



Standardizing Care in the Lupus Patient: Toward Treat to Target

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Instructor Disclosures

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I have these relevant financial relationships to disclose:

	<u>Company</u>	<u>Nature of Relationship</u>
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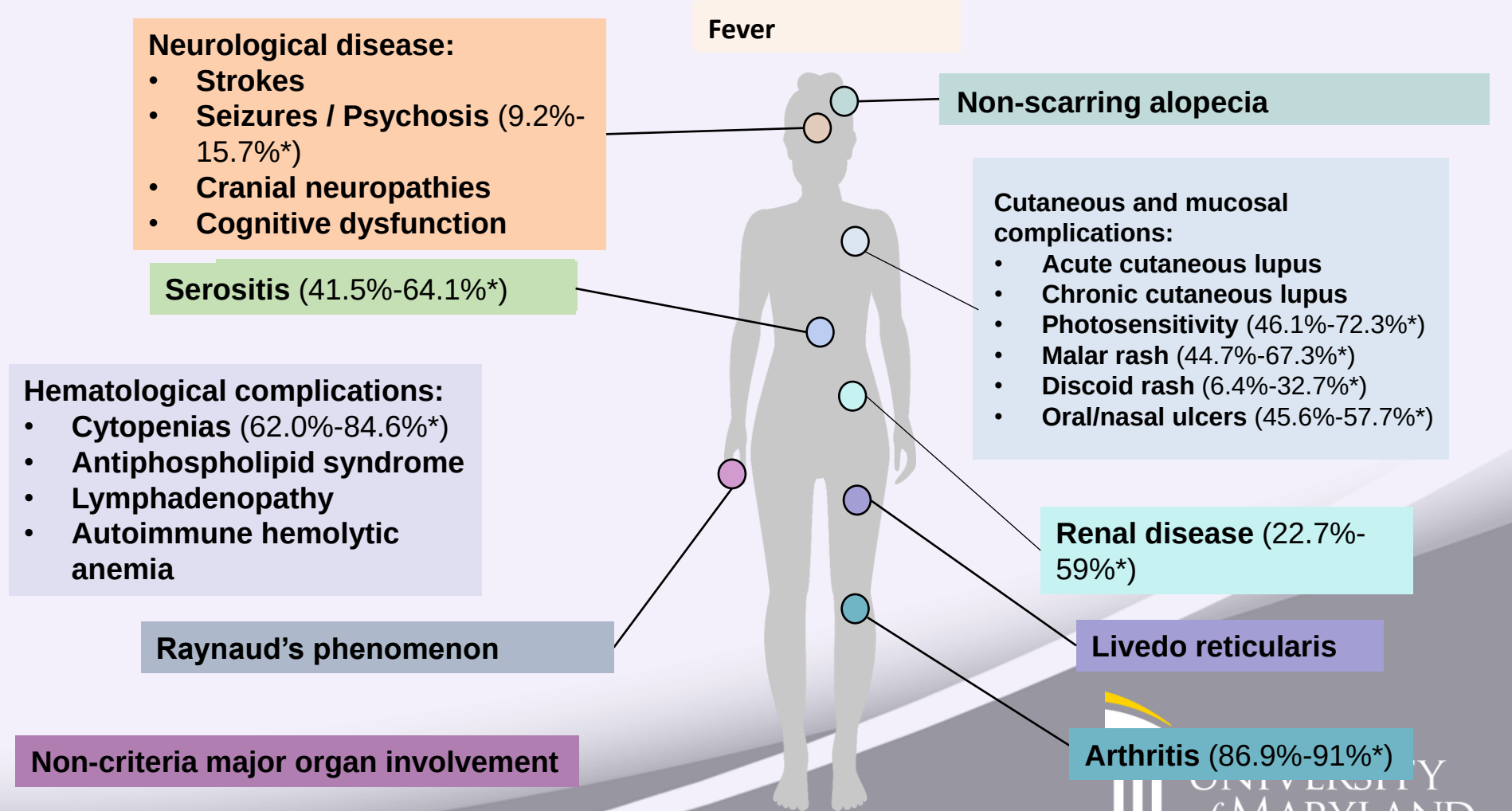
Lupus Research Alliance CDA

Activity Goals

- Discuss the aims of treat to target in SLE
- Explain the need to reduce chronic glucocorticoid use in SLE
- Identify treatment strategies to facilitate treat to target

Lupus Overview: SLE as a Multiorgan System Disease

- Heterogeneous, multi-organ system autoimmune disorder
- Characterized by
 - Production of autoantibodies
 - Immune Complex Deposition



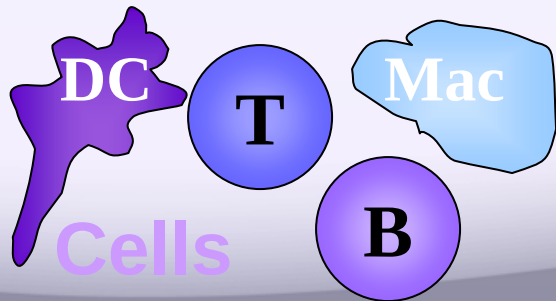
The Nature of Lupus

Clinical Expression is Diverse/ Severity Variable:
330 patients can have 4 different ACR criteria

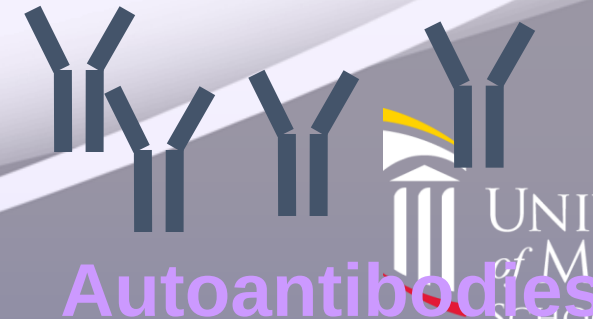
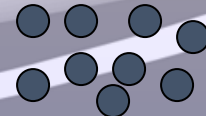
Serositis	Skin	Nephritis	Cytopenias
Arthritis	Central Nervous System		

Therefore.....

Multiple Components in the Innate and Acquired Immune System are Likely to be Candidates:



Cytokines



SLE Disease Activity Comes and Goes but Organ Damage Is Forever



Asymptomatic phase

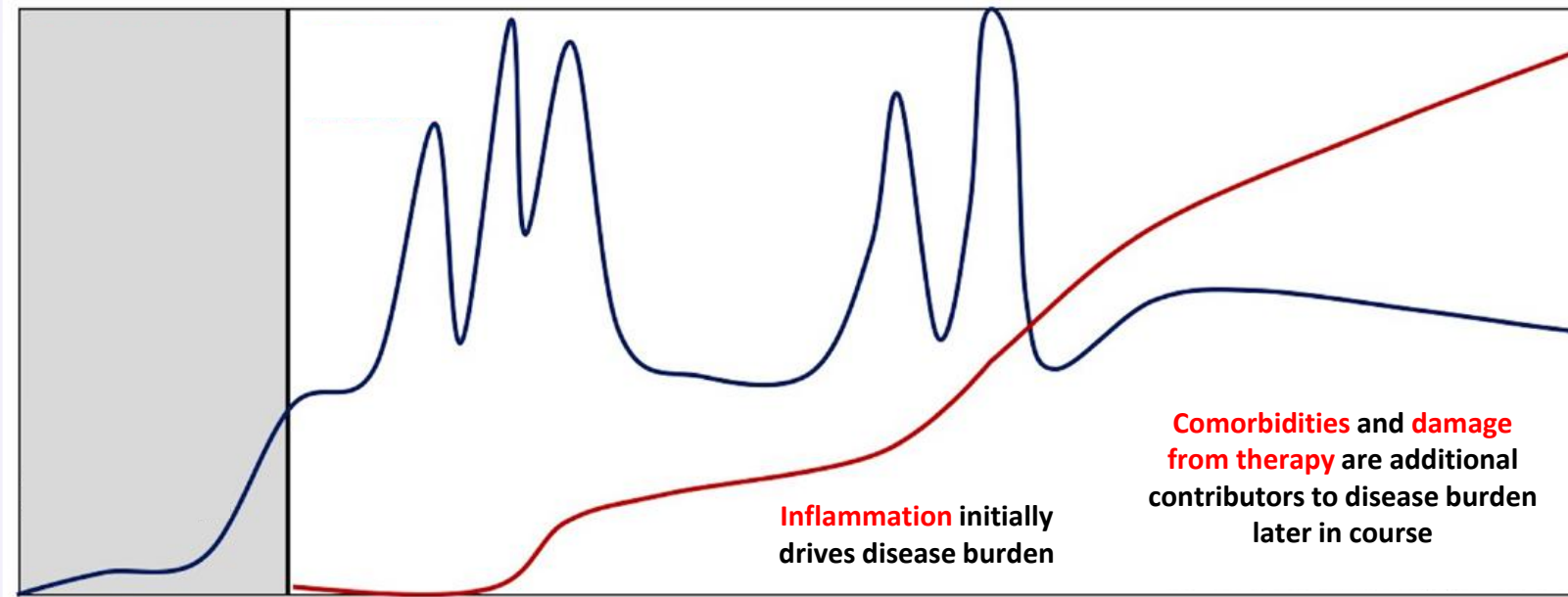
*Accrual of
auto-antibodies*

Symptomatic Phase

*Periods of variable disease activity
resulting in inflammation-driven irreversible damage*

Organ Damage

Inflammation



Inflammation initially
drives disease burden

**Comorbidities and damage
from therapy** are additional
contributors to disease burden
later in course

Time

Safe and effective therapy targeting low disease activity or remission has potential to decrease the frequency of and severity of flares and resulting damage

SLICC/ACR Damage Index (SDI)

Organ system ¹	Item ^{1,2}	Score ^{1,2}
Ocular	Any cataract ever	1
	Retinal change or optic atrophy	1
Neuropsychiatric	Cognitive impairment ^a or major psychosis	1
	Seizures requiring therapy for 6 months	1
	Cerebral vascular accident ever (score 2 >1), resection not for malignancy	1(2) ^b
	Cranial or peripheral neuropathy (excluding optic)	1
	Transverse myelitis	1
Renal	Estimated or measured GFR <50%	1
	Proteinuria ≥3.5 g/24 hrs	1
	ESRD (regardless of dialysis or transplantation)	3
CV	Angina or coronary artery bypass	1
	Myocardial infarction ever (score 2 if >1)	1(2) ^b
	Cardiomyopathy (ventricular dysfunction)	1
	Valvular disease (diastolic, murmur, or systolic murmur >3/6)	1
	Pericarditis for 6 months, or pericardiectomy	1

Organ system ¹	Item ^{1,2}	Score ^{1,2}
Peripheral vascular	Claudication for 6 months	1
	Minor tissue loss (pulp space)	1
	Significant tissue loss ever (eg, loss of digit or limb (score 2 if >1 site)	1(2) ^b
	Venous thrombosis with swelling, ulceration, or venous stasis	1
Gastro-intestinal	Infarction or resection of bowel (below duodenum), spleen, liver or gall bladder ever (score 2 if >1 site)	1(2) ^b
	Mesenteric insufficiency	1
	Chronic peritonitis	1
	Stricture or upper gastrointestinal tract surgery ever	1
	Pancreatic insufficiency requiring enzyme replacement or with pseudocyst ²	1
Pulmonary	Pulmonary hypertension (right ventricular prominence, or loud P2)	1
	Pulmonary fibrosis (physical and X-ray)	1
	Shrinking lung (X-ray)	1
	Pleural fibrosis (X-ray)	1
	Pulmonary infarction (X-ray) or resection not for malignancy ²	1

Organ system ¹	Item ^{1,2}	Score ^{1,2}
Musculo-skeletal	Muscle atrophy or weakness	1
	Deforming or erosive arthritis (including reducible deformities, excluding avascular necrosis)	1
	Osteoporosis with fracture or vertebral collapse (excluding avascular necrosis)	1
	Avascular necrosis (score 2 if > 1)	1(2) ^b
	Osteomyelitis	1
	Ruptured tendons ²	1
Skin	Alopecia	1
	Extensive scarring or panniculum other than scalp and pulp space	1
	Skin ulceration (excluding thrombosis) for >6 months	1
Others	Premature gonadal failure	1
	Diabetes (regardless of treatment)	1
	Malignancy (exclude dysplasia) (score 2 if >1 site)	1(2) ^b

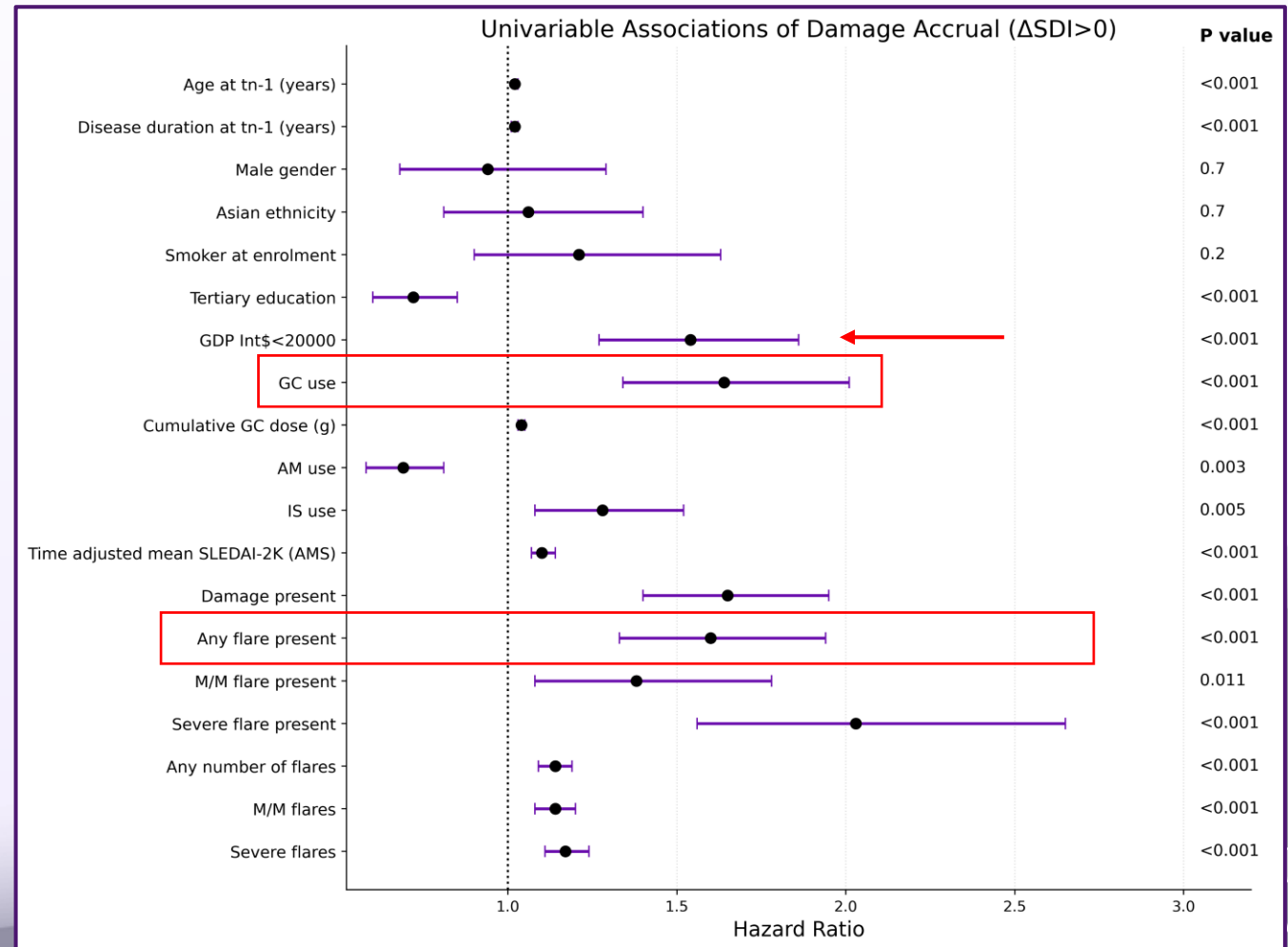
^aMemory deficit, difficulty with calculation, poor concentration, difficulty in spoken or written language, impaired performance level. ^bRepeat episodes must occur at least 6 months apart to score 2.

ACR = American College of Rheumatology; CV = cardiovascular; ESRD = end-stage renal disease; GFR = glomerular filtration rate; SLICC = Systemic Lupus International Collaborating Clinics.

1. Gladman D, et al. Arthritis Rheum. 1996;39(3):363-369. 2. Gladman D, et al. Arthritis Rheum. 1997;40:809-813.

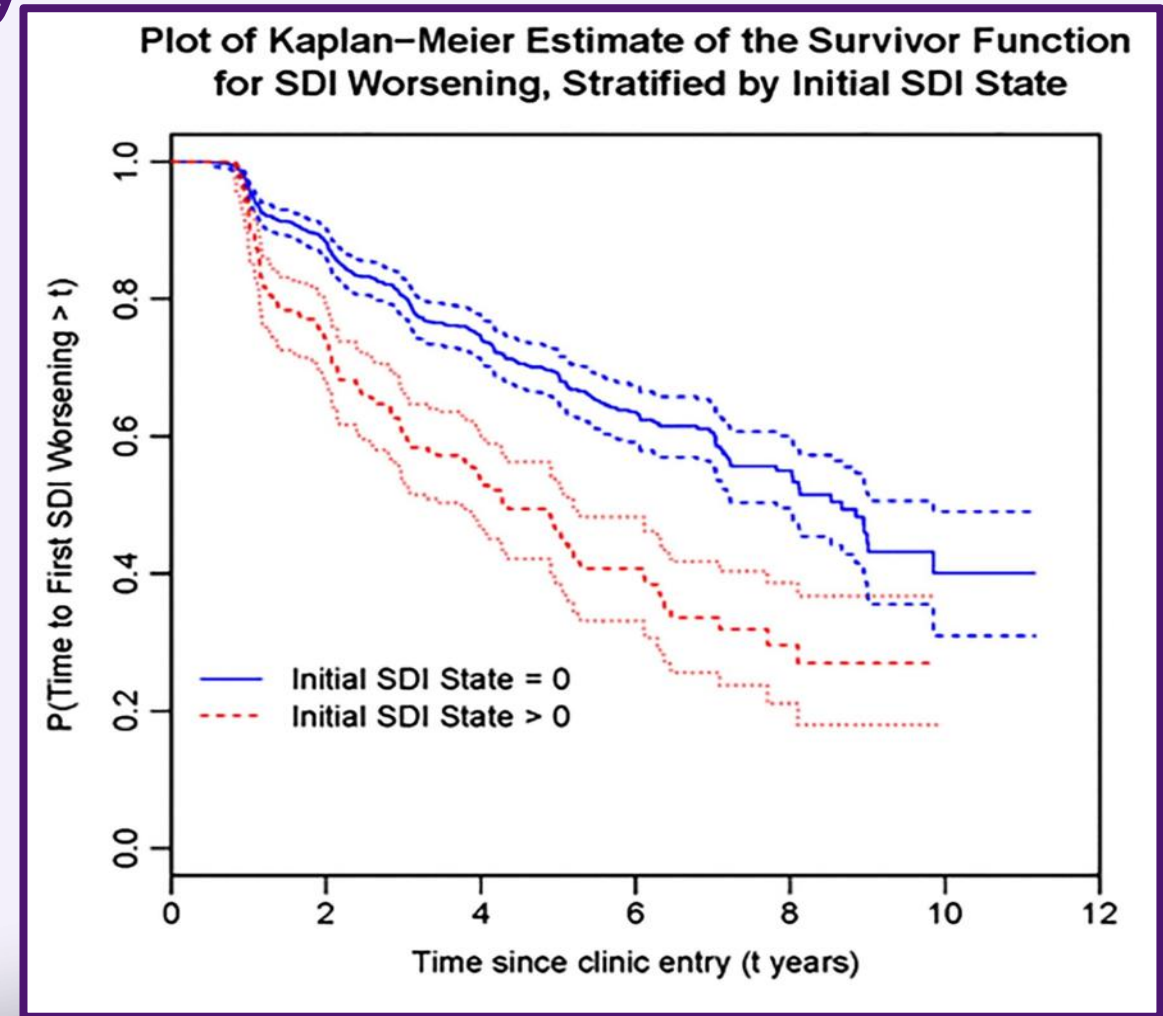
In SLE Permanent Organ Damage Results Both from Disease Activity and Glucocorticoids

- 1556 participants enrolled in the Asia Pacific Lupus Collaboration
- Incidence of damage was 58/1000 person years
- In the multivariable analysis, damage associated with
 - Any flare present
 - Cumulative glucocorticoid dose
 - GDP per capita <\$20,000 international dollars

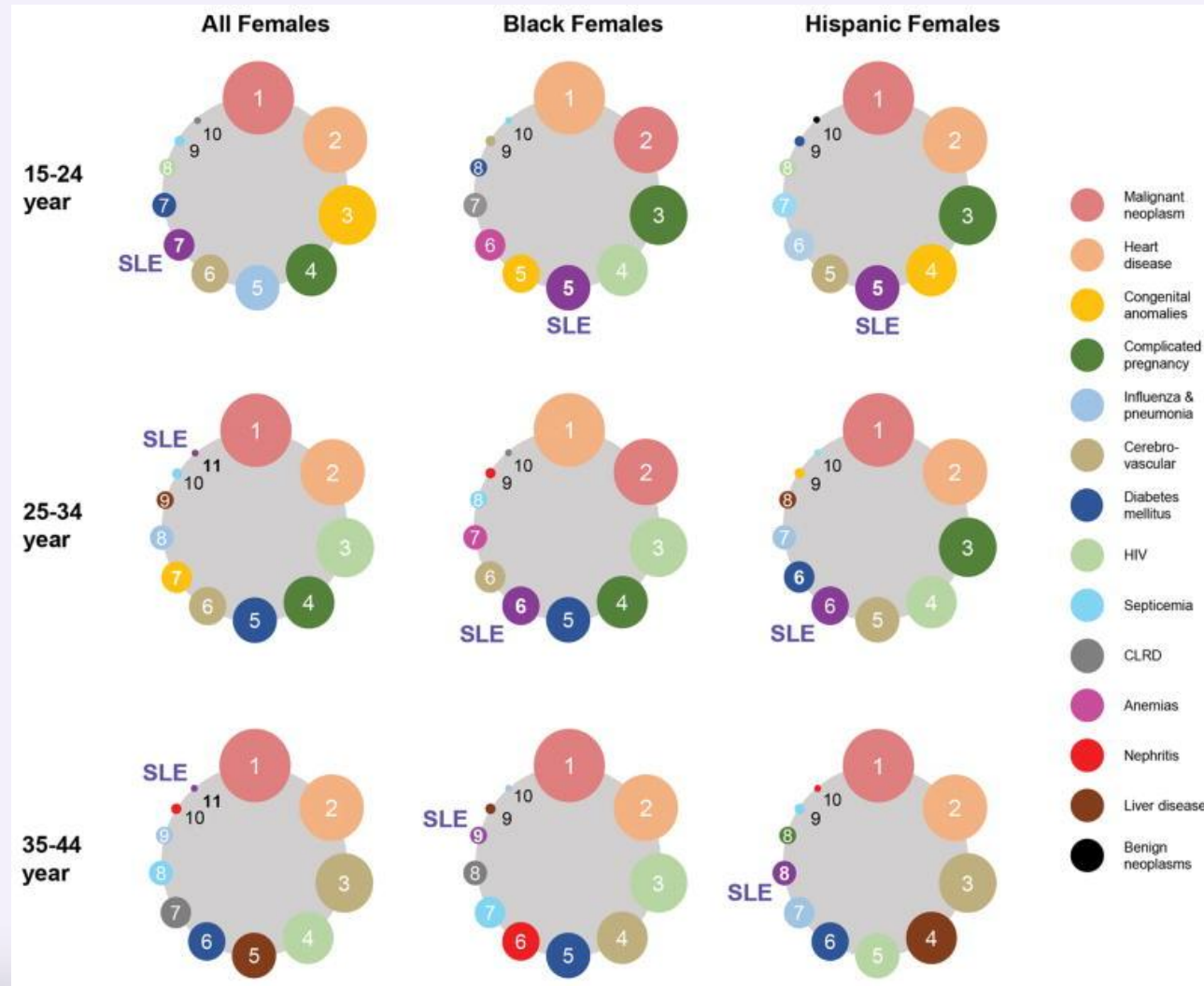


Damage Accrual is Self-Perpetuating and Associates with Mortality

- A “non-zero” Damage index is independently associated with all cause mortality in SLE (Chambers, Allen et al. 2009)
- Renal, neuropsychiatric (including CVA), and cardiovascular outcomes are the most important predictors of mortality (Danila, Pons-Estel et al. 2009)
- The more damage you get, the more damage you get (Bruce, O’Keeffe et al. 2015)

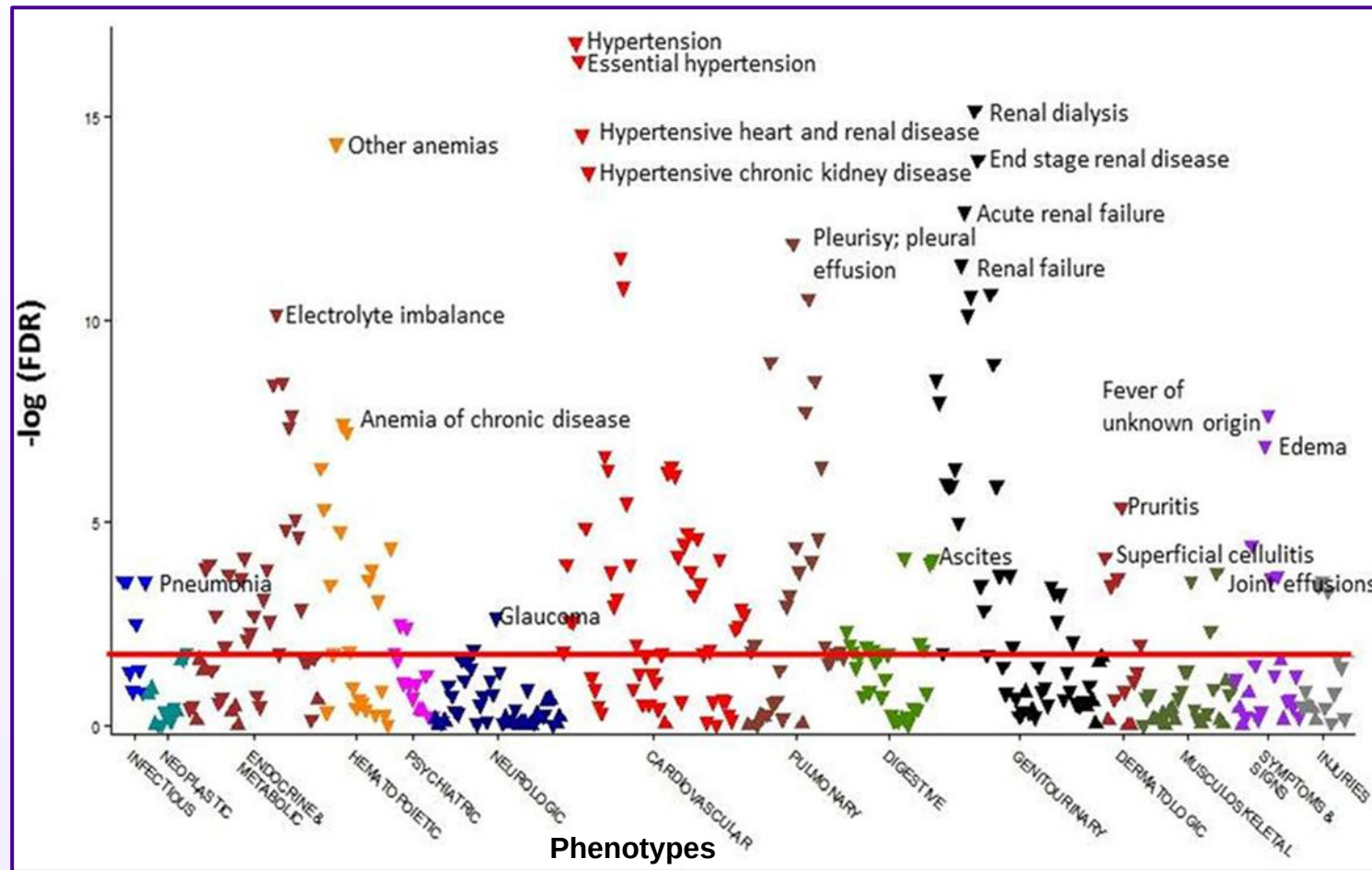


SLE is a Major Cause of Morbidity and Mortality Especially in Minority Women



Leading Causes of Deaths for Females of Reproductive Age by Race/Ethnicity and Age

Patients of Black African Descent Exhibit Increased Burden of Comorbidities



	Black African (n=270)	White (n=715)	P Value
Current age $\pm$ SD	44 $\pm$ 17	53 $\pm$ 17	P<0.001
Age at Diagnosis $\pm$ SD	35 $\pm$ 16	43 $\pm$ 17	P<0.001

Shifting From Race-Based to Race-Conscious

Race-based:

- Race = risk factor
- Conceptualized as rooted in biological differences
- Racial groups thought of as inherently diseased, “bad genes”
- Biased

Race-conscious:

- Racism = risk factor
- Conceptualized as a social & power construct
- Effects of structural racism and consequences on health
- Supportive

(Cerdeña, 2020)

Time to SLE Diagnosis is Delayed in Ethnic Minorities

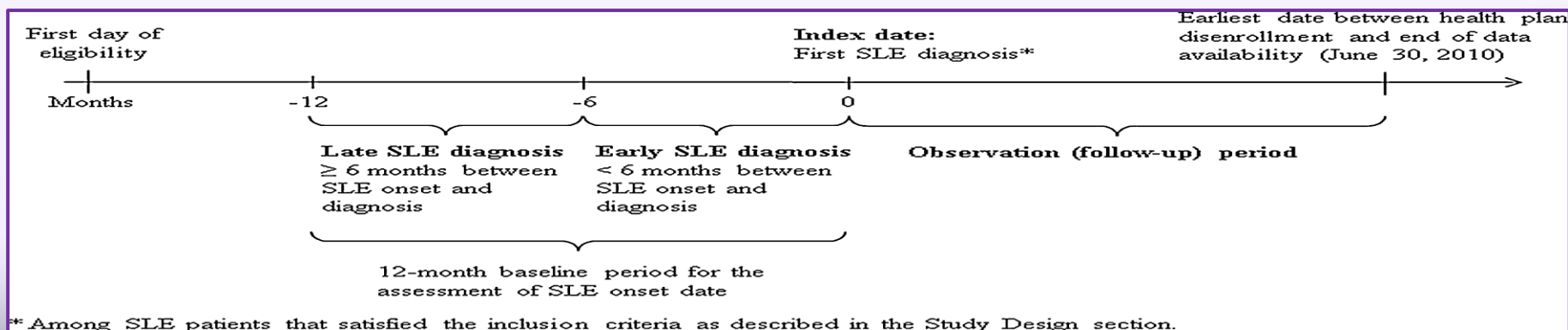


- UCSF CLUES cohort data (196 SLE patients) found that a longer time to SLE diagnosis associated with:
 - African American or Asian race
 - Lower educational attainment
 - Lower socioeconomic status
- Minorities tended to wait over 1 year to receive a diagnosis
- Asian and African American SLE patients were less likely to see a specialist within 3 months (92% of European Americans compared to 64% of AA and 66% of Asian Americans)



SLE Patients Who are Diagnosed Early Experience Fewer Flares

SLE flares	Patients with early	SLE diagnosis (N = 4,166)	Patients with late	SLE diagnosis (N = 4,166)	Rate ratio (95 % CI)	p value
	Number of SLE flares	Incidence rate ^a (per person-year)	Number of SLE flares	Incidence rate ^a (per person-year)		
Any severity	34,136	3.57	37,072	3.75	0.95 (0.94–0.97)	<0.0001
Mild	29,837	3.12	32,615	3.30	0.95 (0.93–0.96)	<0.0001
Moderate	10,316	1.08	11,090	1.12	0.96 (0.94–0.99)	0.0047
Severe	1,677	0.18	1,994	0.20	0.87 (0.82–0.93)	<0.0001



SLE Patients Who are Diagnosed Early Exhibit Fewer Comorbidities

d

Characteristics	Patients with early SLE diagnosis (N = 4,166)	Patients with late SLE diagnosis (N = 4,166)	p value ^a
SLE-related baseline comorbidities excluded from the CCI ^c , n (%)			
Rheumatic disease	2,408 (57.8)	3,500 (84.0)	0.0001
Chronic pulmonary disease	483 (11.6)	681 (16.3)	0.0001
Renal disease	305 (7.3)	411 (9.9)	0.0001
Congestive heart failure	290 (7.0)	386 (9.3)	0.0001
Cerebrovascular disease	233 (5.6)	321 (7.7)	0.0001
Peripheral vascular disease	89 (2.1)	129 (3.1)	0.0060
Acute myocardial infarction	73 (1.8)	94 (2.3)	0.0958
Other SLE-related comorbidities, ^c n (%)			
Hypertension	1,233 (29.6)	1,404 (33.7)	0.0001
Hypothyroidism	560 (13.4)	617 (14.8)	0.0739
Hypercholesterolemia	272 (6.5)	352 (8.4)	0.0009
Osteopenia/osteoporosis	246 (5.9)	586 (14.1)	0.0001

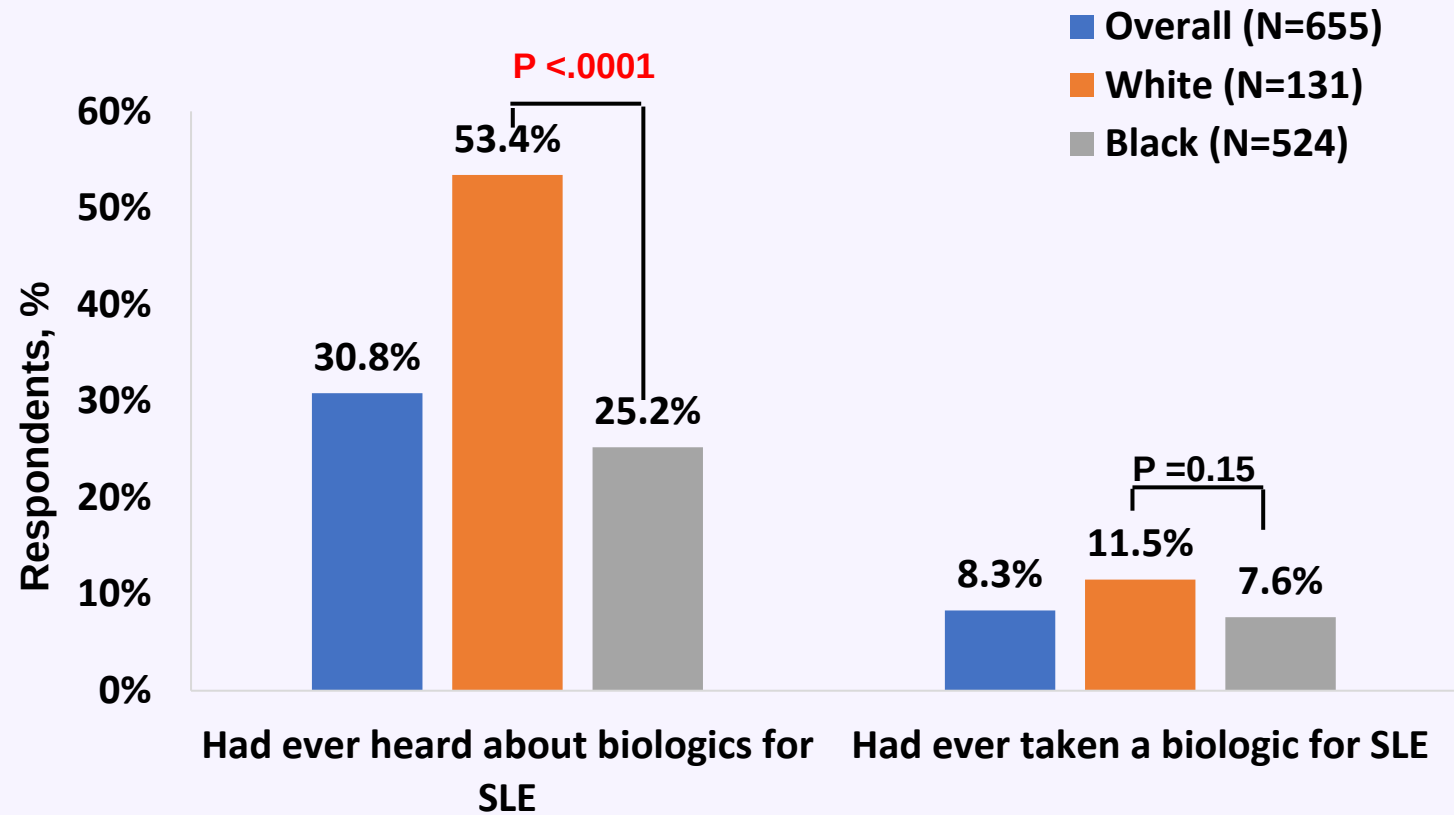
Communicating Treatment Options: SLE Patients of Color are Less Aware of Biologics



SLE disproportionately impacts *women of color*

However, Providers were less likely to Ensure patients of color were aware of all treatment options--including novel biologic therapies.

Cross-sectional Survey of Patients with SLE,
2014-2015

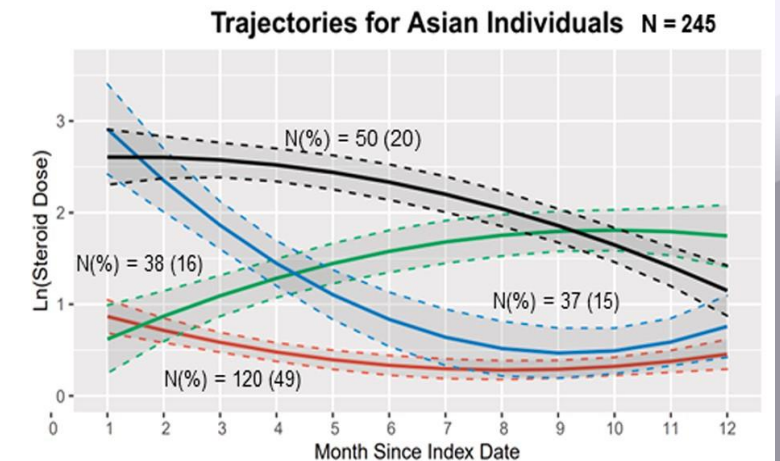
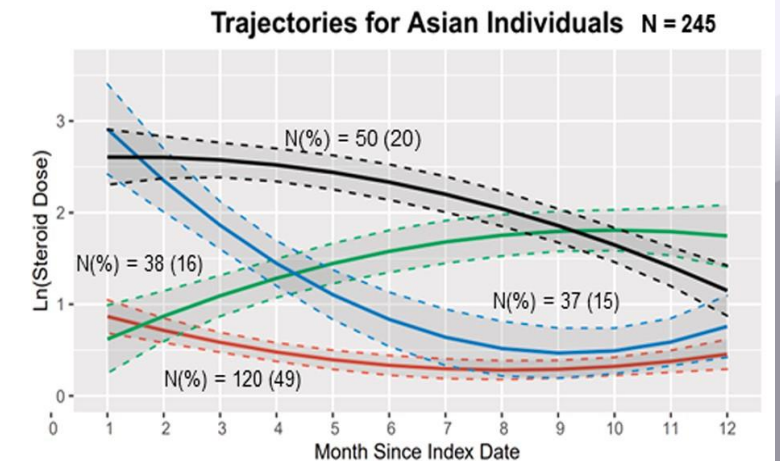
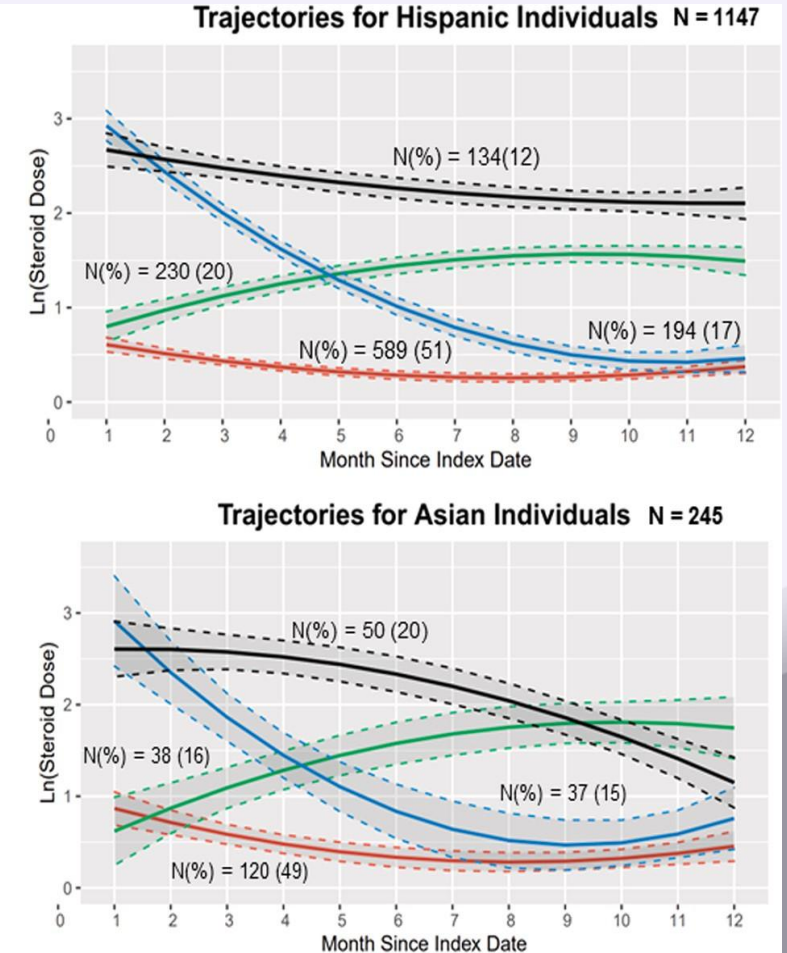
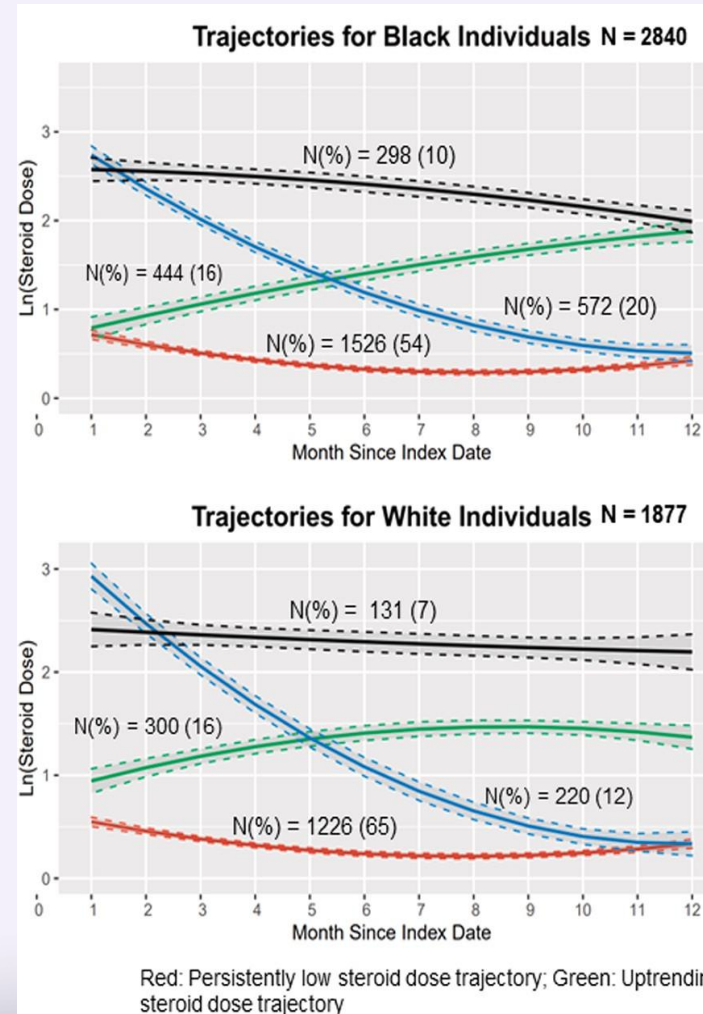


Non-White SLE Patients are More Likely to be Treated with High Dose Glucocorticoids



6,314 Medicaid beneficiaries with ≥ 1 dispensed steroid prescription

- Mean (SD) steroid dose by race:
 - Black: 7 (23) mg/day
 - Hispanic: 7 (26)mg/day
 - Asian 7 (13)mg/day
 - White: 4 (10)mg/day
- Odds of belonging to the highest steroid receiving trajectory compared to white patients:
 - Black: OR 2.07 (95% CI: 1.65-2.61)
 - Hispanic: OR 1.81 (95% CI: 1.38-2.39)
 - Asian OR 2.42 (95% CI: 1.53-3.83)



Complications of SLE are Increased with Even 5mg/day of Glucocorticoids

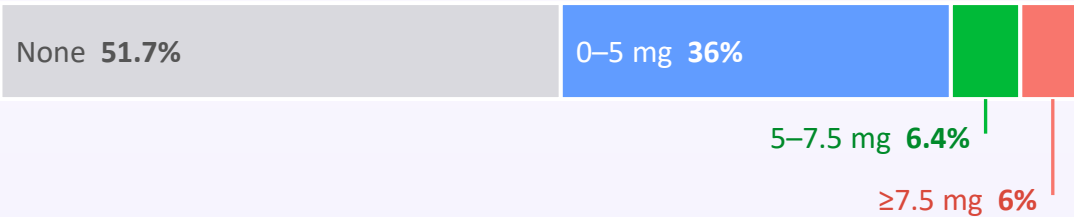
31,852

patients with SLE in the French
national health insurance database
(SNDS)

48.3%

used oral glucocorticoids

Mean daily glucocorticoid dose, all patients



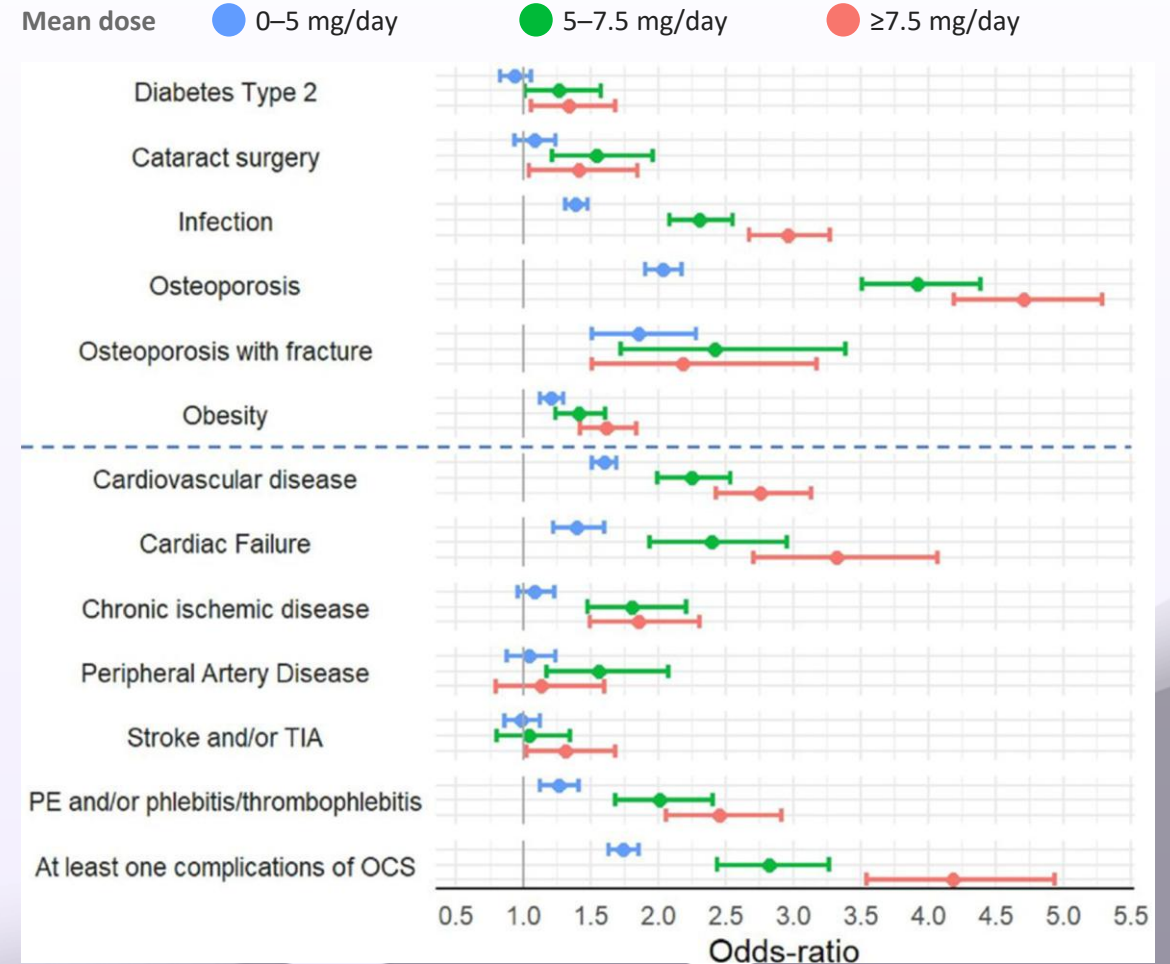
Even 0–5 mg/day

Higher odds of infection, osteoporosis, fracture, cardiovascular disease, heart failure, and venous thrombosis

Odds climb further at each higher dose

Metabolic, bone, infection

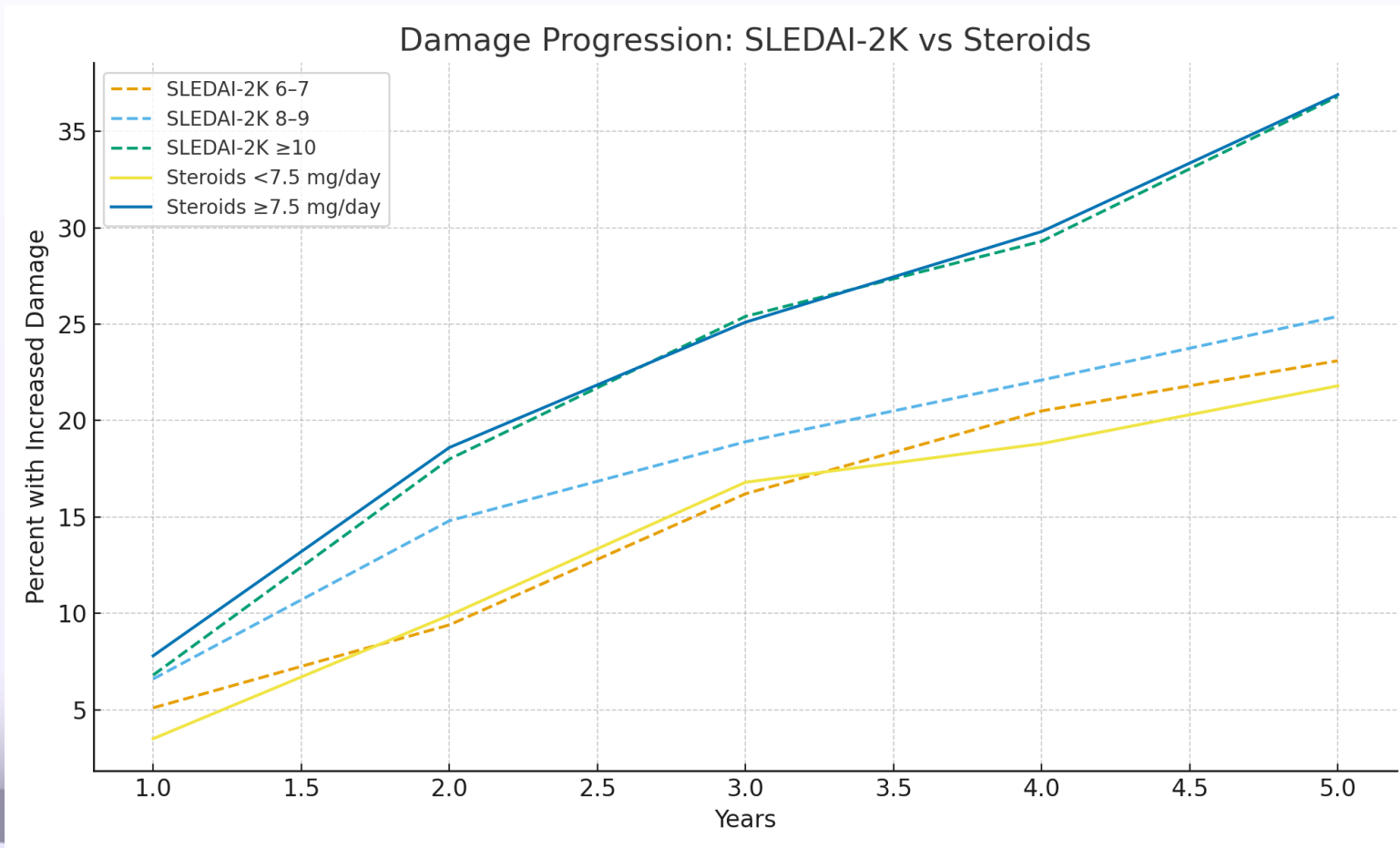
Cardiovascular



Arnaud et al. Lupus Sci Med 2025;12:e001428. SNDS claims data; associations, not causal estimates. Figure from the paper.

Comparison of Damage Progression by SLEDAI-2K vs Corticosteroid Use

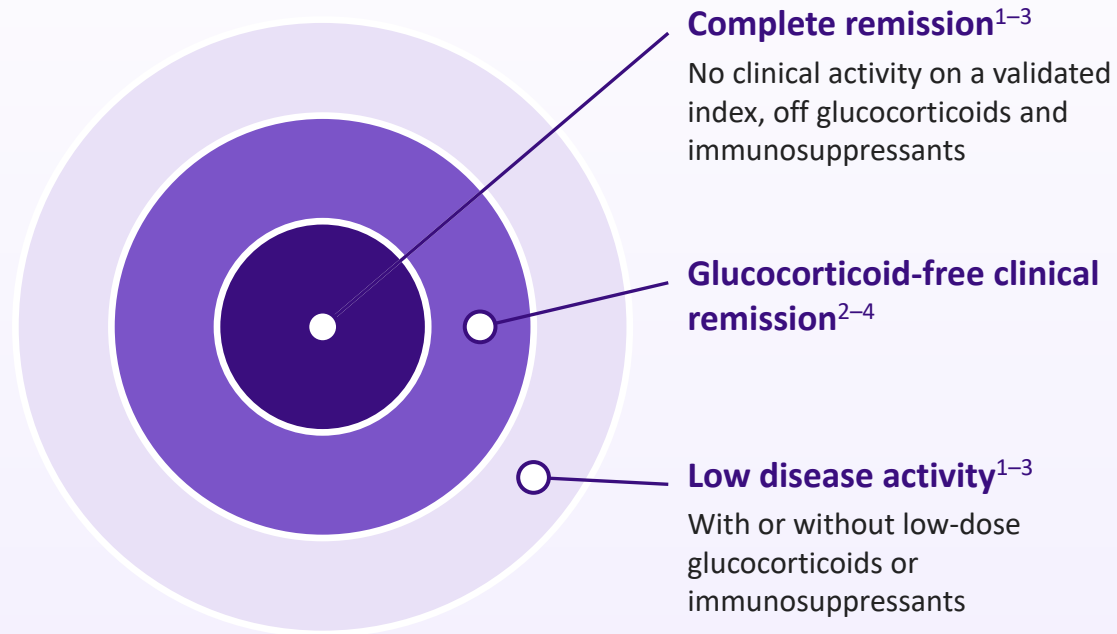
Effect of Disease Activity on Organ Damage Progression in Systemic Lupus Erythematosus: University of Toronto Lupus Clinic Cohort



Treat to Target in SLE: Goals and Objectives

Treatment targets

from ideal to acceptable



Objectives of treat to target⁵



Live longer

- Improve survival
- Limit organ damage accrual



Control disease

- Control disease activity
- Prevent new flares



Treat safely

- Minimize glucocorticoids
- Limit drug toxicity
- Manage comorbidities



Live well

- Improve quality of life

We treat to target to improve long-term outcomes. That means remission, less organ damage, and better quality of life, with minimal drug toxicity.⁴

1. van Vollenhoven RF, et al. Ann Rheum Dis 2017;76:554–561. 2. Doria A, et al. Lupus 2015;24:507–515. 3. Fanouriakis A, et al. Ann Rheum Dis 2019;78:736–745. 4. Doria A, et al. Ann Rheum Dis 2014;73:154–160. 5. van Vollenhoven RF, et al. Ann Rheum Dis 2014;73:958–967.

Defining the Target: LLDAS and DORIS Remission

Most attainable

Most stringent

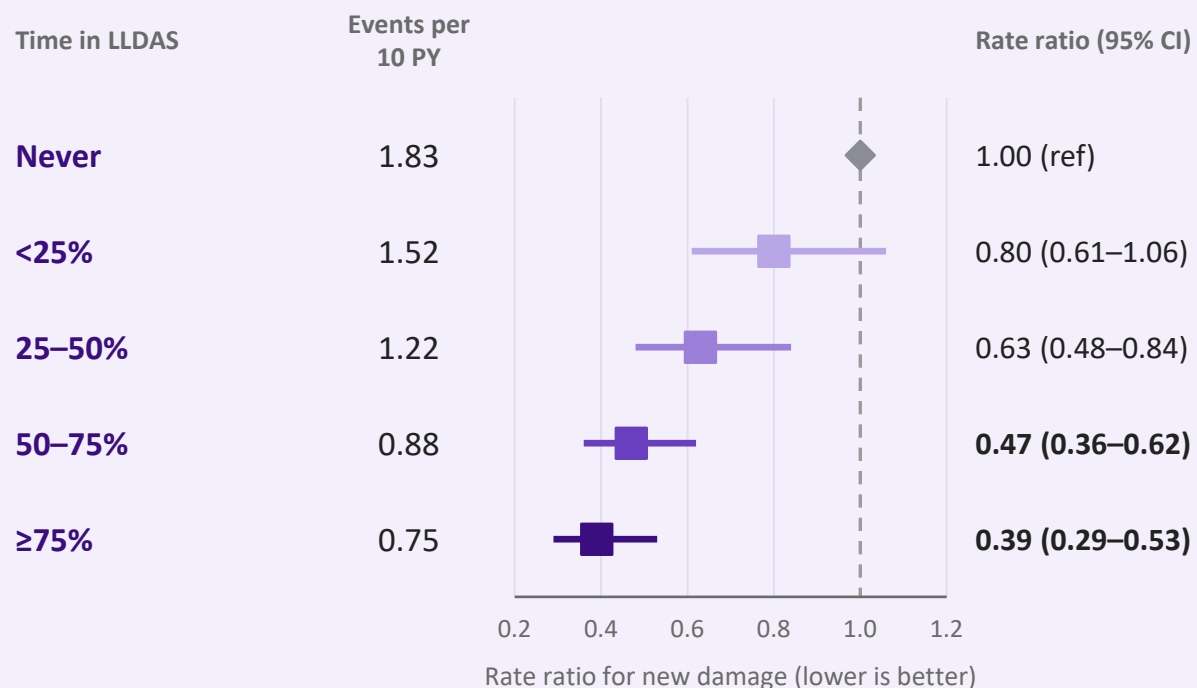
	LLDAS Lupus Low Disease Activity State	DORIS clinical remission on treatment	DORIS complete remission off treatment
 Disease activity	SLEDAI-2K ≤ 4 No major organ activity, no new features	Clinical SLEDAI = 0	Clinical SLEDAI = 0
 Serology	 Activity allowed	 Activity allowed	 No serologic activity
 Physician global	PGA ≤ 1 0–3 scale	PGA < 0.5 0–3 scale	PGA < 0.5 0–3 scale
 Glucocorticoids	Prednisone ≤ 7.5 mg/day	Prednisone ≤ 5 mg/day	None
 Immunosuppressives and biologics	Standard maintenance doses No investigational drugs	Maintenance therapy allowed Antimalarials, IS, stable biologics	Antimalarials only No immunosuppressives or biologics

IS, immunosuppressives. Clinical SLEDAI excludes anti-dsDNA and complement. Serologic activity means anti-dsDNA above normal or C3/C4 below normal. Franklyn K, et al. Ann Rheum Dis 2016;75:1615–1621. van Vollenhoven R, et al. Ann Rheum Dis 2017;76:554–561. van Vollenhoven RF, et al. Lupus Sci Med 2021;8:e000538.



SLE Patients Achieving Low Lupus Disease Activity Exhibit Less Damage Accrual

All new damage, by share of prior visits in LLDAS



Organ Damage

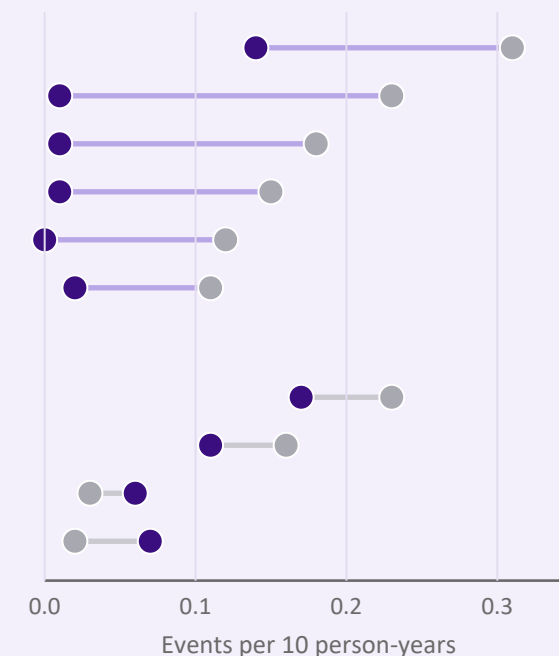
Reduced (trend $P < 0.05$)

Osteoporotic fracture
Avascular necrosis
End-stage renal disease
Erosive arthritis
GFR <50%
Myocardial infarction

Not reduced

Cataract
Pulmonary fibrosis
Pulmonary hypertension
Cognitive impairment

● Never in LLDAS ● LLDAS ≥75% of visits



LLDAS ≥50% of the time cut damage by about half. LLDAS was met at 50% of visits vs 27% for clinical remission on treatment.

African American patients spent less time in LLDAS (41% vs 58% of follow-up) but saw similar benefit.

Petri M, Magder LS. Arthritis Rheumatol 2018;70:1790–1795. Hopkins Lupus Cohort, 1,356 patients, 77,105 person-months. PY, person-years. Damage type rates compare never vs ≥75% of prior visits in LLDAS.



EULAR 2023 Recommendations for Non-Renal SLE



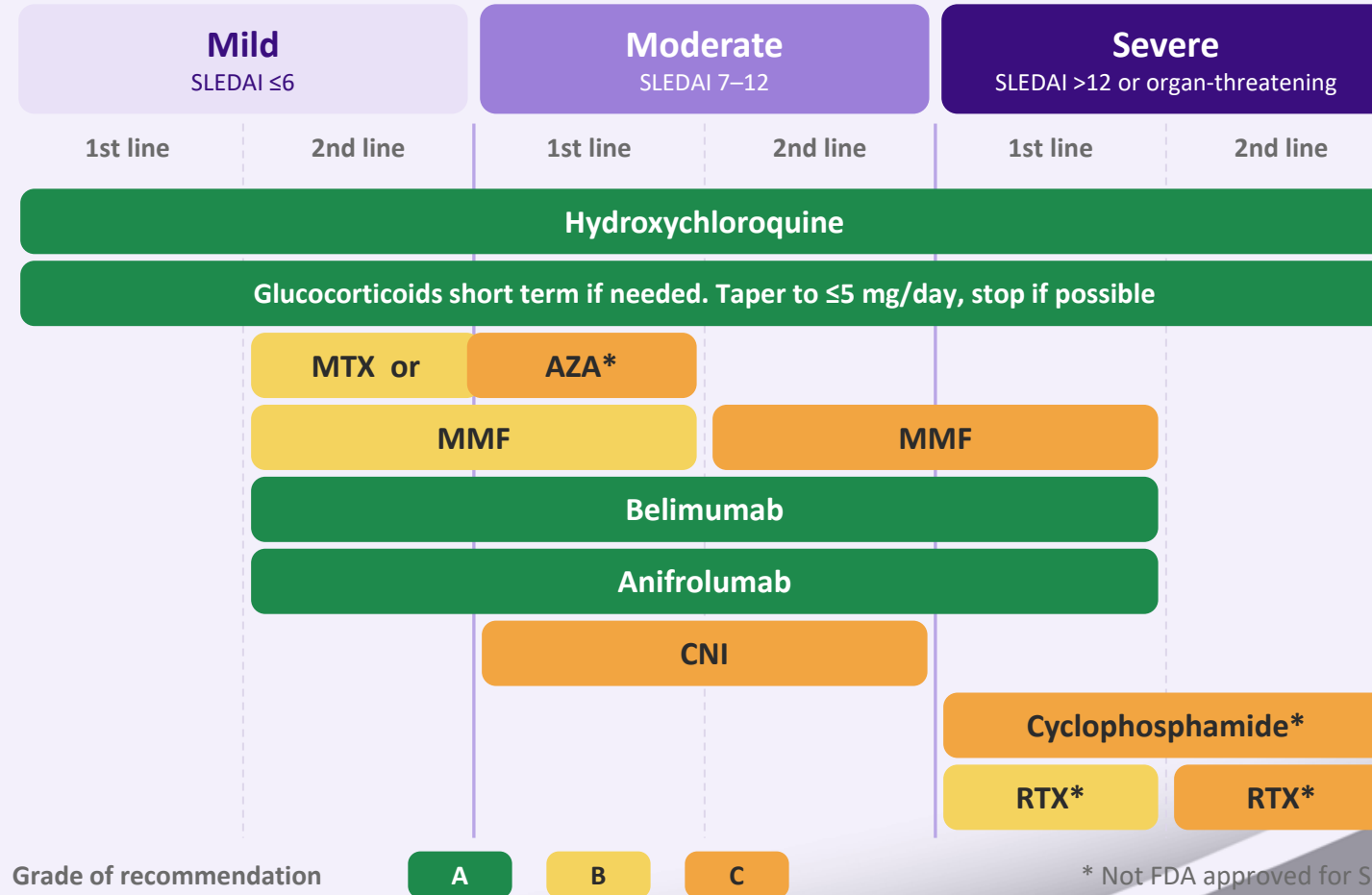
Targets

Remission

- Clinical SLEDAI = 0
- On HCQ
- GC $\leq$ 5 mg/day

Low disease activity

- SLEDAI $\leq$ 4
- On HCQ
- GC $\leq$ 5 mg/day
- Stable, tolerated IS or biologics



For everyone

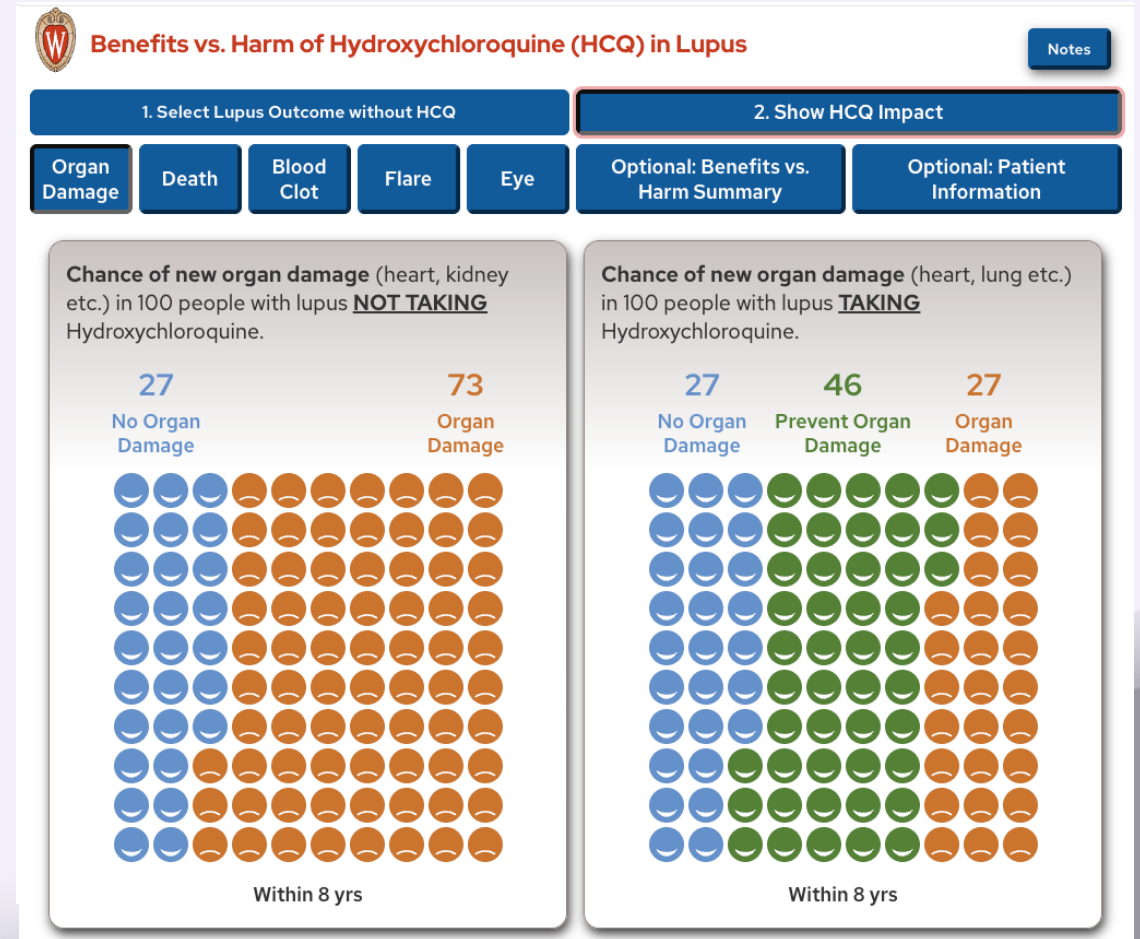
- Sun protection
- Vaccinations
- Exercise
- Smoking cessation
- Body weight
- Blood pressure
- Lipids and glucose
- Antiplatelet or anticoagulant if aPL+

AZA, azathioprine; CNI, calcineurin inhibitor; GC, glucocorticoids; HCQ, hydroxychloroquine; IS, immunosuppressants; MMF, mycophenolate mofetil; MTX, methotrexate; RTX, rituximab. Fanouriakis A, et al. Ann Rheum Dis 2024;83:15–29.



Hydroxychloroquine: SLE Patient's Best Friend

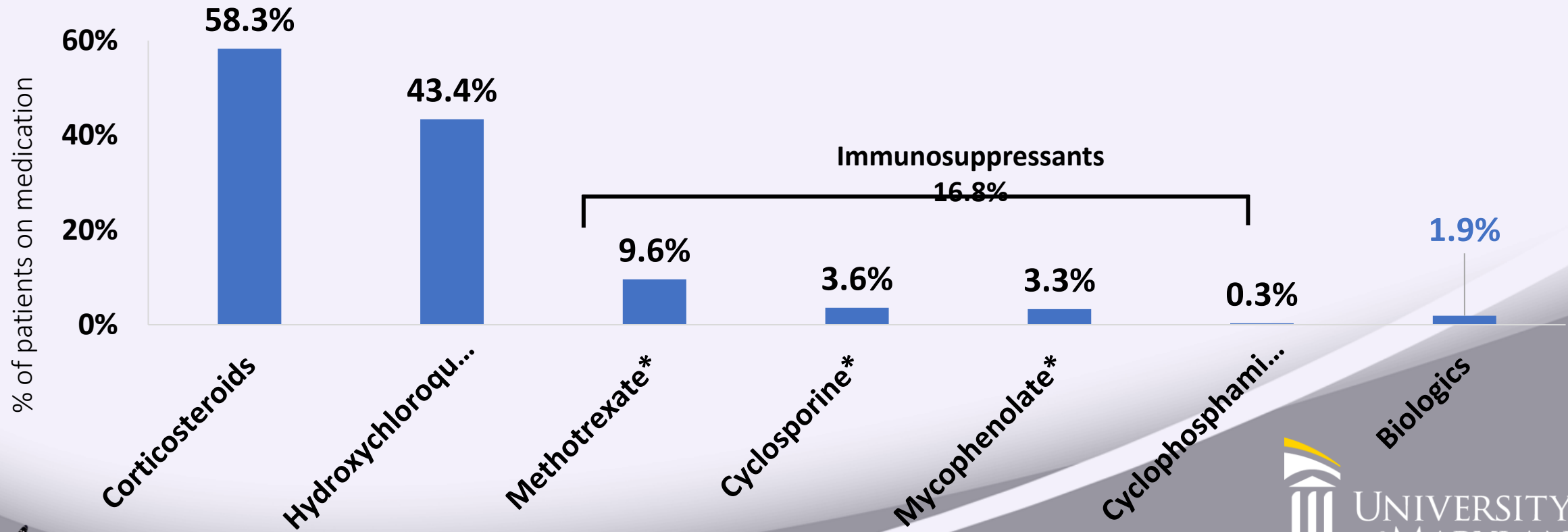
- Most common anti-malarial drug used in lupus.
- Others include:
 - Chloroquine
 - Quinacrine
- Associated with:
 - Fewer Flares
 - Lower mortality
 - Decreased thrombotic risk
 - Less organ damage



Underutilization of Biologics for SLE



SLE medication use in U.S. Commercial Health Plan Population
for one-year following diagnosis
N = 30,086, 2012-2016



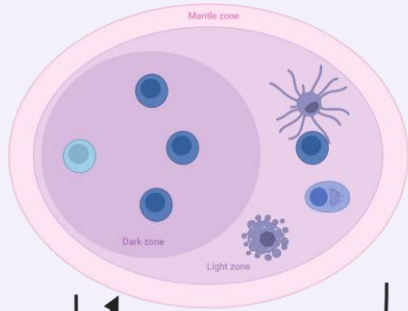
Advanced Therapies in LN Are Associated with Disease Modification and Improved Outcomes

Product	DISEASE MODIFICATION POTENTIAL			DISEASE MODIFICATION CONFIRMED (BEYOND 5 YEARS)
	Outcomes Year 1		Outcomes Years 2-5	Outcomes Year >5
	① Significant reduction in disease activity measured using a validated tool (i.e. SELENA-SLEDAI, BILAG, SRI-4) ② Significant reduction in severe flare measured using a validated tool (i.e. SFI or BILAG) ③ Reduction in use of steroids* and/or immunosuppressants		① Sustained improvement in multiple organ domains/no worsening in multiple organ domains ② Prevention of severe flares ③ Continued reduction in use of steroids* and/or immunosuppressants	No change in SDI or delayed progression
Glucocorticoids	① ② ③		X X ③	X
Hydroxychloroquine†	① ② ③		① ② ③	⑤
Immunosuppressants				
Azathioprine	① ② ③		① ② ③	●
Cyclophosphamide	① ② ③		① ② ③	●
Leflunomide	① ② ③		① ② ③	●
Methotrexate	① ② ③		① ② ③	●
Mizoribine	① ② ③		① ② ③	●
Mycophenolate mofetil	① ② ③		① ② ③	●
Calcineurin inhibitors				
Cyclosporine	① ② ③		① ② ③	●
Tacrolimus	① ② ③		① ② ③	●
Biologics				
Abatacept	① ② ③		① ② ③	●
Anifrolumab	① ② ③		① ② ③	●
Belimumab	① ② ③		① ② ③	●
Rituximab	① ② ③		① ② ③	●

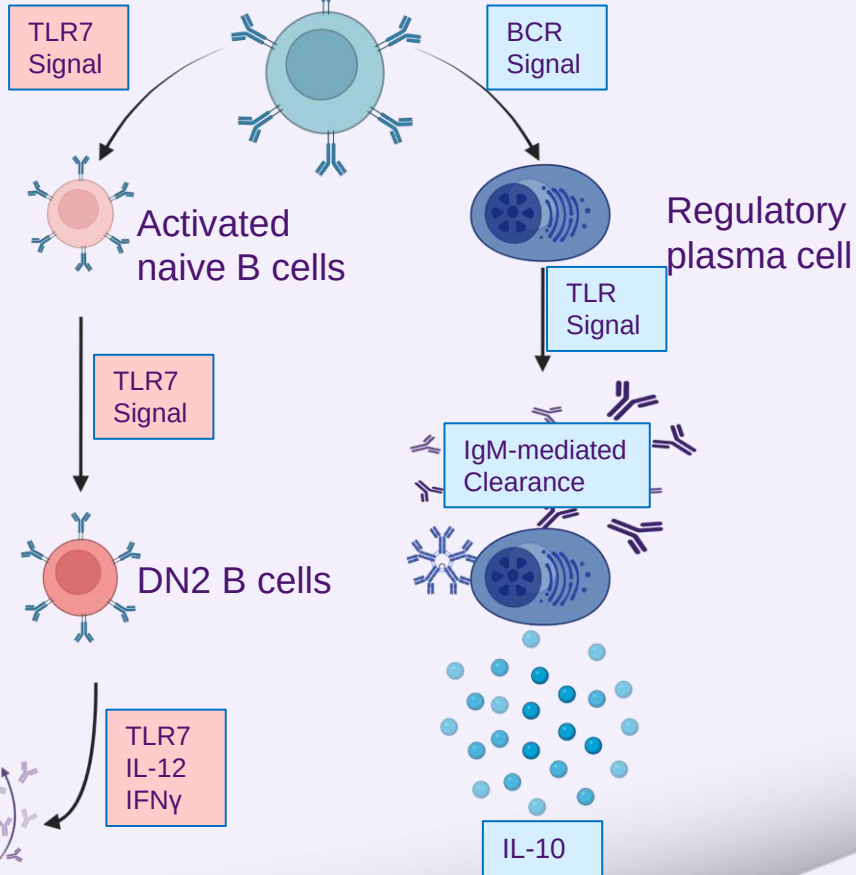
●, criterion met; ⑤, insufficient evidence in the literature to meet the specific criterion, but strong general indications of criterion met; ●, inconclusive; ●, data not available in the literature to support criterion met; X, data were available in the literature, but there was a negative impact on criterion.

Unique Pathologic B Cell Subsets Characterize SLE

Germinal Center-derived memory



Resting naive B cells



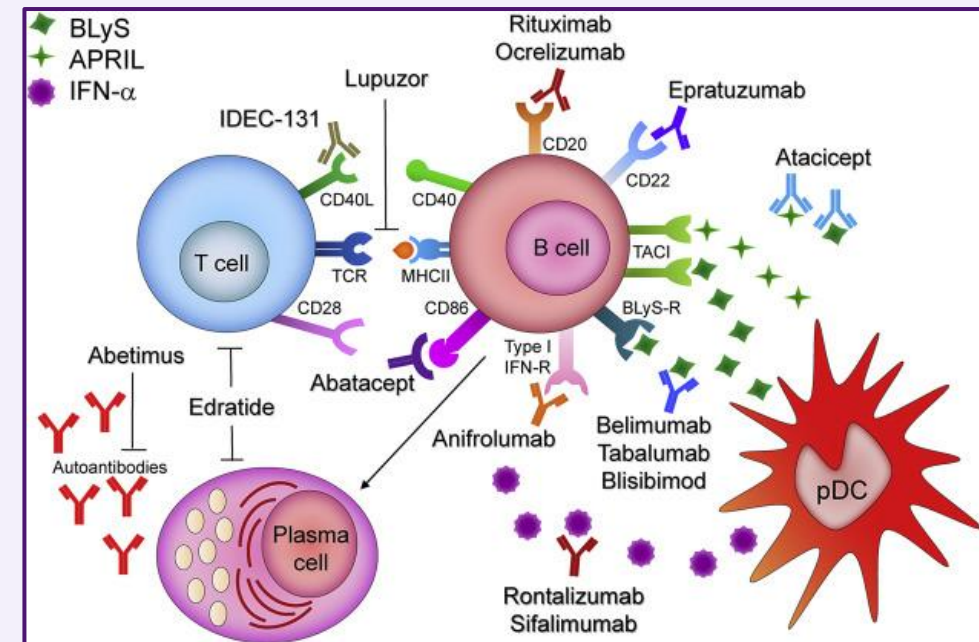
- Two pathways generate pathogenic plasma cells
 - Germinal center
 - Extrafollicular
- Pathologic B-cell production is TLR7 dependent
- Resting naïve B cells can also produce regulatory plasma cells

Anti B-cell Therapy: Where Did We Go Wrong?

- B cells are central to SLE pathogenesis (autoantibody production, T-cell activation, co-stimulatory effect, etc)
- Many open-label trials show efficacy with rituximab
 - Meta-analysis of 11 (201 patients) open-label LN trials using rituximab
 - Pooled CR: 36.1% (95% CI: 25.2–48.6%)
 - Pooled PR: 37.4% (95% CI: 28.5–78.8%)

The Graveyard of Failed B-Cell Targeted Therapy RCTs

ALLEVIATE	EMBRACE	ACCESS
	BELON	LUNAR
CALLIBRATE	G	RITUXILUP
	EXPLORER	



Past therapy Limitations

Incomplete B cell depletion (CD20)
Inability to affect secondary lymphoid organs

Currently B-Cell Therapies in Use for SLE in the US

Belimumab

FDA-approved for SLE and LN

Blocks soluble BAFF. It reduces B-cell survival signals; it does not directly bind or kill B cells.

Most effect on BAFF-dependent transitional and naïve B cells. Mature memory B cells and long-lived plasma cells are relatively spared.

Obinutuzumab

FDA-approved for adults with active LN

Type II anti-CD20 antibody. Marks CD20-positive B cells for depletion.

Targets mature naïve and memory B cells. Does not target most plasmablasts or long-lived plasma cells.

Rituximab

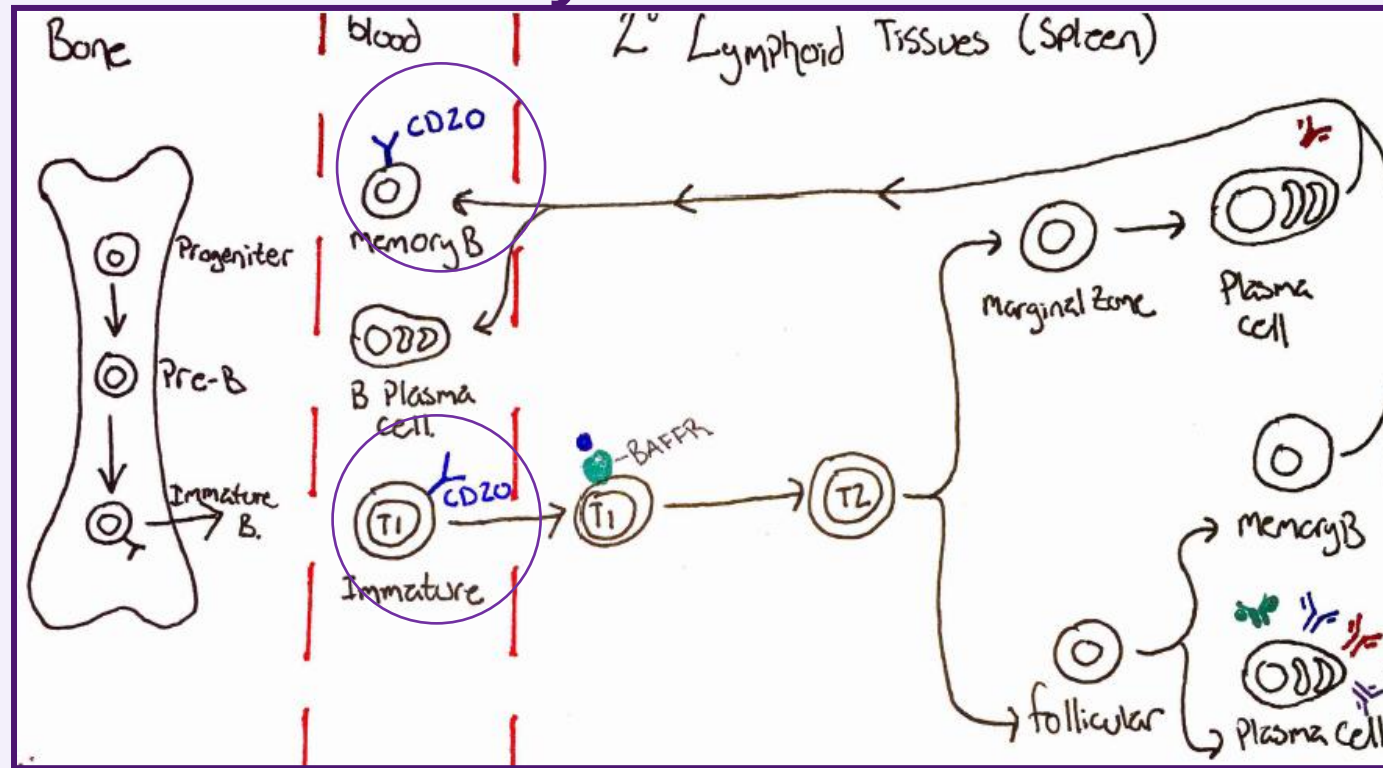
Off-label for refractory SLE/LN

Type I anti-CD20 antibody. Depletes CD20-positive B cells.

Targets mature naïve and memory B cells. EXPLORER and LUNAR missed primary endpoints; still used off-label in selected refractory cases.

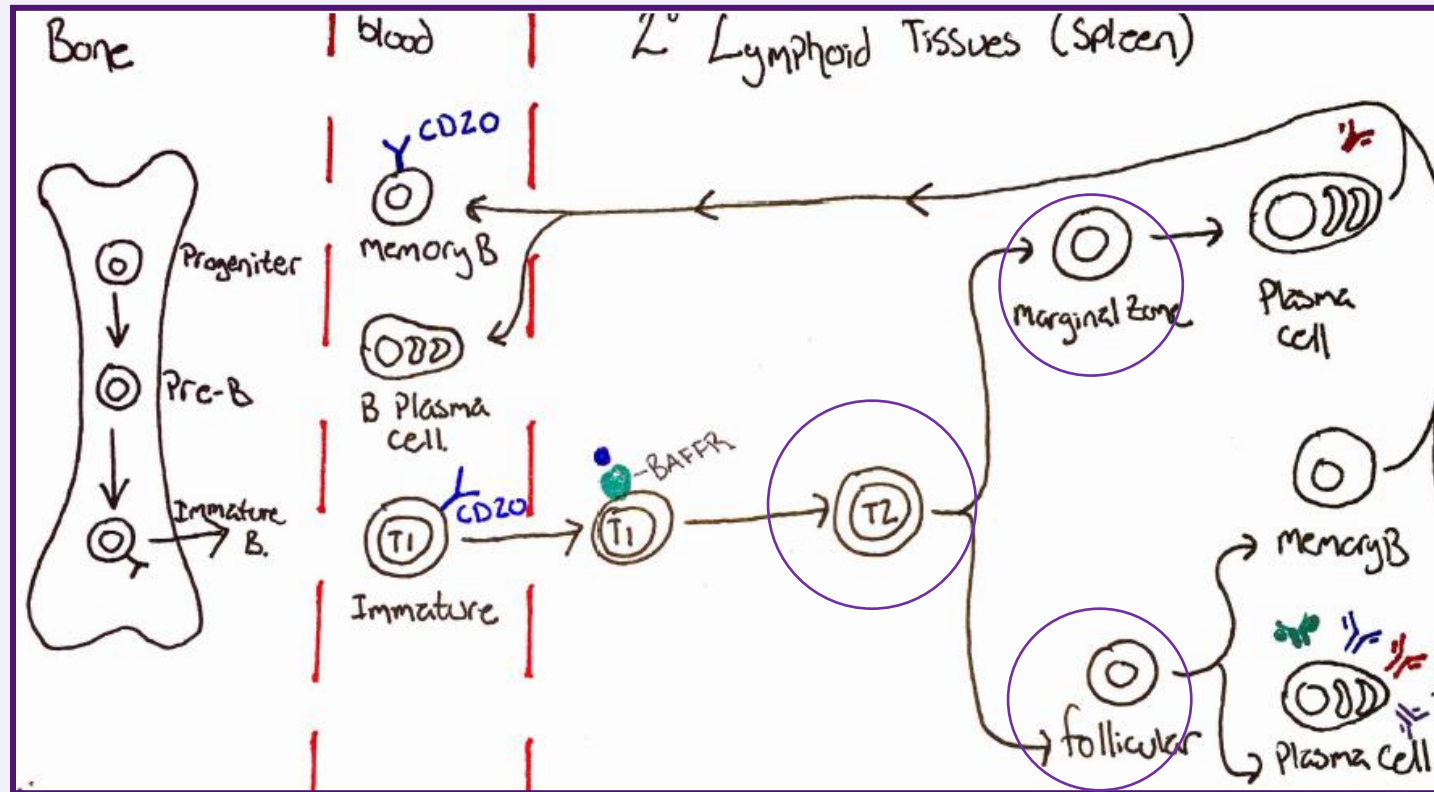
Belimumab changes survival signals. Obinutuzumab and rituximab deplete CD20-positive B cells. None directly removes most long-lived plasma cells.

B-Cell Depletion with Anti-CD20: Aim to Reduce Autoantibody Production



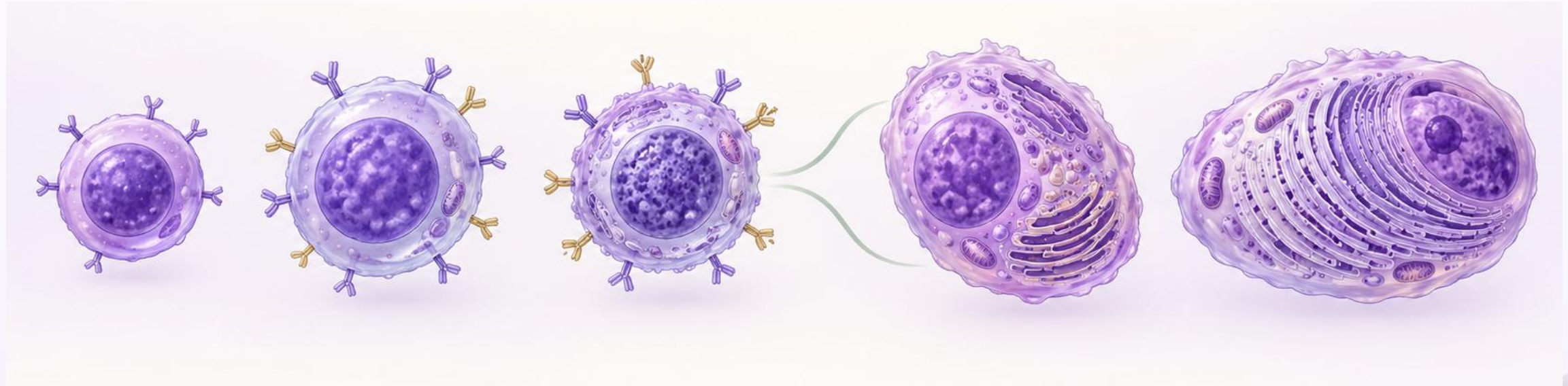
- Chimeric anti-CD20 monoclonal antibody
- Reduces circulating Naïve B cells and Memory B cells
- Spares Plasma cells
- Incomplete clearance of Transitional, Marginal Zone, Germinal Center

Reduced B-Cell Survival with Anti-BAFF: Aim to Reduce Autoantibody Production



- B-Cell Activating Factor
- Stimulates B cell proliferation and differentiation
- Blockade better targets transitional, follicular, and marginal zone B cells

Can New Strategies Lead to Deeper B-Cell Depletion?



Early B cell

Naïve B cell

Memory B cell

Plasmablast

Long-lived plasma cell

BAFF blockade

Changes survival signals, especially for transitional and naïve B cells

CD20 depletion

Mature naïve and memory B cells; little direct reach to most plasma cells

CD19 targeting

Broad CD19-positive B-cell reach, including many plasmablasts

BCMA / CD38

Antibody-secreting cells and plasma cells

Illustration is a teaching schematic. Cell marker expression and depletion vary by subset, tissue, agent and treatment.

The Therapeutic Pipeline for SLE Focuses on B-Cell Mechanisms

Ianalumab

BAFF-R blockade + B-cell depletion

Phase 3 SLE and LN studies

CD19 CAR T

Deep depletion of CD19-positive B cells

Early clinical studies;
investigational

CD19 + BCMA cell therapy

Adds plasma-cell targeting to B-cell depletion

Phase 1 strategies

T-cell engagers

CD3 × CD19 or BCMA × CD3

Early clinical reports and
trials

Anti-CD38 antibodies

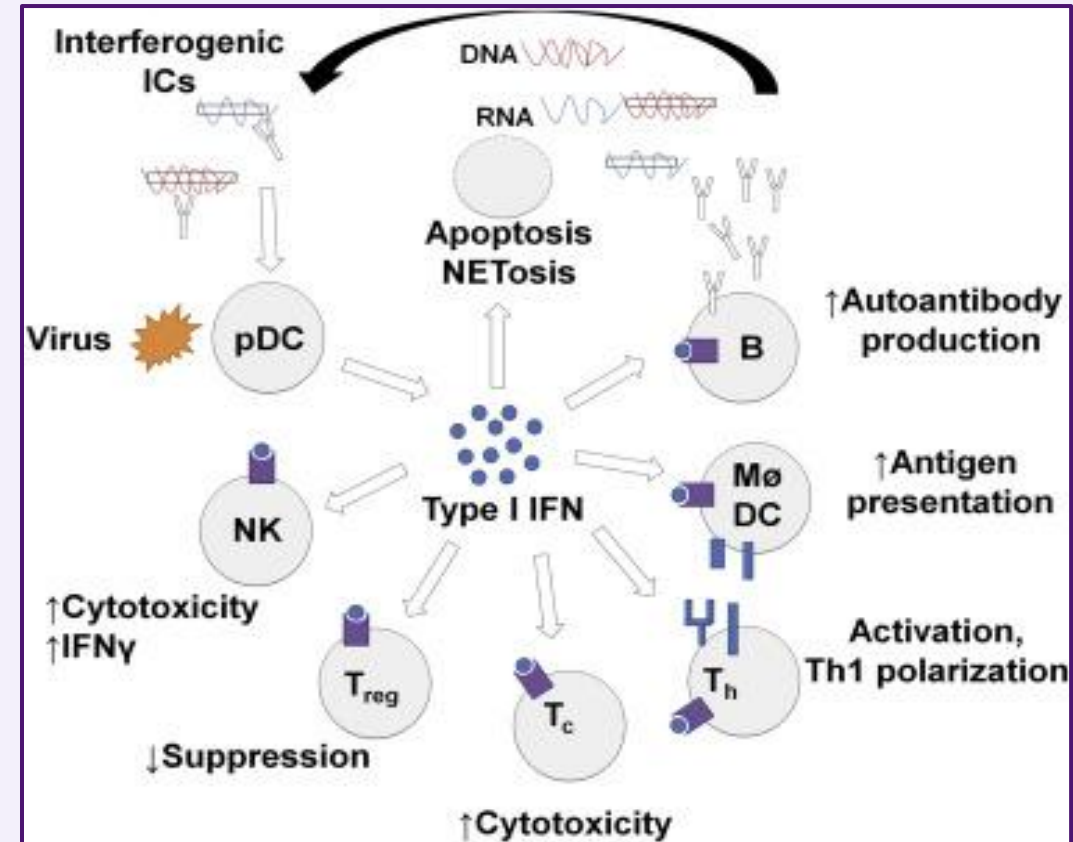
Targets antibody-secreting cells

Daratumumab: phase 2 SLE;
felzartamab: phase 1b LN

All agents on this slide are investigational for SLE/LN in the United States. Trial stage does not establish benefit or approval.

Type I Interferons are at The Center Of SLE Disease Pathogenesis

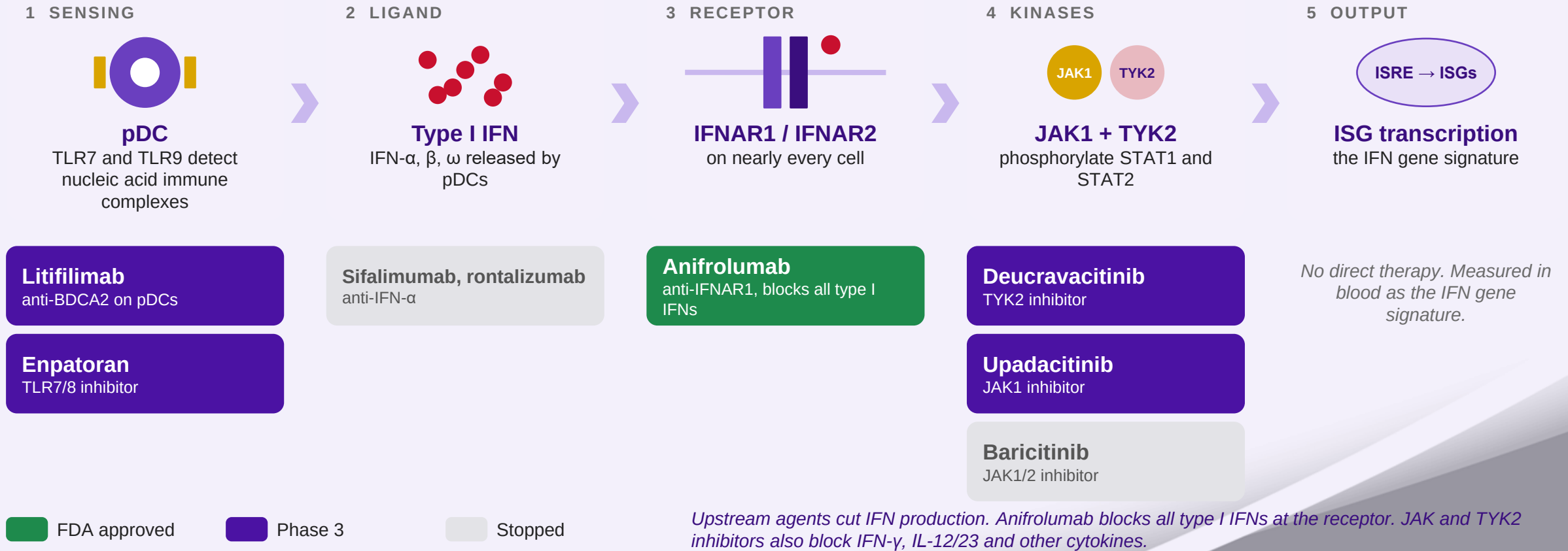
- Immune complexes result in IFN production
- IFN and breaking self-tolerance
 - Promotes autoantibody production
 - Suppresses T regulatory cells
 - Promotes T cell cytotoxicity
- IFNs is a therapeutic target in SLE
 - Anifrolumab
 - Phase 2 LILAC trial (BIIB059)



Schematic: The Role of IFN in SLE Pathogenesis

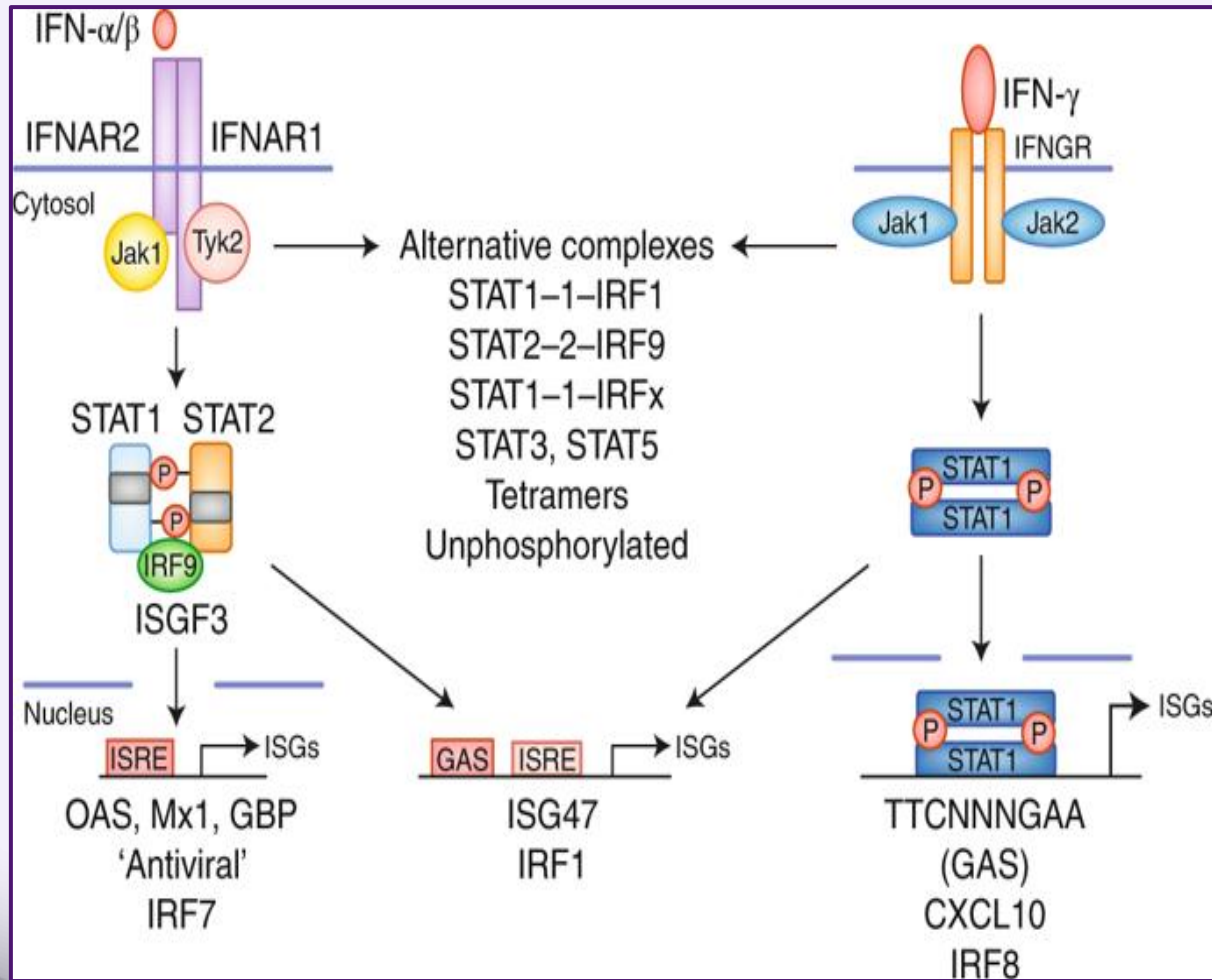
(Hagberg et al, Systemic Lupus Erythematosus Ch 19 (2016))

Several Current and Emerging Therapies Target the IFN Pathway in SLE



BDCA2, blood dendritic cell antigen 2; IFNAR, interferon α/β receptor; ISG, interferon-stimulated gene; ISRE, IFN-stimulated response element; pDC, plasmacytoid dendritic cell; TLR, toll-like receptor.

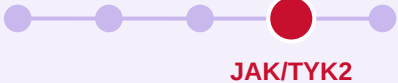
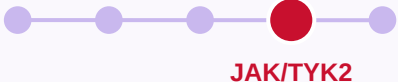
JAK/STAT Pathway may be Targeted to Affect Interferon Signaling



- JAK1 is a signal transducer downstream of IFNAR1/2
- Activated JAKs phosphorylate STATs causing dimerization
- STAT complexes then activate IRFs
- Result: ISG transcription

Emerging Interferon-Pathway Therapies

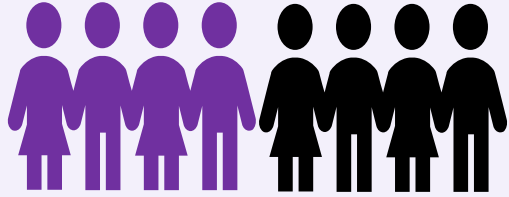


Agent	Where it acts	Phase 2 signal	Phase 3 and next readout
Deucravacitinib oral TYK2 inhibitor	 JAK/TYK2	PAISLEY SRI-4 58% vs 34% at wk 32 (3 mg BID)	POETYK SLE-1 and SLE-2 expected late 2026
Upadacitinib oral JAK1 inhibitor	 JAK/TYK2	SLEek BICLA 53% vs 25% at wk 48 (30 mg)	SELECT-SLE expected December 2026
Litifilimab anti-BDCA2, SC	 pDC/TLR	LILAC fewer active joints in SLE; less skin activity in CLE	TOPAZ-1 and -2 (SLE) expected Q4 2026; CLE in H1 2027
Enpatoran oral TLR7/8 inhibitor	 pDC/TLR	WILLOW improved lupus rash (CLASI-A)	ELOWEN-1 and -2 (skin) FDA breakthrough designation, July 2026
Anifrolumab in LN anti-IFNAR1, IV	 IFNAR	TULIP-LN informed an intensified dosing regimen	IRIS phase 3 in lupus nephritis, ongoing
Stopped in SLE Baricitinib (JAK1/2; SLE-BRAVE-II missed, 2023). Sifalimumab and rontalizumab (anti-IFN-α).			

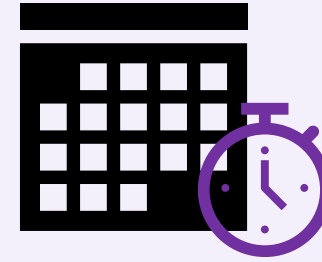
Morand EF, et al. Arthritis Rheumatol 2023;75:242–252 (PAISLEY). Merrill JT, et al. Arthritis Rheumatol 2024 (SLEek). Furie R, et al. N Engl J Med 2022;387:894–904 (LILAC). Merck KGaA, July 2026 (enpatoran). Readout timing from sponsor disclosures as of 2026.



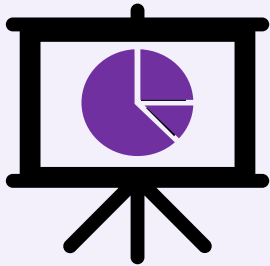
Lupus Nephritis Burdens and Outcomes



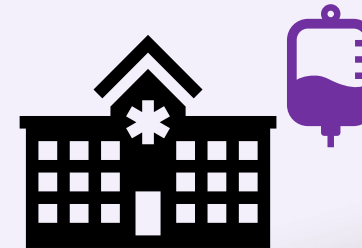
50-60% of patients with SE develop **lupus Nephritis (LN)**



Most patients develop LN within **5 years** of diagnosis

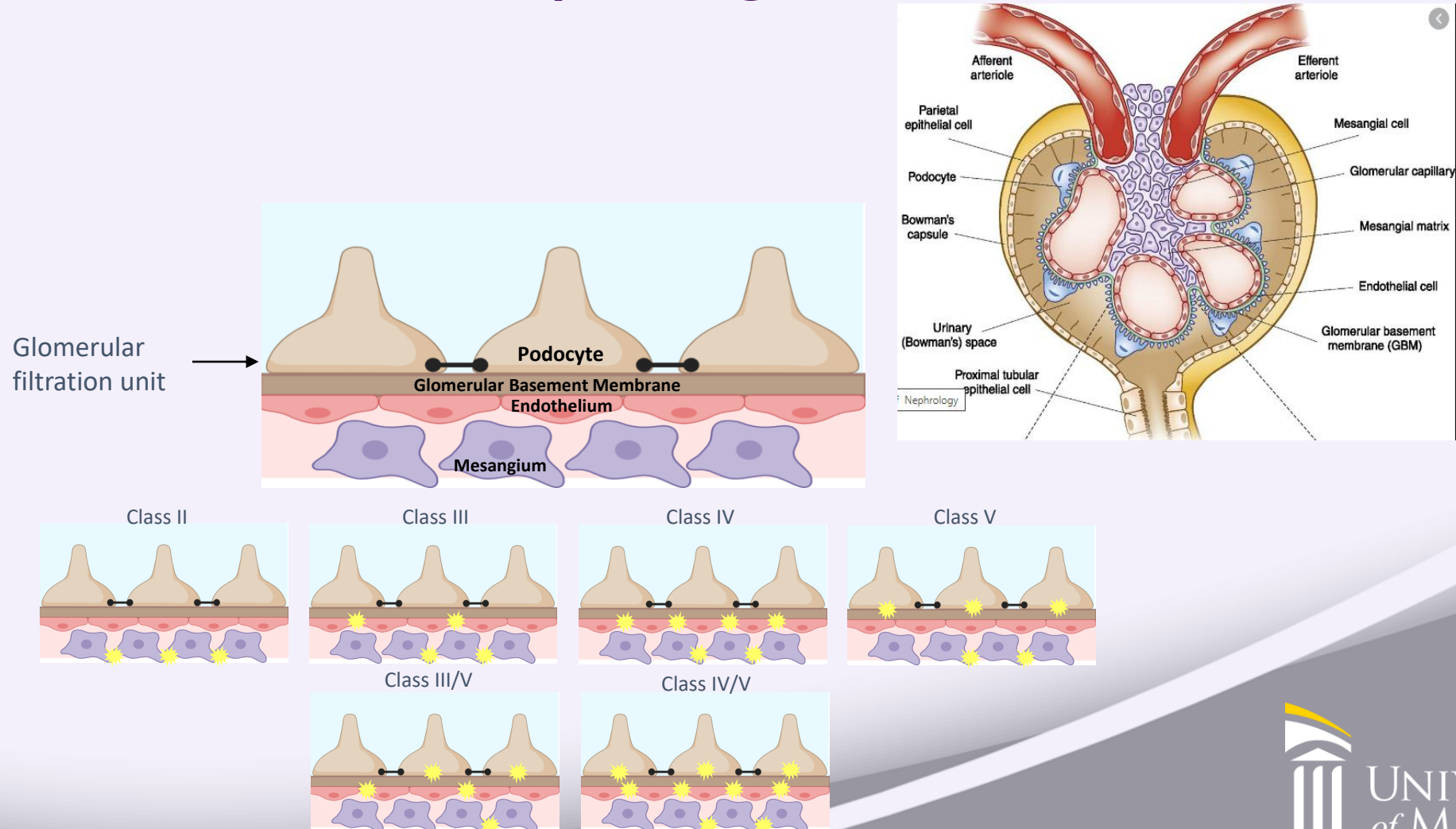


Fewer than 40% achieve **complete remission** after 1 year of treatment



Up to **30%** of people with LN progress to **ESRD**

Schematic: Lupus Nephritis Classes Requiring Treatment



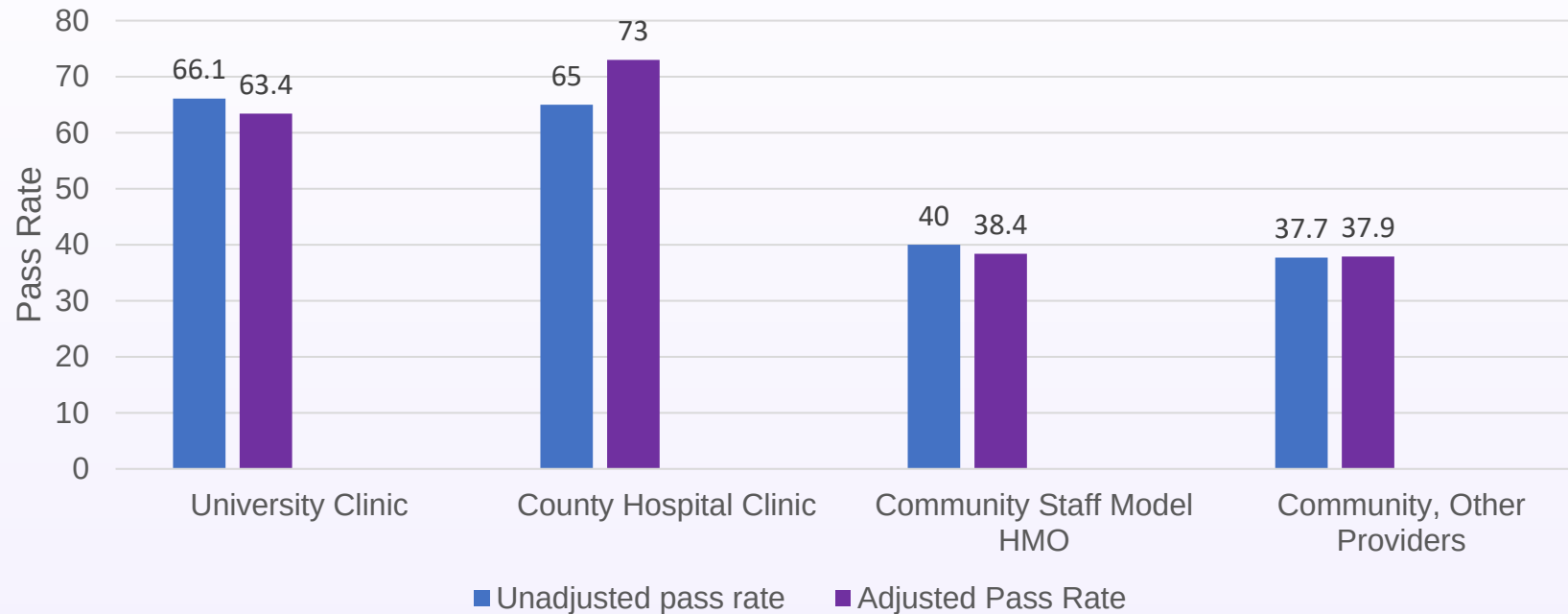
The CDC and ACR have partnered to Improve Quality Care in SLE: Healthy People with Lupus 2030 Campaign

Healthy People with Lupus 2030 Quality Metrics

Goal	Eligible patients should take Hydroxychloroquine	Avoid Prednisone dose > 7.5mg/day for more than 6 months	Laboratory Screening for lupus nephritis	Functional Status Evaluation	Depression Screen
Measure	Pharmacy record screen	Pharmacy record screen	• Blood Pressure • C3, C4, dsDNA • UA, UPCR	• PROMIS* physical function scale • MDHAQ**	• PHQ*** • PROMIS* depression Scale
Interval	Continuously	Continuously	Every 6 months	Every Year	Every Year

* Patient reported outcomes measurement information system ** Multi-dimensional health assessment questionnaire *** Patient health questionnaire

Compared to Academic Centers, Community Care Centers are Less Likely to Screen for Lupus Nephritis



- N= 148 SLE patients in the CLUES Cohort participants with no history of LN
- Screening “pass” was defined as being screened every 6 months for:
 - LN nephritis labs (UA, UPCR, creatinine)
 - SLE activity serologies (C3 or C4, dsDNA levels)
 - Blood pressure

LN presents a major risk for morbidity and mortality with progression to ESKD¹

Uncontrolled **LN flares accelerate nephron loss** and potentiate the **risk for early ESKD**.¹

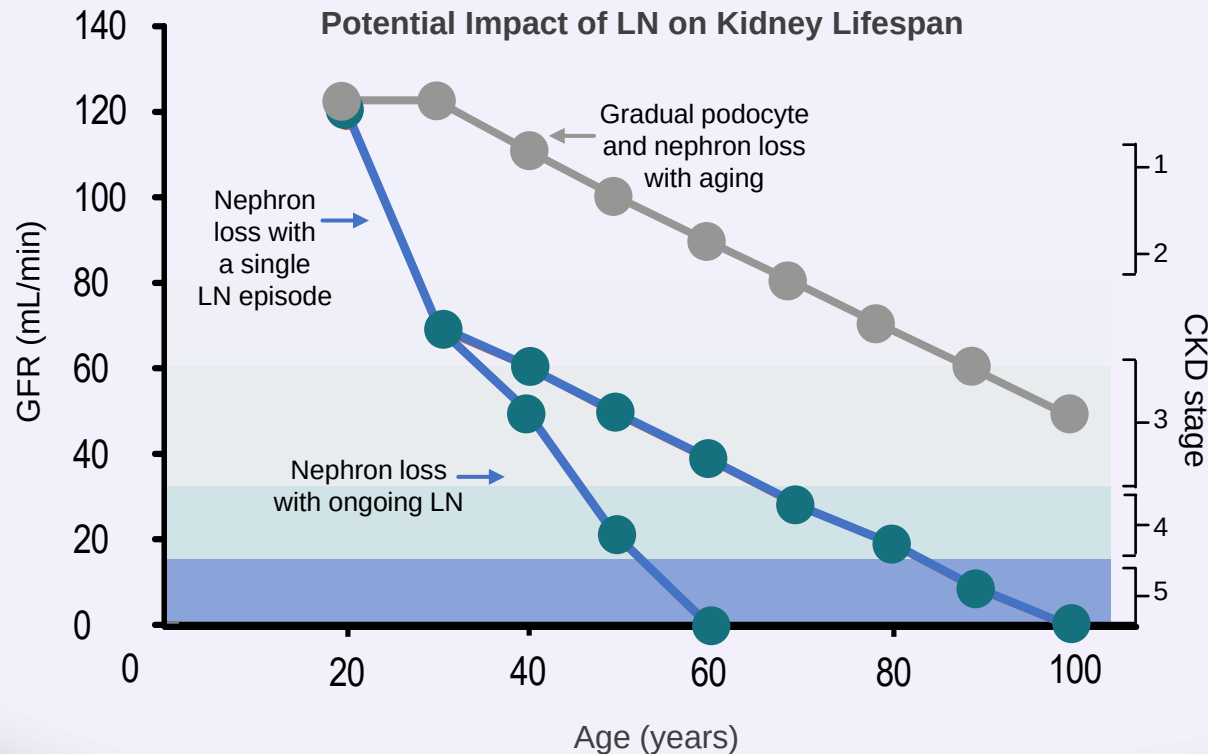


Figure reprinted from Anders HJ, *Kidney Int.* 2016;90(3):493-501.

^aSerum creatinine of ≤ 1.4 mg/dl and proteinuria of ≤ 0.33 g/d within 5 years of entering the study.

CKD = chronic kidney disease; ESKD = end-stage kidney disease; GFR = glomerular filtration rate; LN = lupus nephritis.

1. Anders HJ, Rovin B. *Kidney Int.* 2016;90(3):493-501; 2. Almasani S, et al. *Clin J Am Soc Nephrol.* 2017;12(5):825-835;
3. 2024 ACR Guideline Summary for the Screening, Treatment, and Management of Lupus Nephritis. Accessed February 22, 2025. <https://assets.contentstack.io/v3/assets/bltee37abb6b278ab2c/blt4db6d0b451e88caf/lupus-nephritis-guideline-summary-2024.pdf>



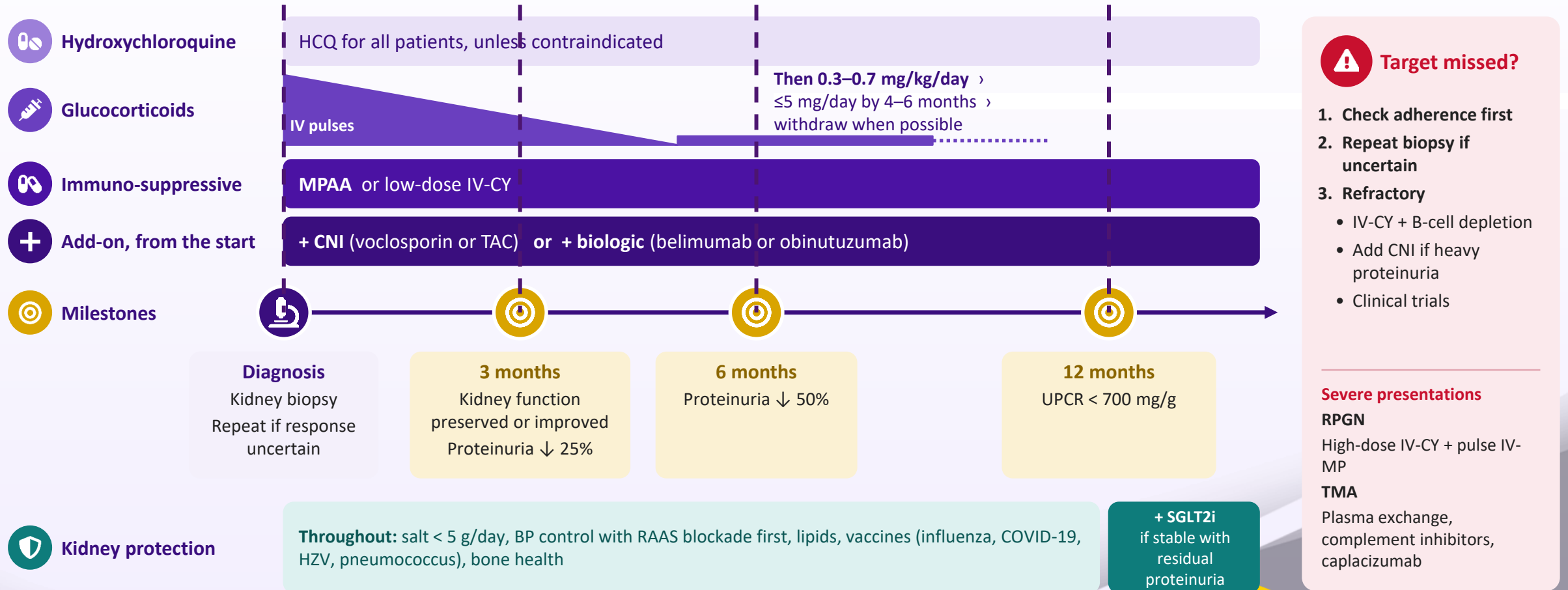
10-year survival has been shown to improve from 46% to 95% if disease remission can be achieved^{2,a}

Preserving kidney function and reducing morbidity/mortality while minimizing medication-related toxicities have been recommended as treatment goals³



UNIVERSITY
of MARYLAND
SCHOOL OF MEDICINE

EULAR 2025 LN Recommendations: Treat to Target



Fanouriakis A, et al. EULAR recommendations for SLE with kidney involvement: 2025 update. Ann Rheum Dis 2025. doi:10.1016/j.ard.2025.09.007

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Changes in the EULAR LN Guidelines from 2023 vs 2025

2023 SLE recommendations



Initial immune therapy

MMF or low-dose CYC. Add belimumab or CNI as an option



Biologics

Belimumab. Rituximab reserved for refractory disease



Glucocorticoids

Pulse, then 0.3–0.5 mg/kg/day. Taper to ≤ 5 mg/day as quickly as possible



Targets

UPr $\downarrow$ 25% at 3 mo, $\downarrow$ 50% at 6 mo, UPr < 0.5 – 0.7 g/day at 12–24 mo



Kidney protection

ACEi/ARB. Consider SGLT2i if decreased eGFR



Refractory and TMA

High-dose CYC. Rituximab

2025 kidney update



Early combination for most patients. MPAA plus belimumab, CNI, or obinutuzumab, with GC



Obinutuzumab added alongside belimumab as first-line add-on

NEW



Pulse, then 0.3–0.7 mg/kg/day. **≤ 5 mg/day by 4–6 months, then withdraw when possible**



Kidney function preserved by 3 mo. $\downarrow$ 25% at 3 mo, $\downarrow$ 50% at 6 mo, **UPCR < 700 mg/g by 12 mo**



Salt < 5 g/day, RAAS blockade first. **SGLT2i in stable disease with residual proteinuria**



Adherence check first. IV-CY + B-cell depletion, add CNI. **TMA pathway** (plasma exchange, complement inhibitors, caplacizumab)

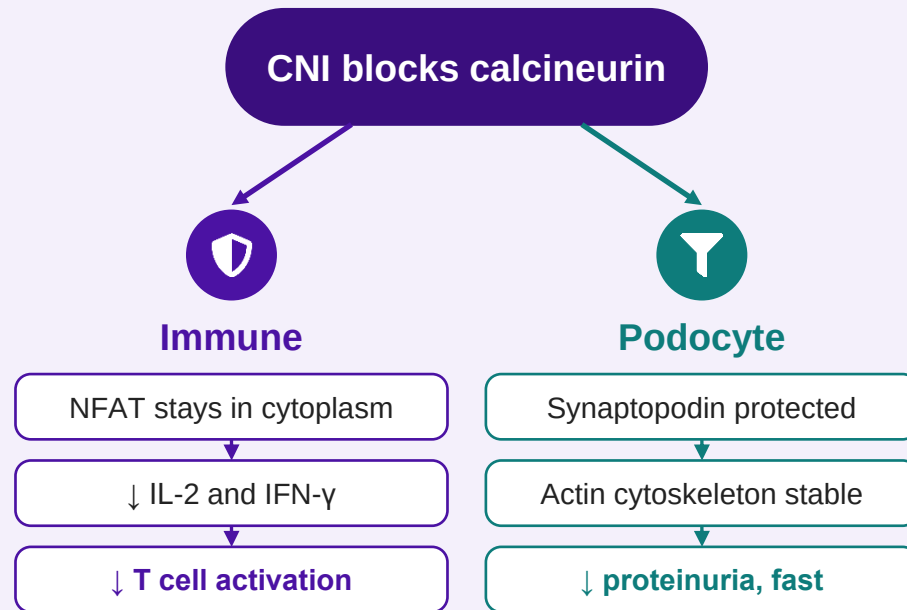
NEW

2023: Fanouriakis A, et al. Ann Rheum Dis 2024;83:15-29.

2025: Fanouriakis A, et al. Ann Rheum Dis 2025. doi:10.1016/j.ard.2025.09.007

Calcineurin Inhibitors Improve Complete Remission Rates in Lupus Nephritis

Two sites of action



Masking ongoing injury? Paired biopsies at 18 months in AURORA 2 (16 voclosporin, 10 control) showed no difference in activity or chronicity indices.

Choosing a CNI

	Voclosporin	Tacrolimus	Cyclosporine
Drug levels	● Not needed	● Required	● Required
Effect on MMF	● Minimal	● Minimal	● ↓ MPA ~40%
Kidney toxicity	● Lower; reversible eGFR dip	● Moderate	● Higher
Pregnancy	● Avoid	● Compatible	● Compatible



Best fit

- Class III/IV ± V with heavy proteinuria
- eGFR >45 at start
- Goal of fast proteinuria control



Monitor and avoid

- eGFR every 2 weeks for 1 month, then every 4 weeks
- Blood pressure
- Not studied with cyclophosphamide

Rovin BH, et al. Arthritis Rheumatol 2025 (AURORA 2 repeat biopsies). Lupkynis prescribing information. Kidney Int 2021 (cyclosporine lowers MPA exposure). Faul C, et al. Nat Med 2008 (CNI and podocyte actin). ACR 2020 reproductive health guideline.

In Summary

- SLE is an under recognized cause of morbidity and mortality especially in young women of color
- Diagnosing SLE requires a high index of suspicion
- Early referral to a specialist can be life-saving
- Late mortality due to SLE is highly related to the accumulation of comorbidities
- Comorbidities in SLE should be co-managed by the rheumatologist and the primary care physician
- Treat to target and early implementation of advanced therapies prevents morbidity and mortality in SLE