH, Desai A, Alarcón GS, et al. *Arthritis Rheum*. 2011;63(6):1681-1688.

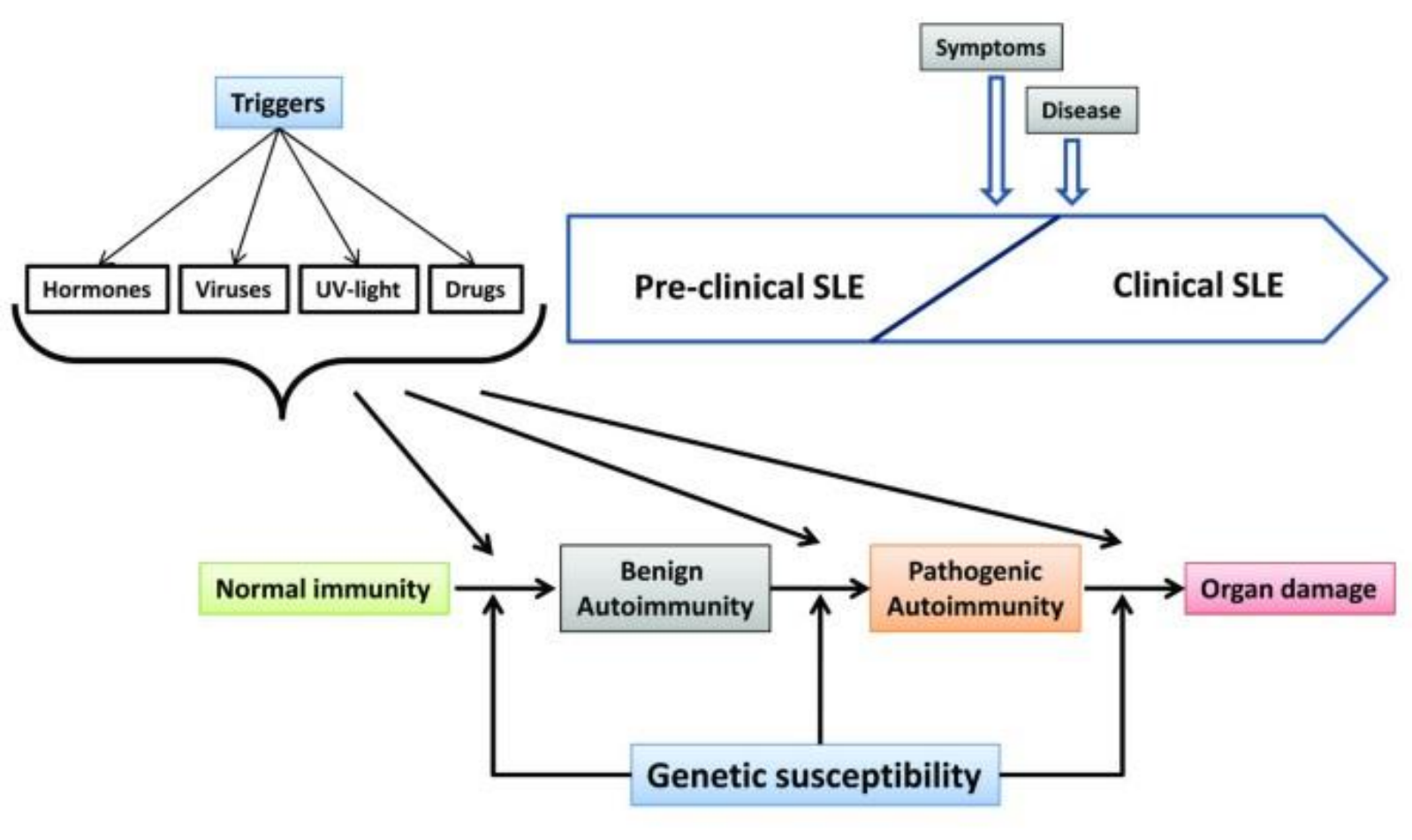


Racial Disparities in Mortality Associated with Systemic Lupus Erythematosus — Fulton and DeKalb Counties, Georgia, 2002–2016

Weekly / May 10, 2019 / 68(18);419–422

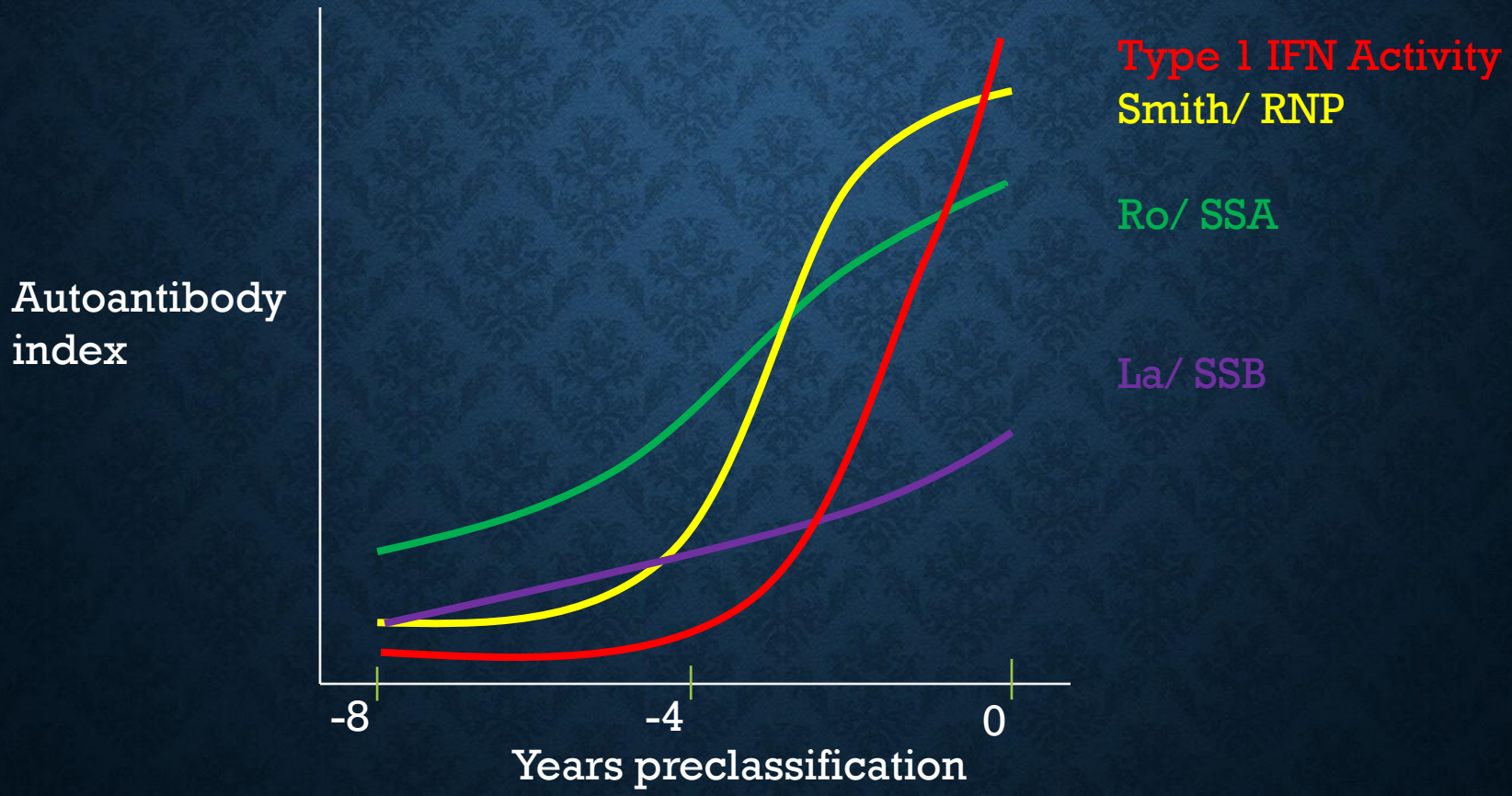
S. Sam Lim, MD[1]; Charles G. Helmick, MD[2]; Gaobin Bao, MPH[1]; Jennifer Hootman, PhD[2]; Rana Bayakly, MPH[3]; Caroline Gordon, MD[4]; Cristina Drenkard, MD, PhD[1]

WHAT CAUSES LUPUS?

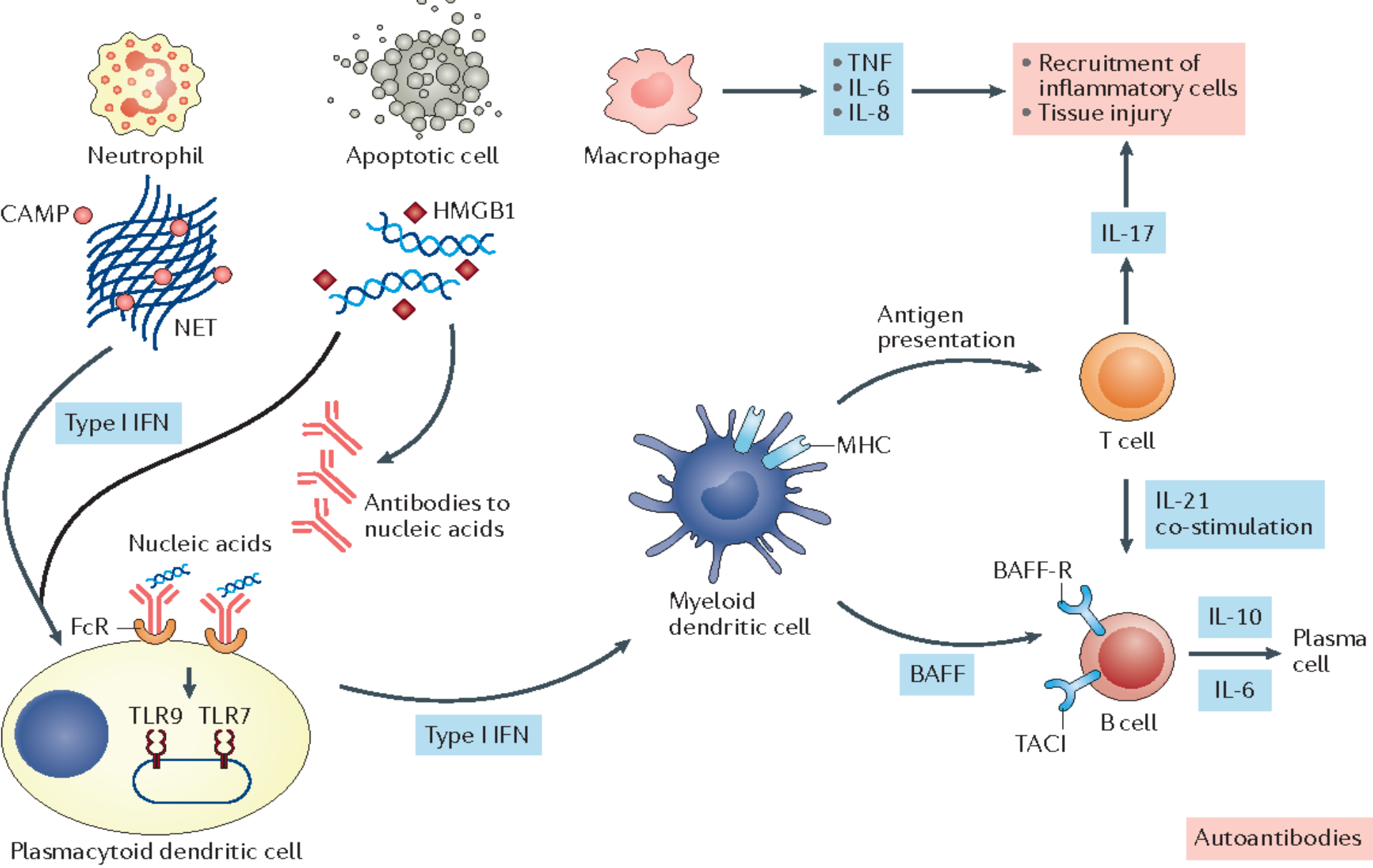


Autoantibodies and Type 1 IFN Present Before Clinical Manifestations of SLE.

Longitudinal changes in serum level/activity preceding SLE classification in patients with SLE (n=55)



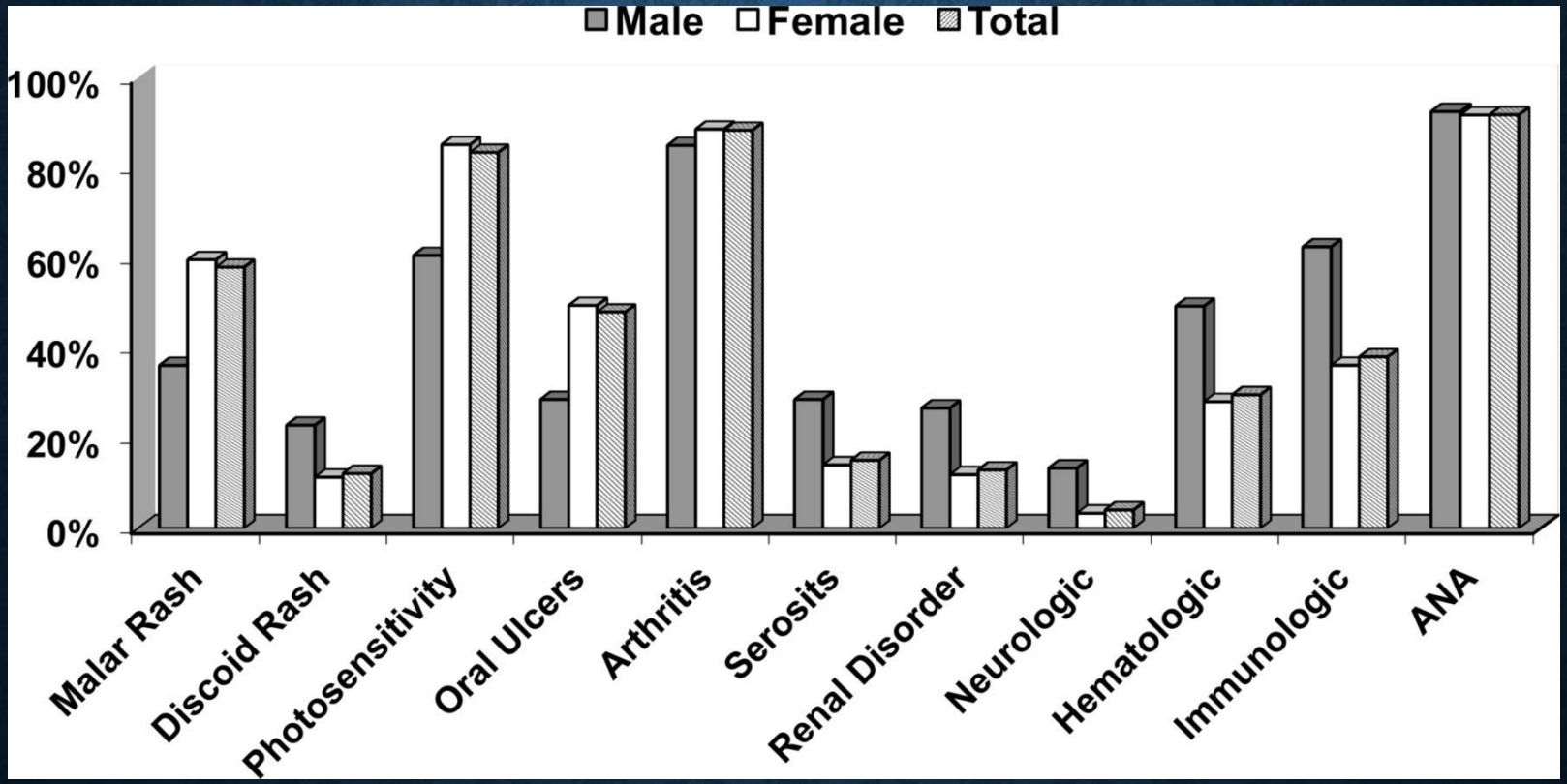
Munroe ME, et al., Ann Rheum Dis. 2016; 75 (11): 2014-2021.

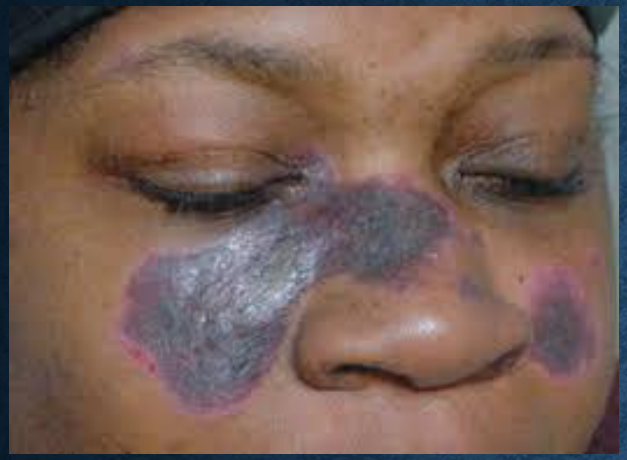


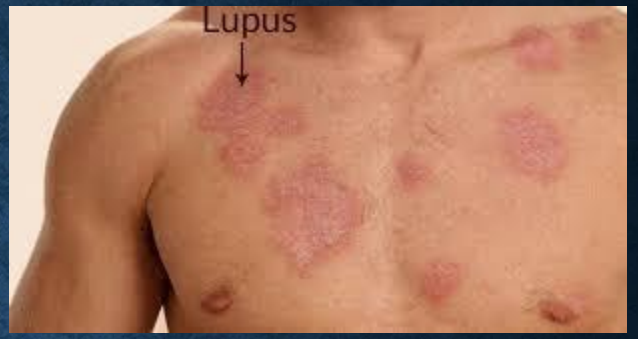
PUBLISHED IN NATURE REVIEWS RHEUMATOLOGY 2016

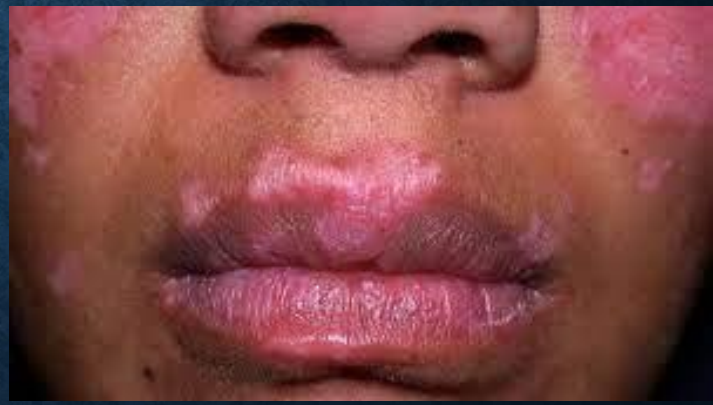
NEW INSIGHTS INTO THE IMMUNOPATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS G. TSOKOS, M. LO, P. C. REIS, K. SULLIVAN

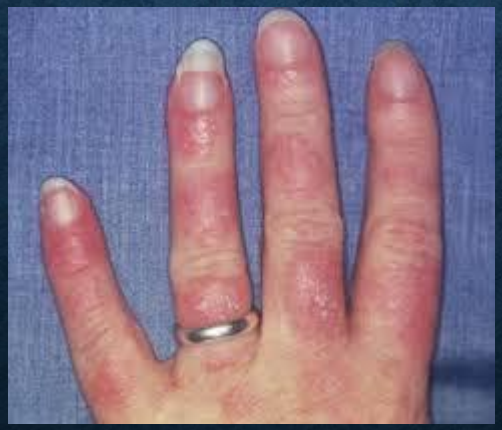
SYMPTOMS OF LUPUS

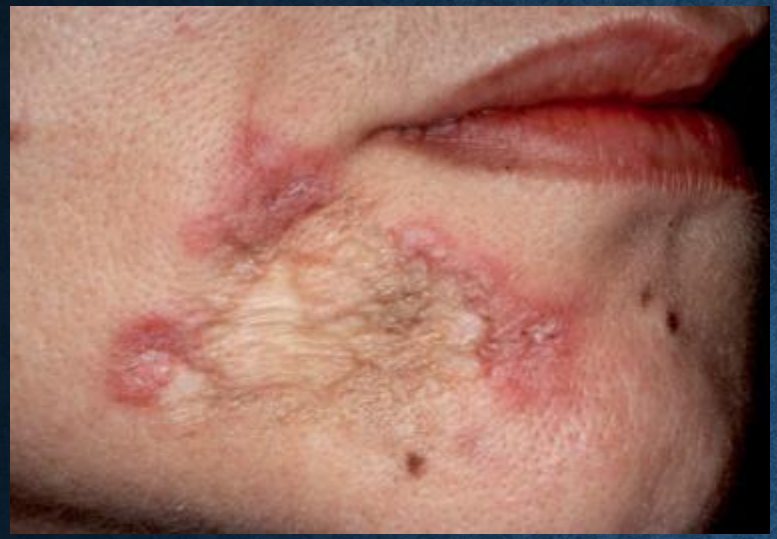


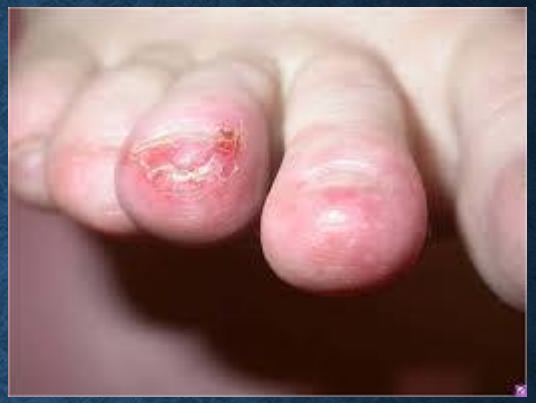


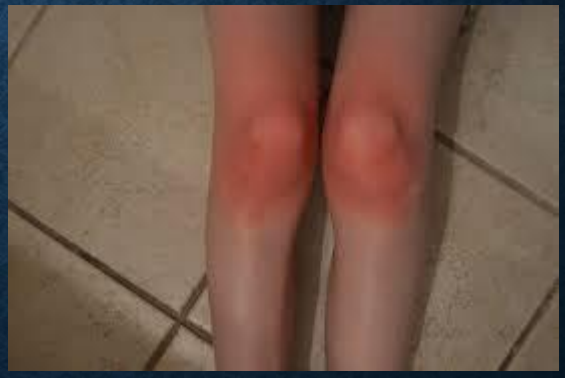

Lupus

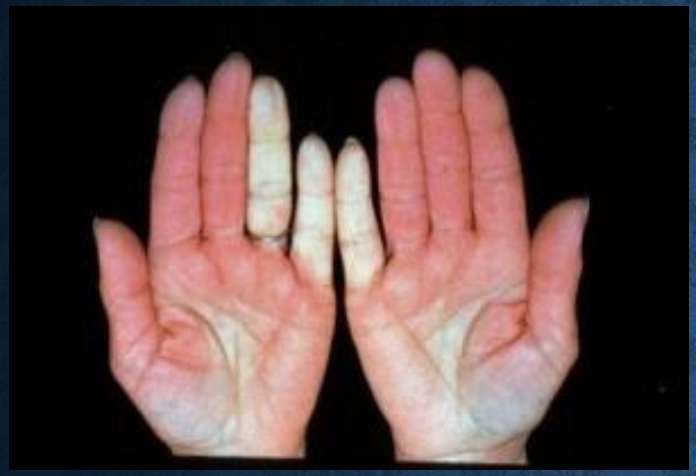


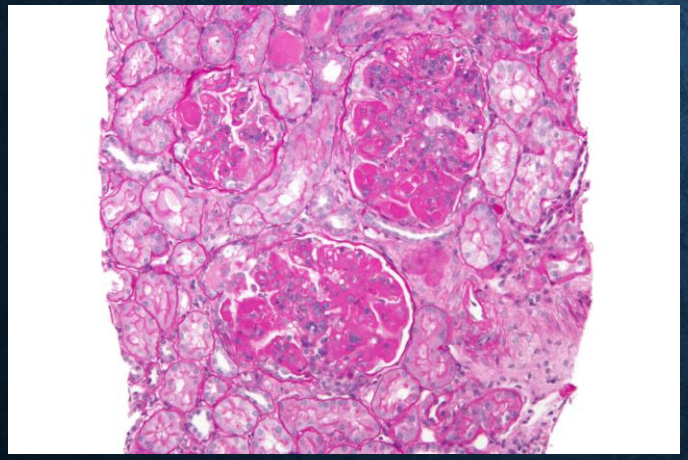


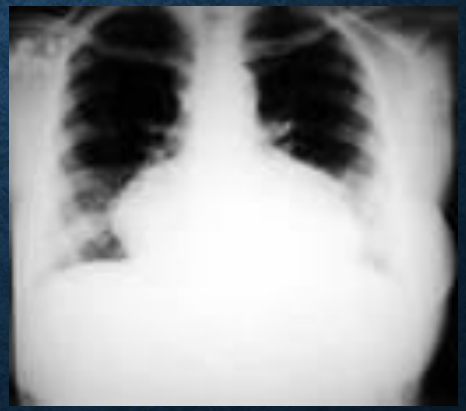












New ACR and EULAR criteria for classification of SLE

All patients classified as having systemic lupus erythematosus must have a serum titer of antinuclear antibody of at least 1:80 on human epithelial-2–positive cells or an equivalent positive test. In addition, a patient must tally at least 10 points from these criteria. A criterion is not counted if it has a more likely explanation than SLE. Occurrence of the criterion only once is sufficient to tally the relevant points, and the time when a patient is positive for one criterion need not overlap with the time when the patient is positive for other criteria. SLE classification requires points from at least one clinical domain, and if a patient is positive for more than one criterion in a domain only the criterion with the highest point value counts:

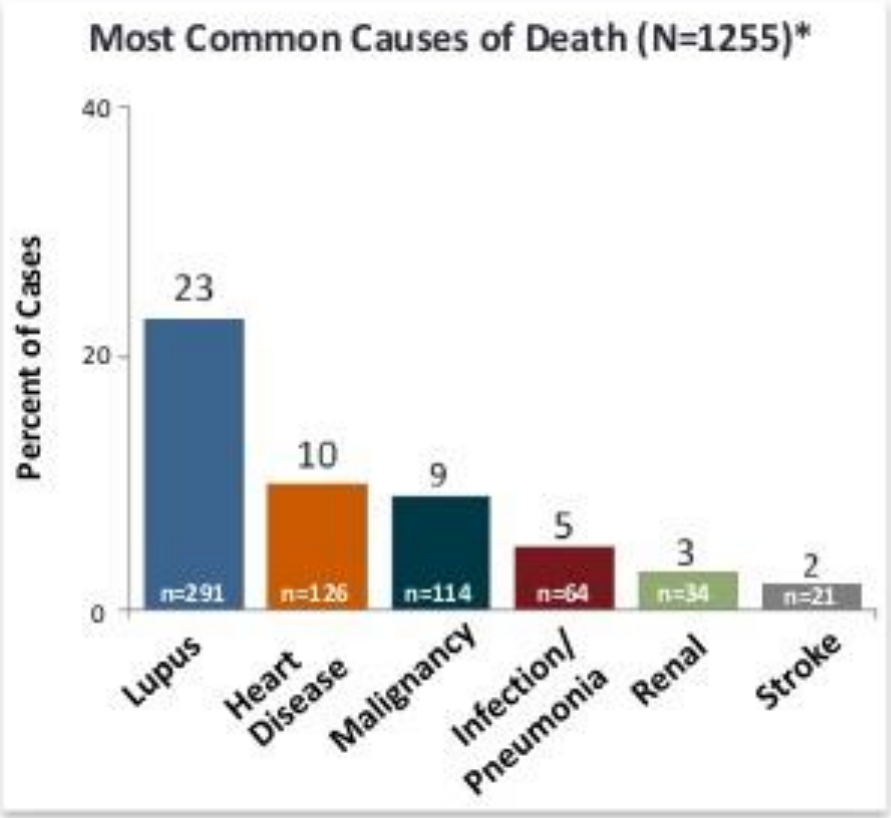
Clinical domains	Points
Constitutional domain	
Fever	2
Cutaneous domain	
Nonscarring alopecia	2
Oral ulcers	2
Subacute cutaneous or discoid lupus	4
Acute cutaneous lupus	6
Arthritis domain	
Synovitis in at least two joints or tenderness in at least two joints, and at least 30 min of morning stiffness	6
Neurologic domain	
Delirium	2
Psychosis	3
Seizure	5
Serositis domain	
Pleural or pericardial effusion	5
Acute pericarditis	6
Hematologic domain	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Renal domain	
Proteinuria >0.5g/24 hr	4
Class II or V lupus nephritis	8
Class III or IV lupus nephritis	10

Immunologic domains	Points
Antiphospholipid antibody domain	
Anticardiolipin IgG >40 GPL or anti-β2GP1 IgG >40 units or lupus anticoagulant	2
Complement proteins domain	
Low C3 or low C4	3
Low C3 and low C4	4
Highly specific antibodies domain	
Anti-dsDNA antibody	6
Anti-Smith antibody	6

Source: Dr. Johnson

Cardiovascular Events, Malignancies, and Infections Are Among the Most Common Causes of Death in SLE

- A range of organ systems are implicated in SLE mortality
  - Mortality data from 9547 patients followed 1958-2001; total of 1255 deaths occurred
  - Patients followed for 76,948 person-years
- Mortality rates were significantly higher for some of the most common causes of death than those seen in the general population
  - ~8x higher for renal causes
  - ~5x higher for infections
  - Almost 2x higher for heart disease



*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 (e.g., cardiovascular disease or infection), but the patient's preexisting diagnosis of SLE may have led to this being listed as the cause of death

Bernatsky S, et al. *Arthritis Rheum*. 2006;54:2550-2557.

COMPLICATIONS OF LUPUS.

- Cardiovascular disease.
- Malignancy.
- Infections.
- Renal Failure.
- Vasculitis.
- Drug Effects – cancer, avascular necrosis, osteoporosis.
- Pregnancy related – Hypertension, Lupus flare, kidney disease, fetal loss.

TREATMENT OF LUPUS

PREVENTION

Careful and frequent medical evaluation.

Anti-inflammatory diet.

Avoid direct exposure to sunlight, Echinacea, drugs – Hydralazine, Sulfa, TNF inhibitors.

Use a sunscreen with at least SPF 30.

Use of anti-oxidants – Vitamin E, Fish Oil, Flaxseed, Vitamin D.

Avoid smoking.

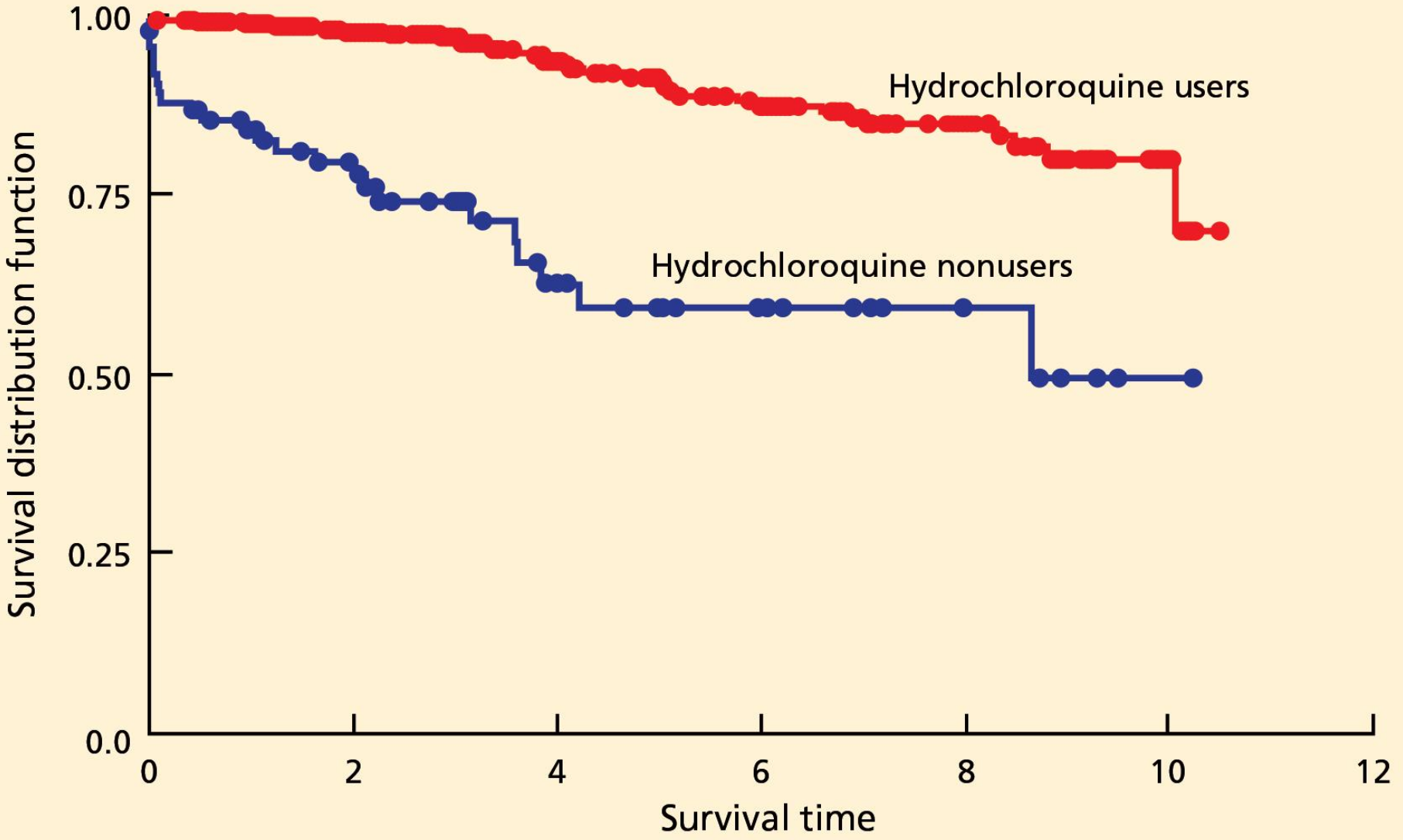
Screening with SS-A antibody in pregnancy.

Early pre-natal care.

Lupus Treatment Options

NSAIDs Ibuprofen, naproxen, & Diclofenac	Tablet
Antimalarials Hydroxychloroquine, Chloroquine, & Quinacrine	Tablet
Corticosteroids Methylprednisolone & Prednisone	Tablet
Biologics Rituximab & Belimumab	IV Infusion
Immunosuppressants Azathioprine, Methotrexate, Mycophenolate, Mofetil, & Cyclophosphamide	Tablet

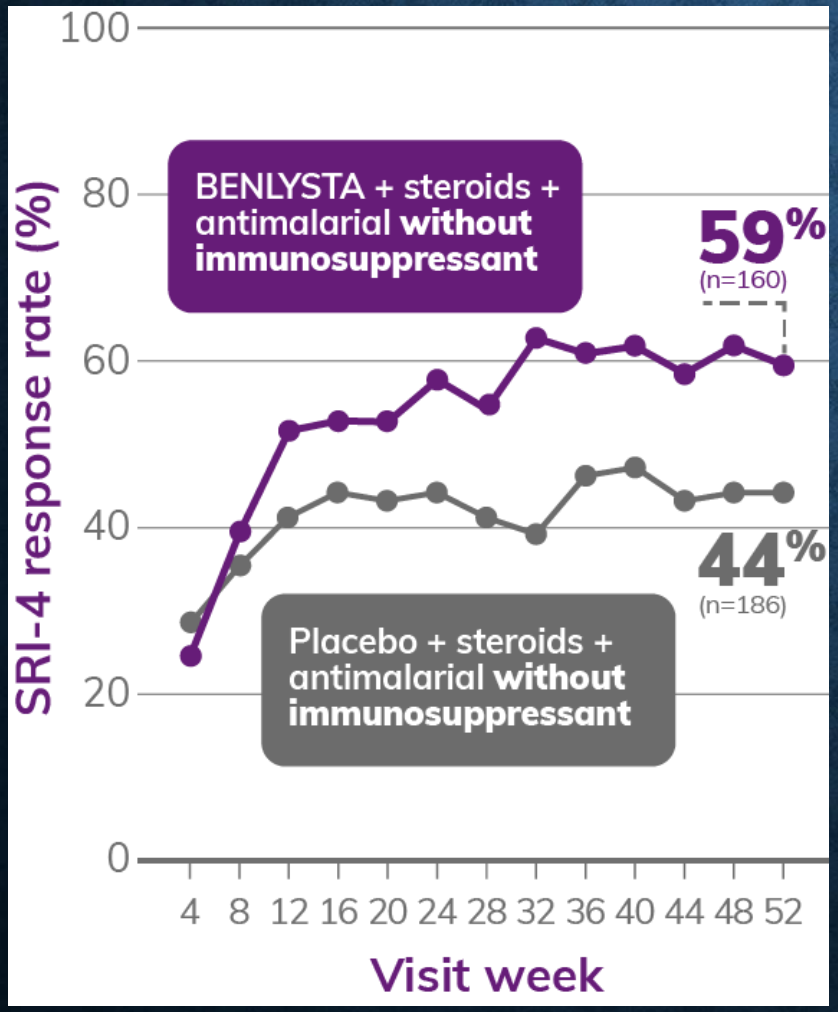
An antimalarial drug increases survival in patients with lupus



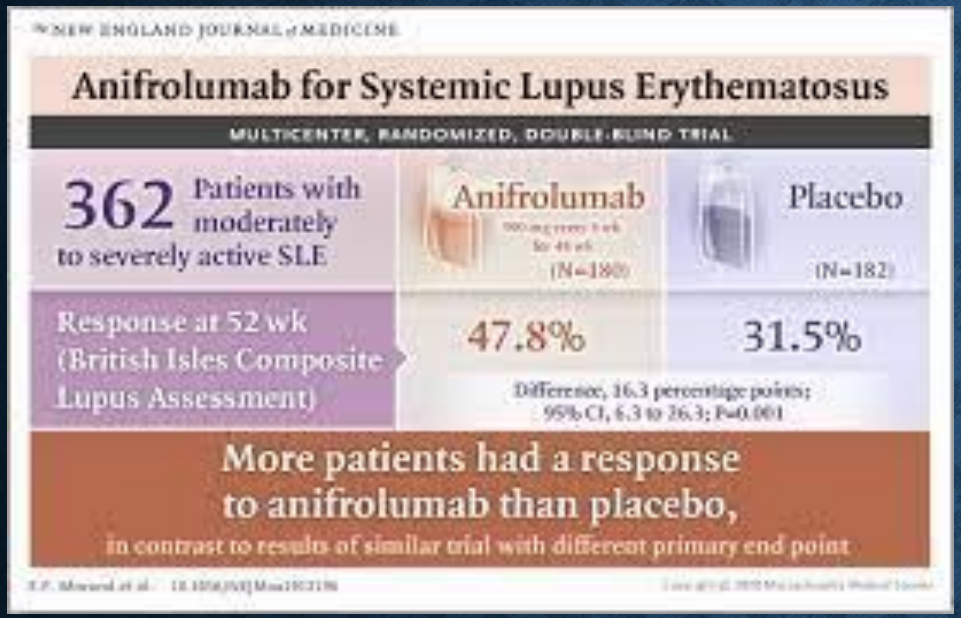
DRAWN FROM DATA FROM ALARCÓN GS, MCGWIN G, BERTOLI AM, ET AL; LUMINA STUDY GROUP. EFFECT OF HYDROXYCHLOROQUINE ON THE SURVIVAL OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM LUMINA, A MULTIETHNIC US COHORT (LUMINA L). ANN RHEUM DIS 2007; 66:1168–1172.

Benlysta (belimumab)

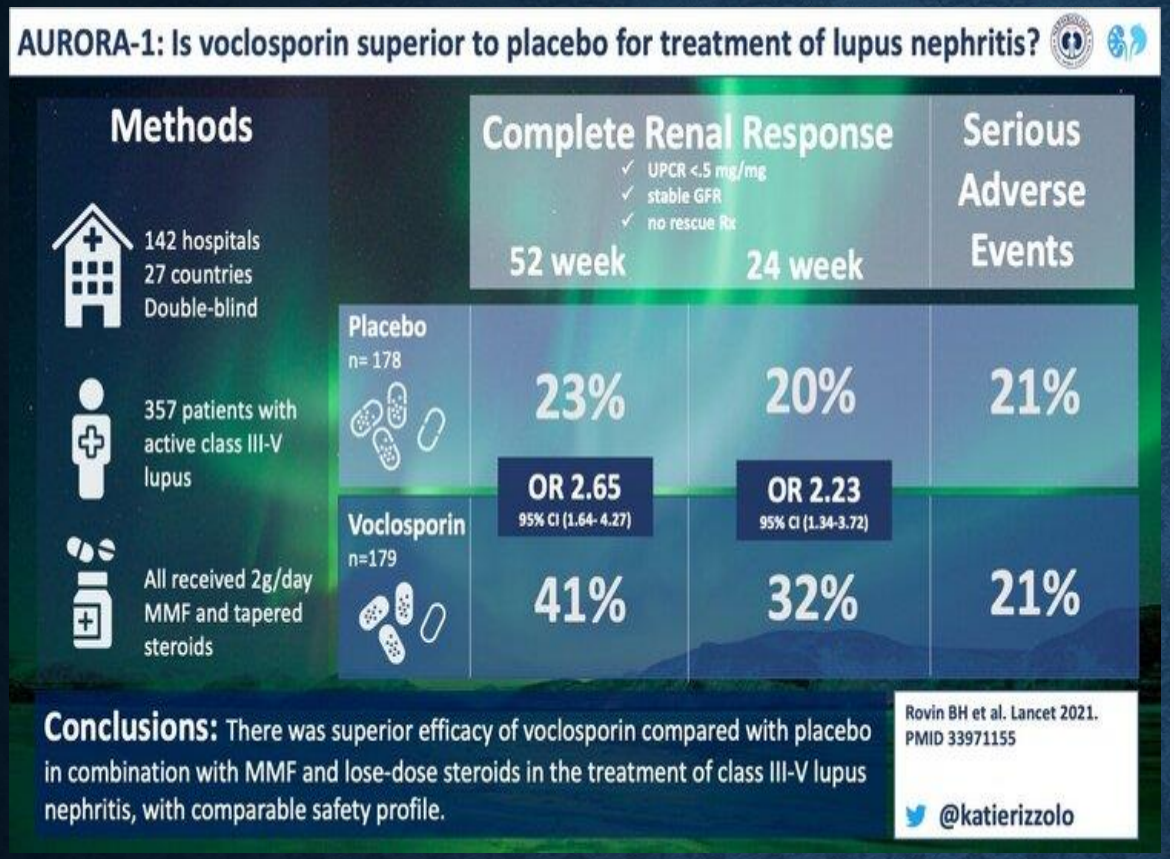
Intravenous Use 120 mg/vial
Subcutaneous Use 200 mg/mL



Adverse Event	BENLYSTA 10 mg/kg (n=674)	Placebo (n=675)
Nausea	**15%**	12%
Diarrhea	**12%**	9%
Pyrexia	**10%**	8%
Nasopharyngitis	**9%**	7%
Bronchitis	**9%**	5%
Insomnia	**7%**	5%
Pain in extremity	**6%**	4%
Depression	**5%**	4%
Migraine	**5%**	4%
Pharyngitis	**5%**	3%
Cystitis	**4%**	3%
Leukopenia	**4%**	2%
Gastroenteritis viral	**3%**	1%



ADVERSE REACTION	SAPHNELO + ST (N=459),%	PLACEBO + ST (N=466),%
Upper respiratory tract infection†	34	23
Bronchitis‡	11	5.2
Infusion-related reactions§	9.4	7.1
Herpes zoster	6.1	1.3
Cough	5.0	3.2
Respiratory tract infection‖	3.3	1.5
Hypersensitivity	2.8	0.6



	Voclosporin group (n=178)	Placebo group (n=178)
Adverse event summary		
Adverse event	162 (91%)	158 (89%)
Serious adverse event	37 (21%)	38 (21%)
Serious adverse event of infections and infestations	18 (10%)	20 (11%)
Treatment-related serious adverse event	8 (4%)	8 (4%)
Adverse event leading to study drug discontinuation	20 (11%)	26 (15%)
Death*	1 (<1%)	5 (3%)
Treatment-related adverse event leading to death	0	0
Adverse events (reported ≥4% of patients)		
Infections and infestations	115 (65%)	101 (57%)
Gastrointestinal disorders	83 (47%)	61 (34%)
Investigations and infestations	60 (34%)	31 (17%)
Nervous system disorders	47 (26%)	27 (15%)
Skin and subcutaneous tissue disorders	42 (24%)	31 (17%)
Musculoskeletal and connective tissue disorders	40 (22%)	46 (26%)
Vascular disorders	38 (21%)	23 (13%)
General disorders and administration site conditions	36 (20%)	32 (18%)
Blood and lymphatic system disorders	35 (20%)	29 (16%)
Respiratory, thoracic, and mediastinal disorders	26 (15%)	17 (10%)
Renal and urinary disorders	26 (15%)	37 (21%)
Metabolism and nutritional disorders	25 (14%)	37 (21%)

Adverse events are defined as an adverse event that occurs on or after the day of the first dose and up to 30 days after the last dose of voclosporin or placebo, with the exception of death. *Includes two deaths in placebo group and one death in voclosporin group that occurred >30 days after discontinuation of study drug.

Table 3: Adverse events (safety population)

Table 5. Follow-Up and Monitoring for Selected Complications of SLE

Complication	*Frequency of follow-up*	*Prevention, monitoring, and management*
None; mild, stable SLE[8]	Every three to six months	History for features of SLE, physical examination, CBC, creatinine level, urinalysis, anti-dsDNA, complements; keep all health maintenance screenings and vaccinations up to date
Cardiovascular abnormalities[49,57]	Every visit	Optimal lupus control with minimal glucocorticoid use; judicious use of antimalarial and other immunosuppressive agents; smoking cessation, adequate exercise, low-cholesterol diet, lipid-lowering therapy, blood pressure control, screening for diabetes mellitus
Infection[8,57]	Every visit	Assure that vaccinations are up to date; judicious use of immunosuppressive agents
Malignancy[57,58]	Yearly	Assure that routine cancer screenings are up to date; screen for high-risk cancers (e.g., hematologic, non-Hodgkin lymphoma, lung, cervical)
Moderate to severe SLE with complications[8]	Frequent	Monitor in conjunction with rheumatologist and lupus care subspecialists
New-onset nephritis[8,27]	Monthly or more frequently	Urinalysis, 24-hour urinary protein level, creatinine clearance, CBC, levels of cholesterol, calcium, phosphorus, alkaline phosphatase, sodium, and potassium; useful to assess complements and anti-dsDNA
Receiving high-dose glucocorticoids[8,57]	Every visit	Consider steroid-sparing agent; use lowest dose possible to achieve optimum disease control; glucose testing every three to six months; cholesterol testing annually; DEXA every one to two years; maintain high index of suspicion for avascular necrosis if patient has acute joint pain
Receiving hydroxychloroquine (Plaquenil)[8,36]	Every six to 12 months	Ophthalmologic examination to screen for retinal toxicity; keep dosage to no more than 6.5 mg per kg per day
Receiving immunosuppressive or cytotoxic agents[8]	Every one to two weeks initially, then every one to three months	CBC and liver function testing at baseline, then every one to two weeks at initiation of therapy, then one to three months; judicious use of immunosuppressive medications, vigilance for signs and symptoms of infection; routine cancer screening; avoidance of live vaccines; if live vaccines are needed, administer one month after therapy completion
Receiving low-dose glucocorticoids[8]	Every visit to every one to two years	Keep dosage as low as possible; healthy diet with adequate physical activity; smoking cessation; annual cholesterol and glucose testing; consider DEXA every one to two years for patients receiving long-term therapy
Renal abnormalities[8,27,54]	Every three months or more frequently, depending on disease state	Regular screening for proteinuria and hematuria; regular serum creatinine level; for patients with chronic kidney disease, vaccination with 13-valent pneumococcal conjugate vaccine (Prevnar) or 23-valent pneumococcal polysaccharide vaccine (Pneumovax), as indicated
Severe hemolytic anemia[8]	Weekly	Hematocrit and reticulocyte count; may require transfusion
Severe thrombocytopenia (< 50,000 cells per mm^3)[8]	Weekly	Platelet count weekly initially; may require transfusion

Anti-dsDNA = anti–double-stranded DNA antibodies; CBC = complete blood count; DEXA = dual energy x-ray absorptiometry; SLE = systemic lupus erythematosus.

Information from references 8, 27, 36, 49, 54, 57, and 58.

SUMMARY

- Lupus is an autoimmune disease affecting multiple organ systems and may co-exist with other autoimmune diseases.
- African American and Hispanic women tend to develop lupus at a younger age, experience more serious complications, and have higher mortality rates.
- Multiple factors contribute to disease expression including genetic and environmental.
- Common symptoms include polyarthritis and cutaneous manifestations.
- Treatment is multi-dimensional including lifestyle and pharmacologic options.
- Monitoring of Lupus patients require a comprehensive approach addressing disease, complications and medications.