



Szisztémás lupus erythematosus

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Clinical Manifestations of Systemic Lupus Erythematosus (SLE)

Neuropsychiatric Symptoms

- Aseptic Meningitis
- Cerebrovascular Disease
- Plexopathy
- Seizure Disorders
- Demyelinating Syndrome
- Cognitive Dysfunction
- Psychosis
- Myasthenia Gravis

Dermatological Symptoms

- Malar Rash
- Erythematous Macules
- Permanent Hair Loss
- Periorbital Edema

Musculoskeletal Symptoms

- Transient Arthralgias
- Erosive Arthritis
- Non-Deformative, Non-Erosive Arthritis
- Jaccoud's Arthropathy
- Myositis

Cardiovascular Symptoms

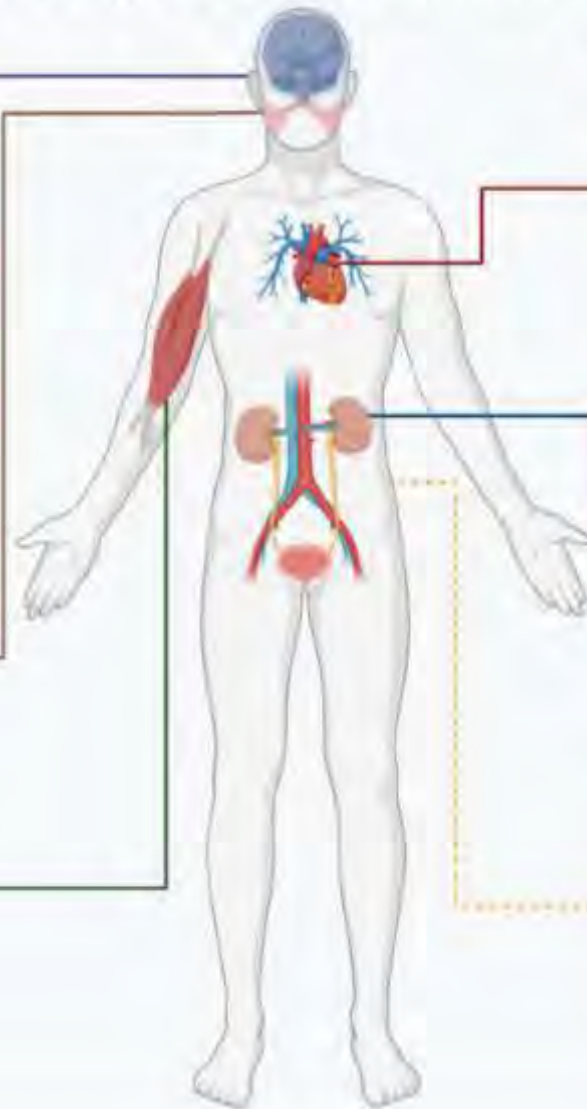
- Pericarditis
- Myocarditis
- Atherosclerosis
- Valvular Disease
- Arrhythmias
- Hypertension
- Endocarditis

Renal Symptoms

- Lupus Nephritis
- Hematuria
- Proteinuria
- Increased Creatine Levels

Constitutional Symptoms

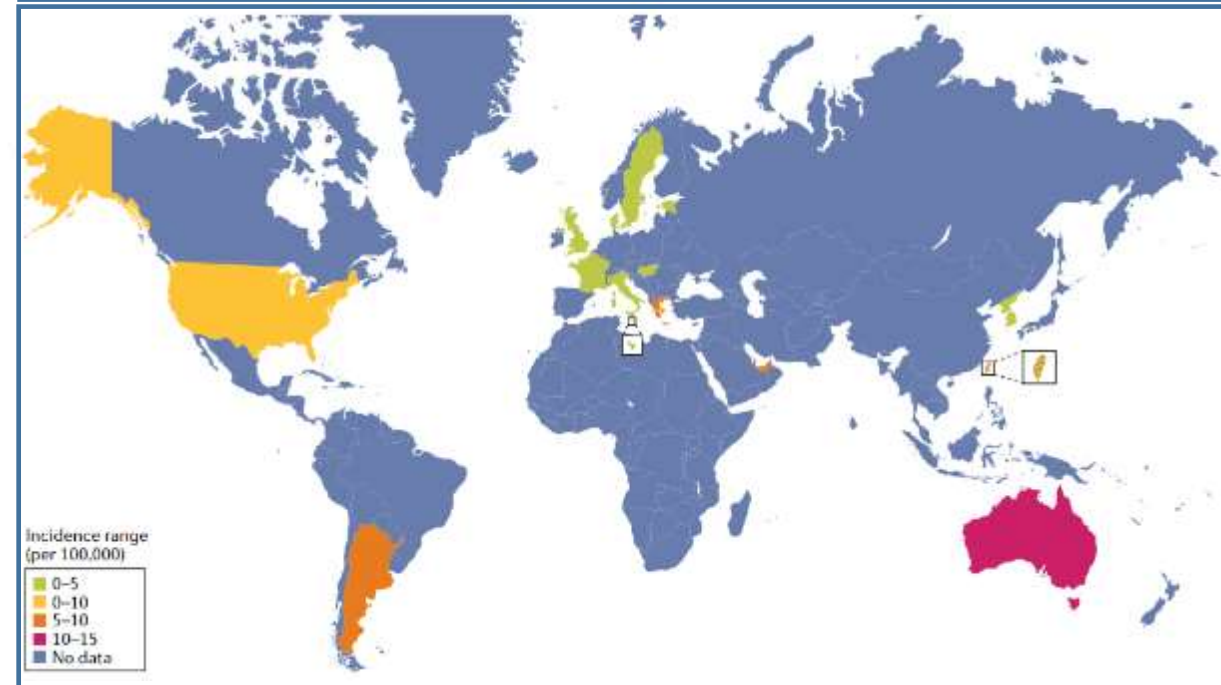
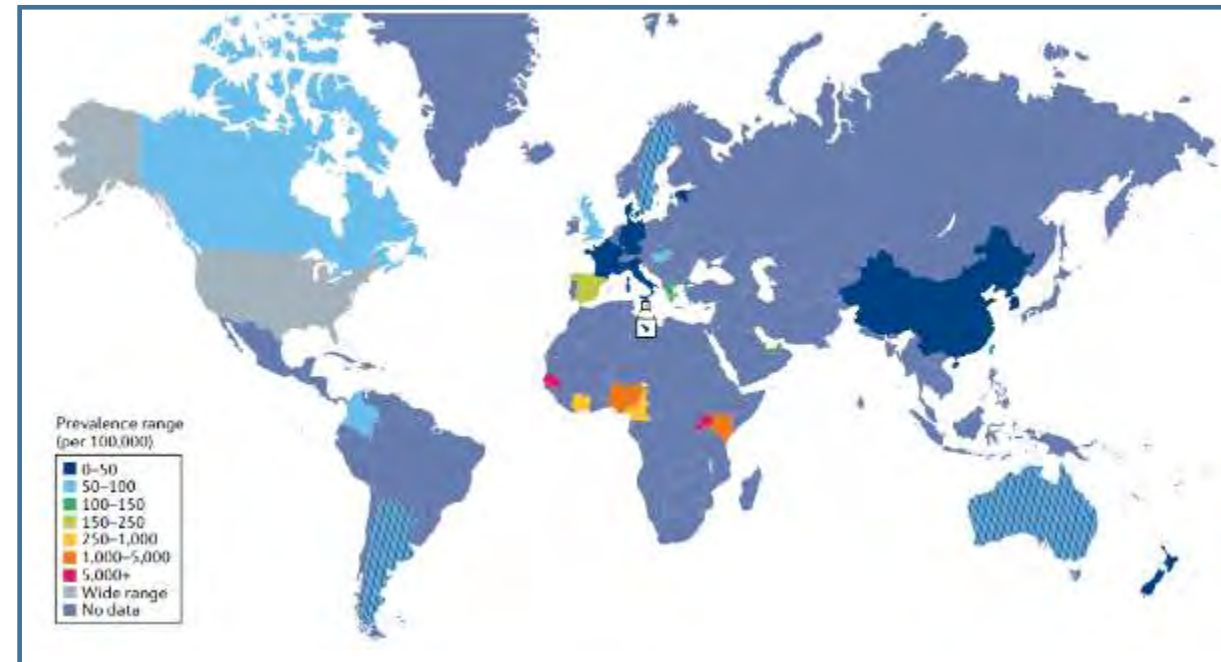
- Fatigue
- Fever
- Headaches
- Sores
- Dizziness
- Abdominal Pain



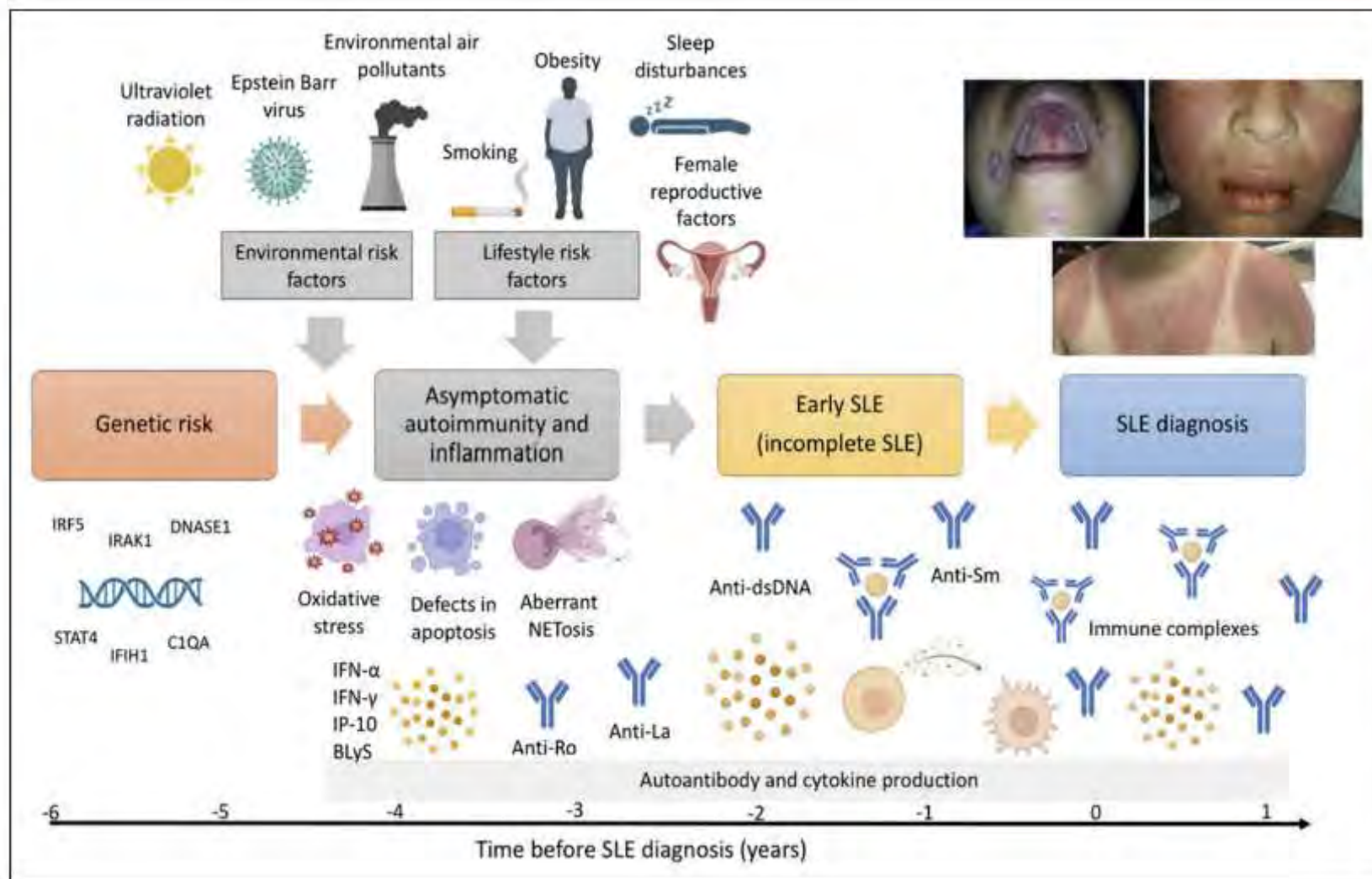
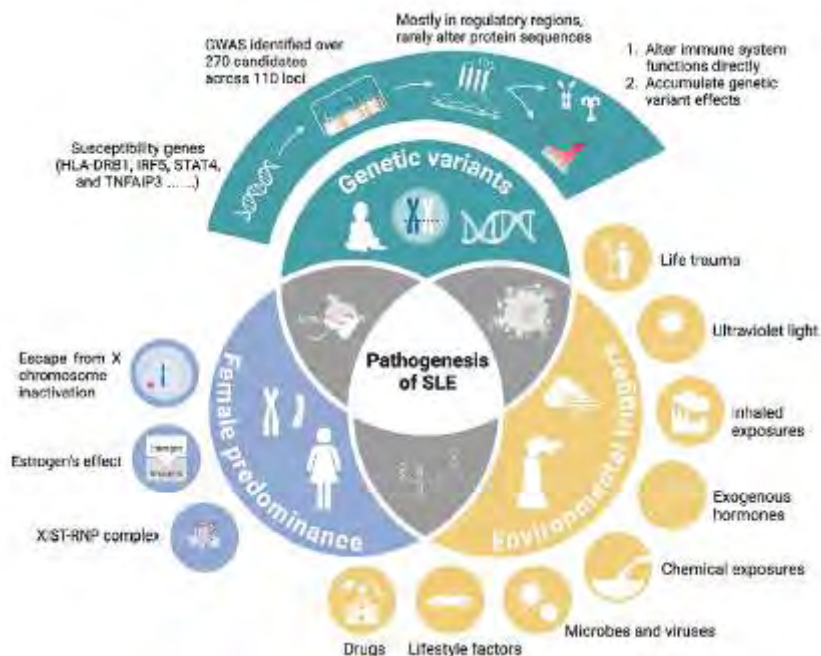
Epidemiológia

- Prevalencia: 50-100 /100.000
- Incidencia: 2-7 /100.000/year
- Betegség kezdet: 20-30 év
- nő:férfi arány: 9-10:1

Barber MRW et al, Nat Rev.Rheumatol, 2021.



SLE kialakulása

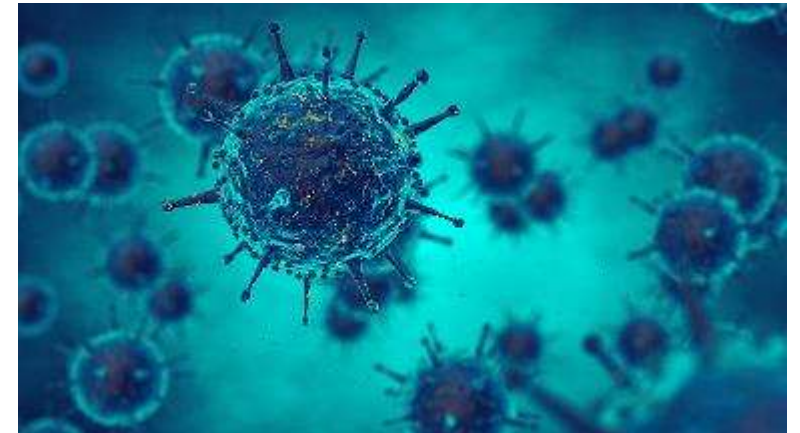


Gonzales L et al, *Lupus*, 2023.

Tian J et al., *MedComm*, 2024.

Etiológia

- Provokáló faktorok
 - napfény, UV fény
 - fertőzések
 - hormonális státusz: ösztrogén, prolaktin
 - gyógyszerek
 - Isoniacide
 - Hidantoin
 - Hydralazin
 - Procainamide
 - D penicillinamin
 - Penicillins
 - Sulphonamids
 - TNF alpha gátlók



Infektív ágensek

➤ Rizikó tényezők

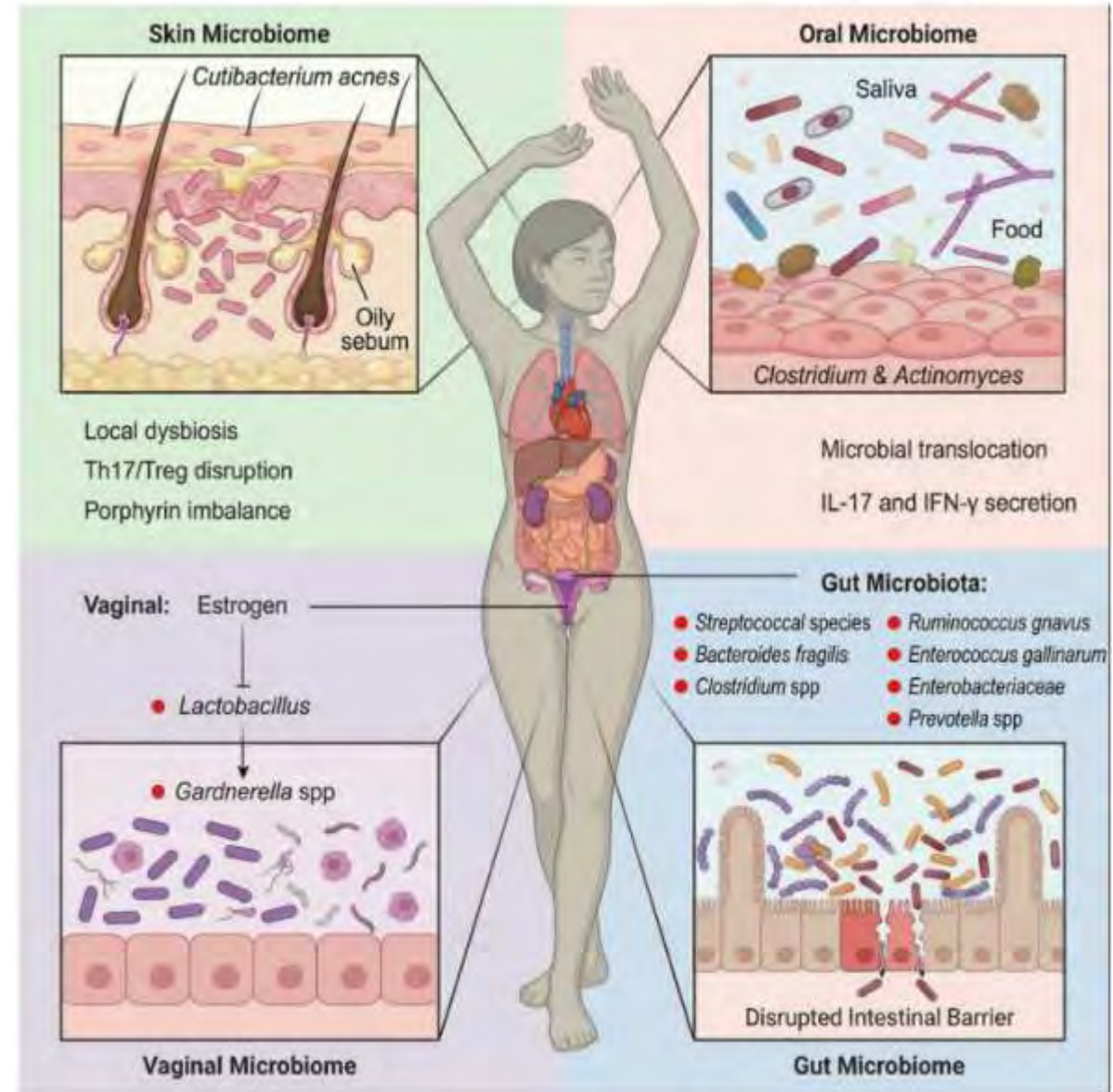
- EBV
- CMV

➤ Protektív hatás

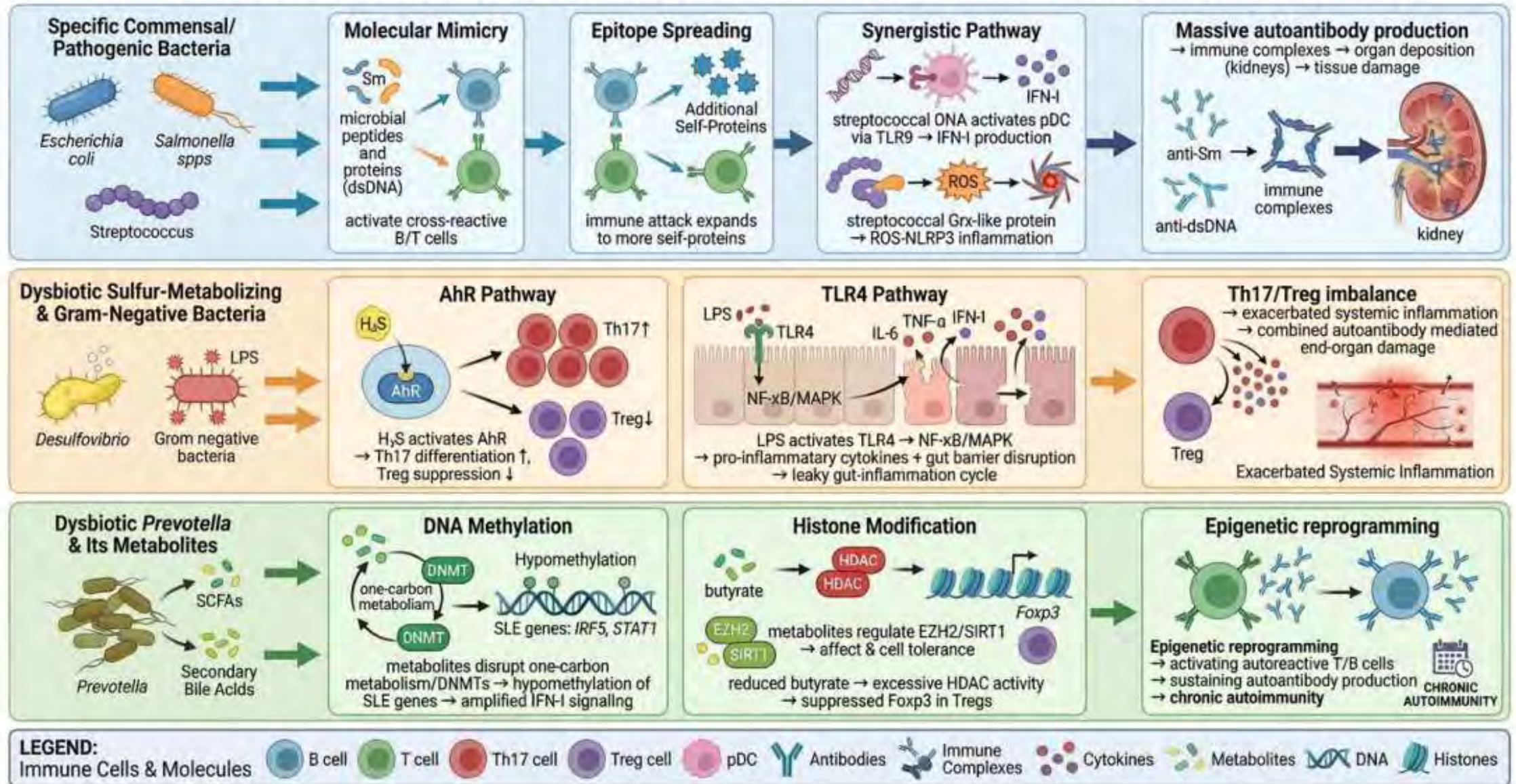
- *Helicobacter pylori*
- Hepatitis B
- Paraziták

➤ Mikrobiom

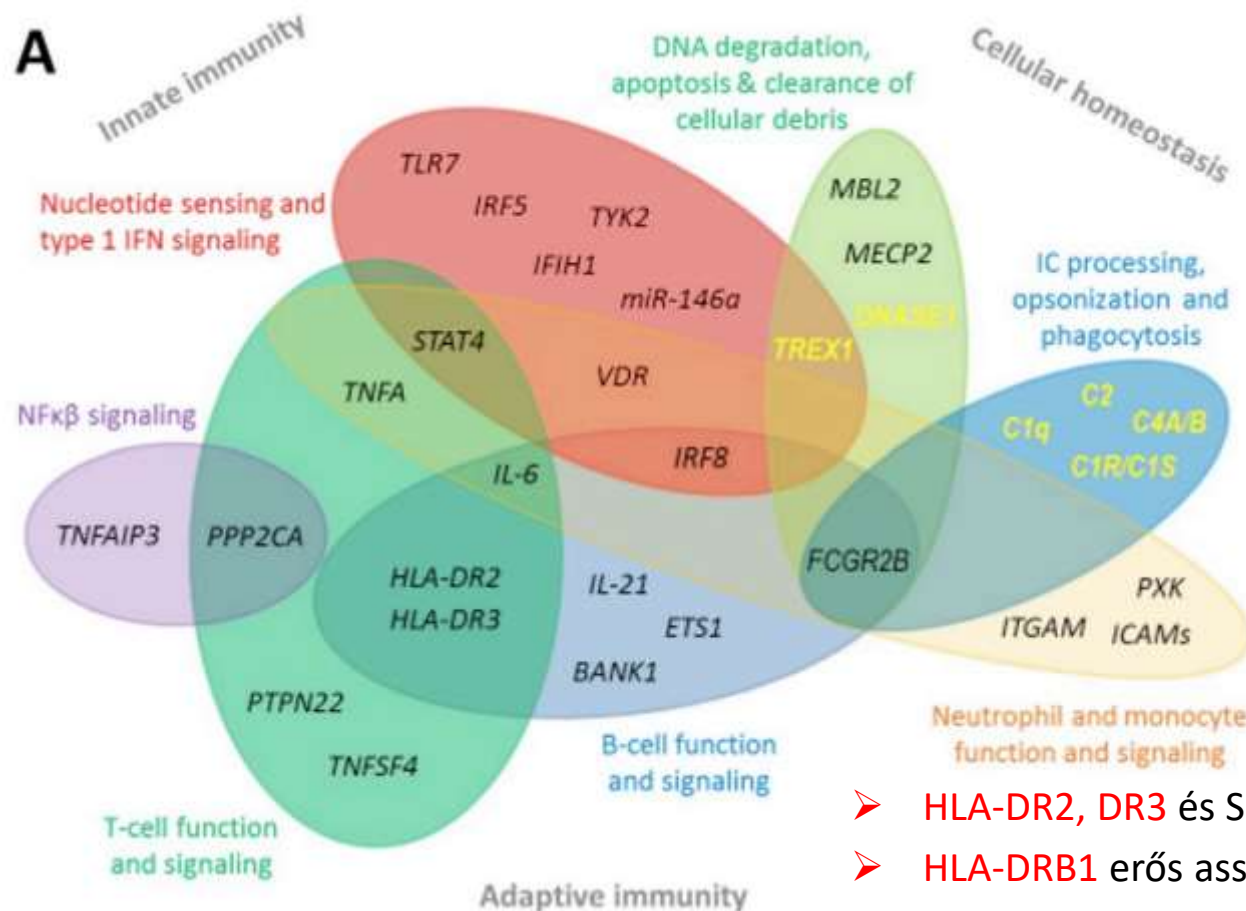
- Alacsonyabb Firmicutes/Bacteriodes arány
- Emelkedett Bacteriodes species



GUT MICROBIOTA MECHANISMS IN AUTOIMMUNE DISEASES (SLE)



Genetikai faktorok: MHC és nem MHC gének



- **HLA-DR2, DR3** és SLE
- **HLA-DRB1** erős asszociáció
- HLA-DRB1*1401, DRB1*1501, DQB2
- HLA-DR3 anti-dsDNS pozitivitás
- HLA DRB1*03:01:anti-SSA, anti-SSB pozitivitás
- DRB1*1501 kaukázusi és ázsiai populáció,
- DRB1*1503 afro-amerikai populáció

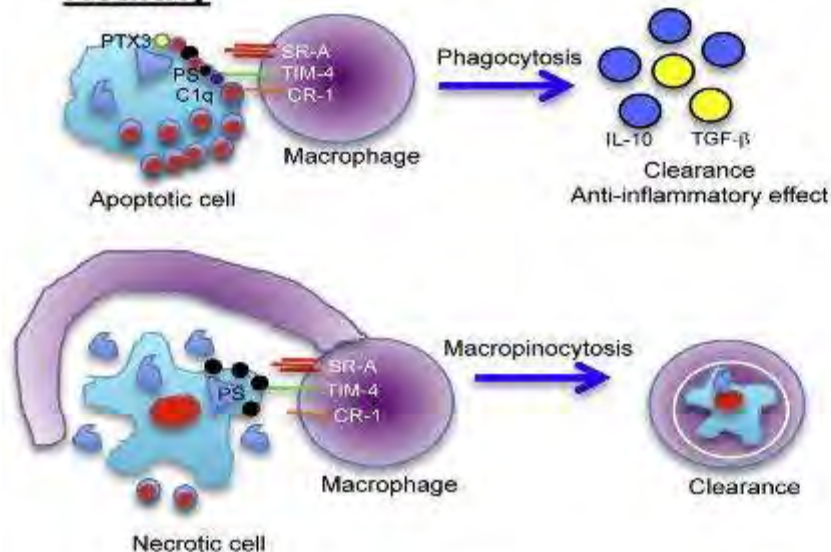
TABLE 1: Genetic variants associated with disease manifestations.

Disease phenotypes	Genetic variants associated with related SNPs
Skin involvement	ITGAM rs1143679 FCGR2A rs1801274 IL-6 174G/C VDR rs1168268
Serositis	TRAF3IP2 rs33980500, rs13190932, and rs13196377 PTPN2 rs2542151
Kidney involvement	HLADR2, HLADR3 rs2187668 STAT4 rs7574865, rs11889341, rs7568275, and rs7582694 ITGAM rs1143683, rs1143679 IRF5 rs2004640, rs2079197, and rs10488631 IRF7 rs4963128 TNFS4 rs2205960 DNase I Q222R
Neurologic disorder	TREX1 rs922075, rs6776700, rs6442123, rs2242150, and rs11797
Joint involvement	ITGAM rs1143679 FCGR2A, FCGR3A VDR rs3890733 Mir146a rs2910164
Hematological features	IL-21 rs907715 STK17A haplotype TAGTC
Immunologic disorders	Anti-dsDNA HLADR2, HLADR3 rs2187668 STAT4 rs7582694, rs7574865 ITGAM rs1143679, rs9888739 IRF5 rsrs10488631 SSA/SSB ITGAM rs1143679 IRF7 rs4963128 HCP5 rs3099855 HLADR3 rs2187668 RNP ITGAM rs1143679 Sm ITGAM rs7574865 aC1 HCP5 rs3099844 C3 reduction Mir146a rs2910164 C1 reduction TRAF3IP2 rs33980500

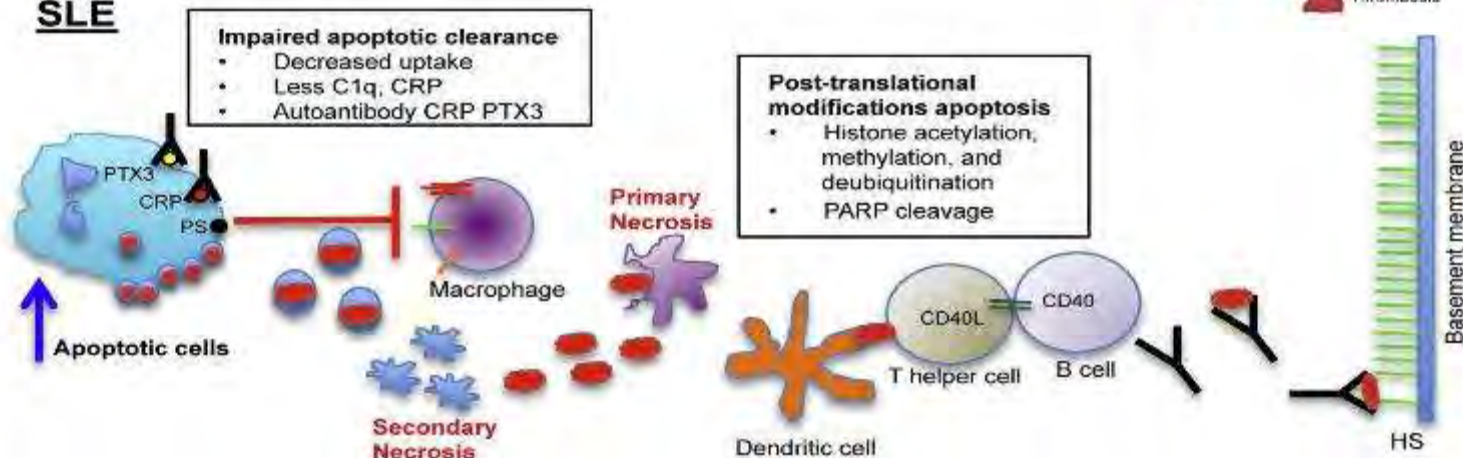
Fokozott antigén kínálat SLE-ben

Apoptosis and Necrosis

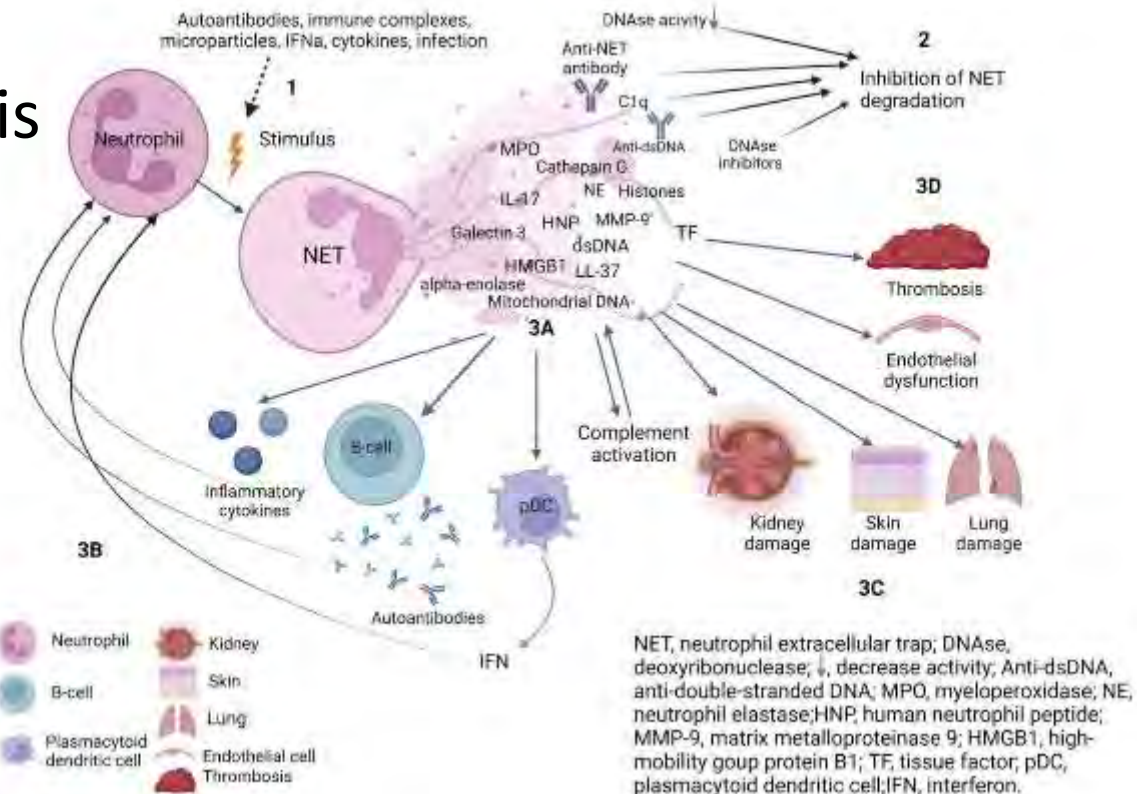
Healthy



SLE



NETosis



Antigén targetek SLE-ben

- **Nukleáris antigének:** ssDNA, dsDNA, histon, Sm, RNP
- **Cytoplazmában antigének:** SS-A, SS-B, ribosoma p protein, ANCA

- **Sejtfelszíneken:**

endothel sejtek,

vörösvértest,

neutrophilek,

lymphocyták,

trhobocyták

- **Egyéb antigének:**

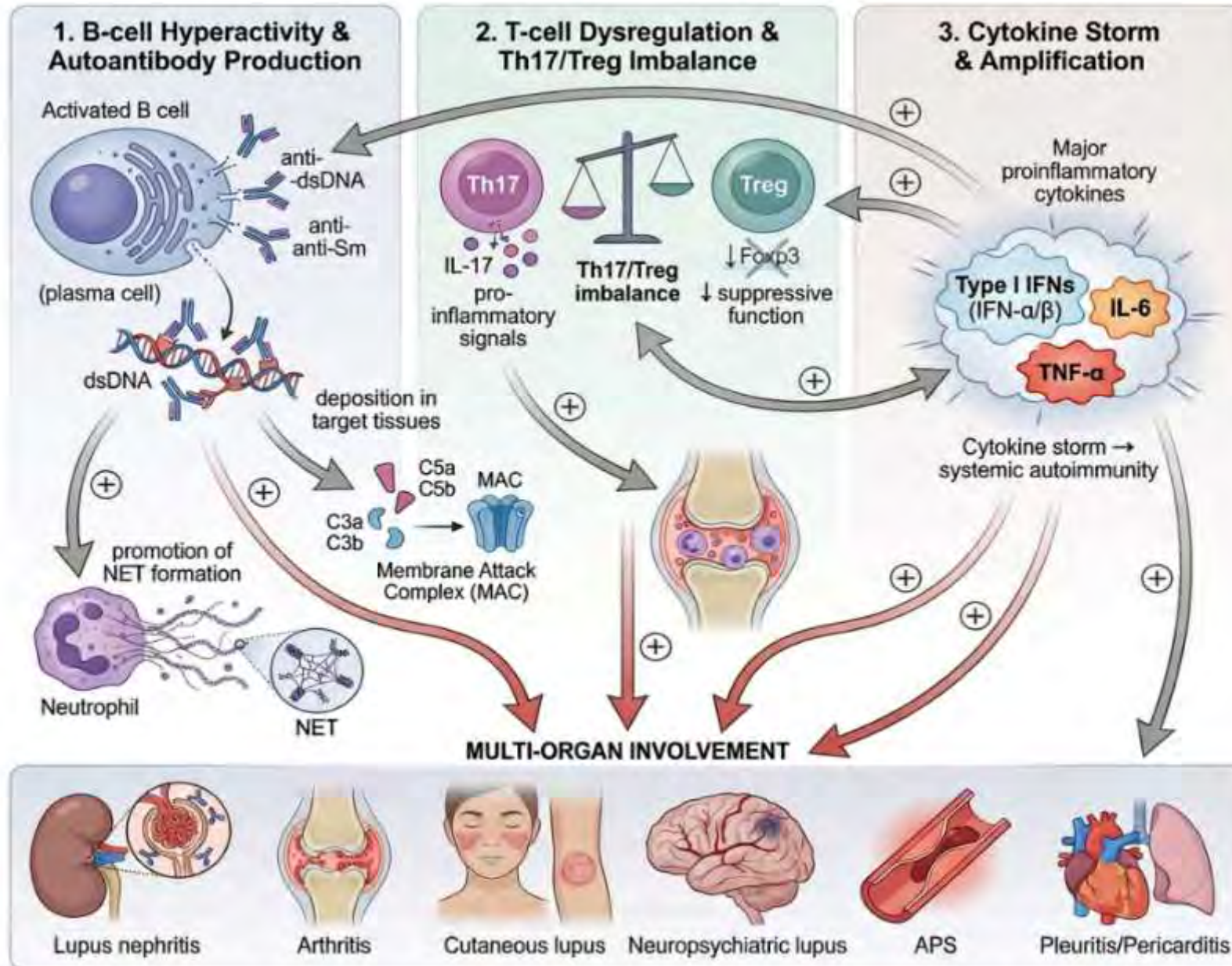
Beta-2 glycoprotein I,

foszfolipidek,

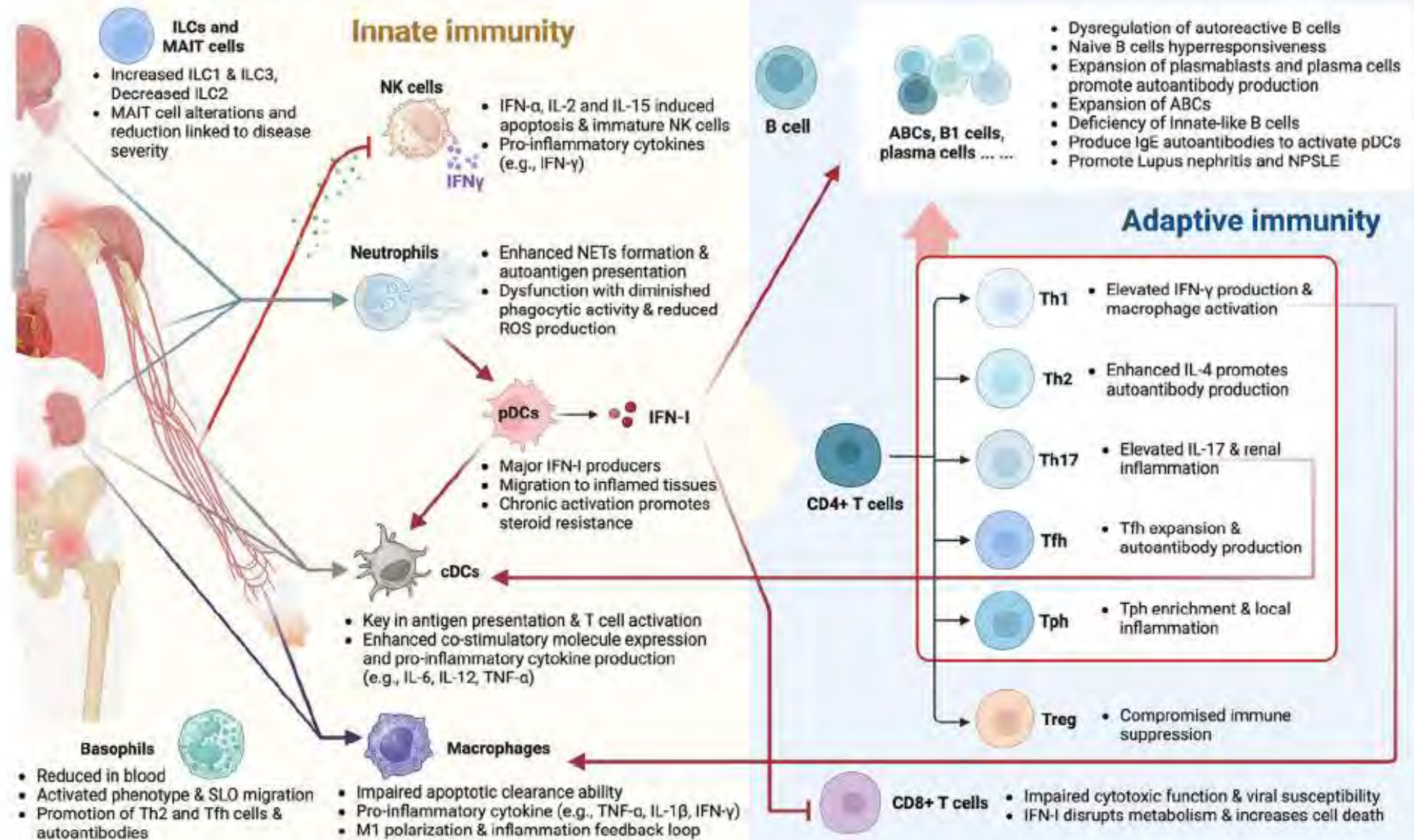
immunglobulinok

Antitest	Prevalencia	Szenzitivitás	Specificitás
anti-DNA	43-92 %	8-54 %	89-99 %
anti-nukleosome	59,8-61,9 %	52-61 %	87,5-95,7 %
anti-Sm	15-55,5 %	10-55 %	98-100 %
anti-hisztin	50-81 %	-	-
anti-C1q	4-60 %	28 %	92 %
anti-ribosome P protein	12-60 %	36 %	97-100 %
anti-SSA	36-64 %	-	-
anti-SSB	8-33,6 %	25.7 %	96,7 %
anti-RNP	23,3-49 %	8-69 %	25-82 %

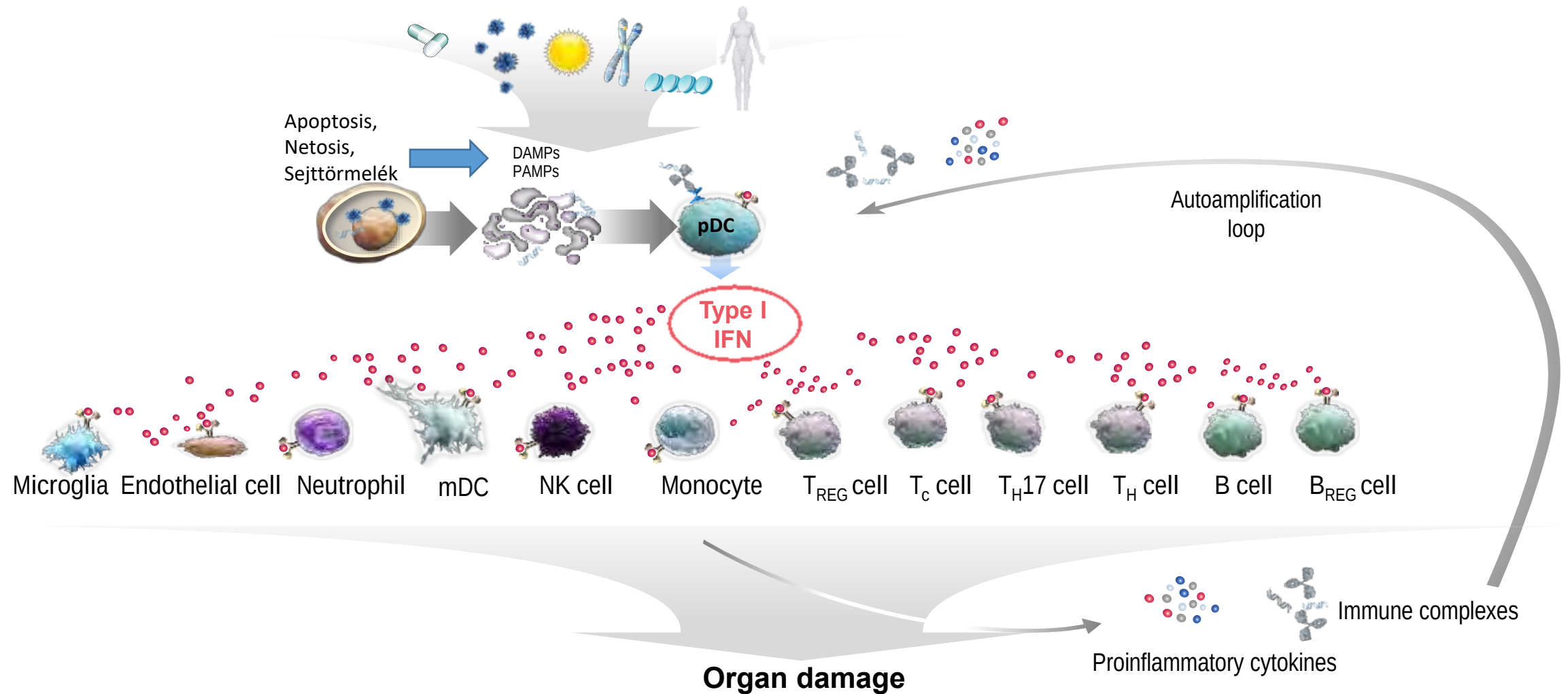
SLE pathogenesis



Altered immunoregulation in SLE



Az I-es típusú interferon az SLE pathomechanizmusában



Bőrtünetek



Mozgásszervi tünetek

- Kéz- és láb kis ízületeinek szimmetrikus nem errozív, nem deformáló polyarthritise
- Aszeptikus csontelhalás
- Myositis

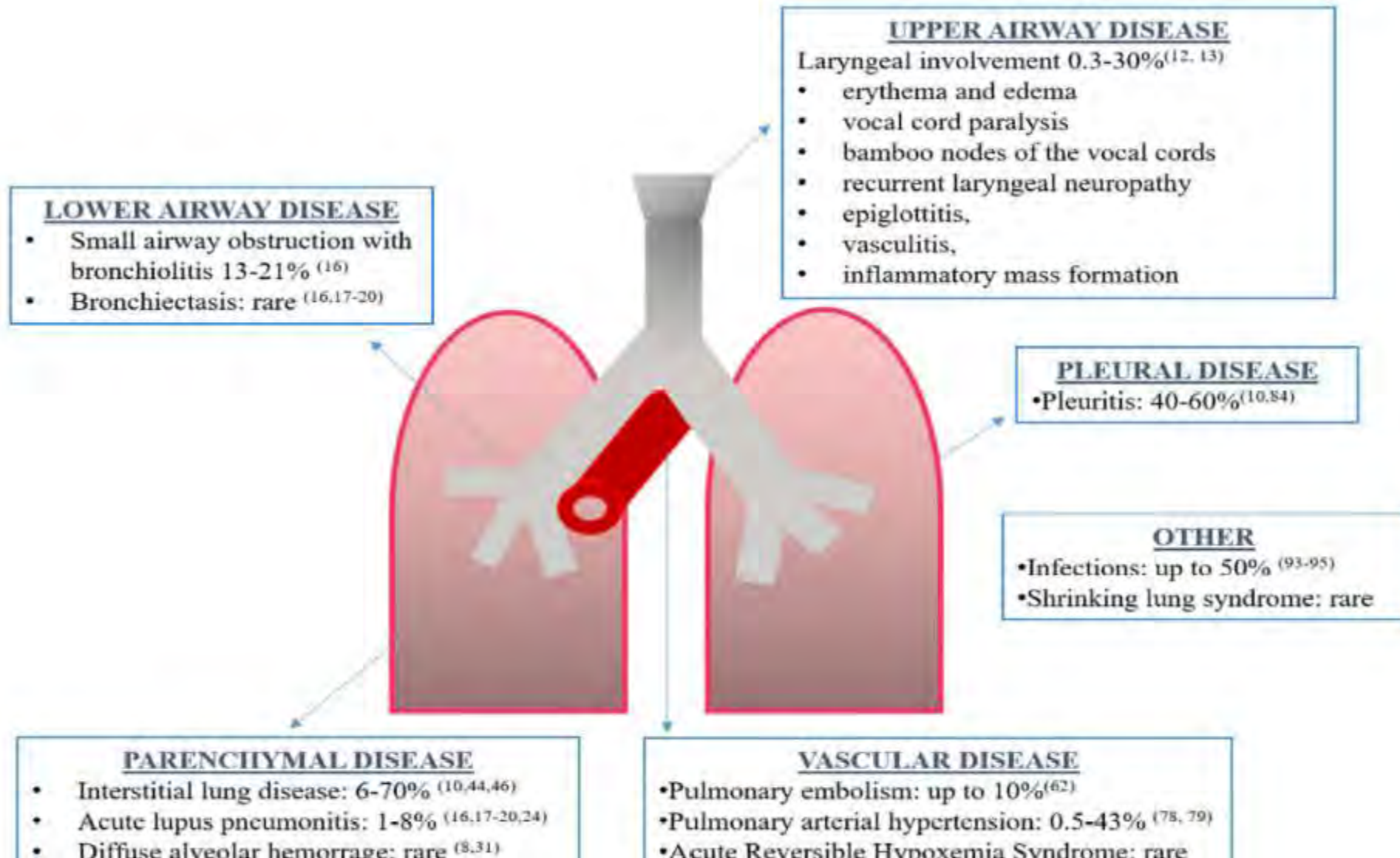


polyarthrititis



Jaccoud arthropathia

Légzőszervi eltérések



Kardiális eltérések

Vezetési zavarok

- Az anti-Ro/SSA pozitív anyák gyermekeinek 2 %-a érintett lehet
- Szinusz tachycardia
- AV blokk és szárblokk

Endokarditisz ~ 50-60 %

- Atípusos verrukózus endokarditisz
- Aktív léziók, melyek fibrin sapkát, fokális nekrozist és mononukleáris sejt infiltrációt tartalmaznak
- Gyógyult léziók, melyre vaszkularizált fibrózus szövet és néha kalcifikáció jellemző
- Valvulopátiák

Ateroszklerózis – rizikófaktorok

- Hagyományos kardiovaszkuláris rizikófaktorok
- Nagydózisú hosszantartó kortikoszteroid terápia
- Hosszú betegség fennállás
- Magas betegségaktivitás
- Magas gyulladásos markerek
- Immunológiai eltérések (anti-béta2 glikoprotein1, anti-ox LDL, anti-HsP 60/65), lipoproteinek, koagulációs paraméterek

Miokarditisz ~ 5-10 %

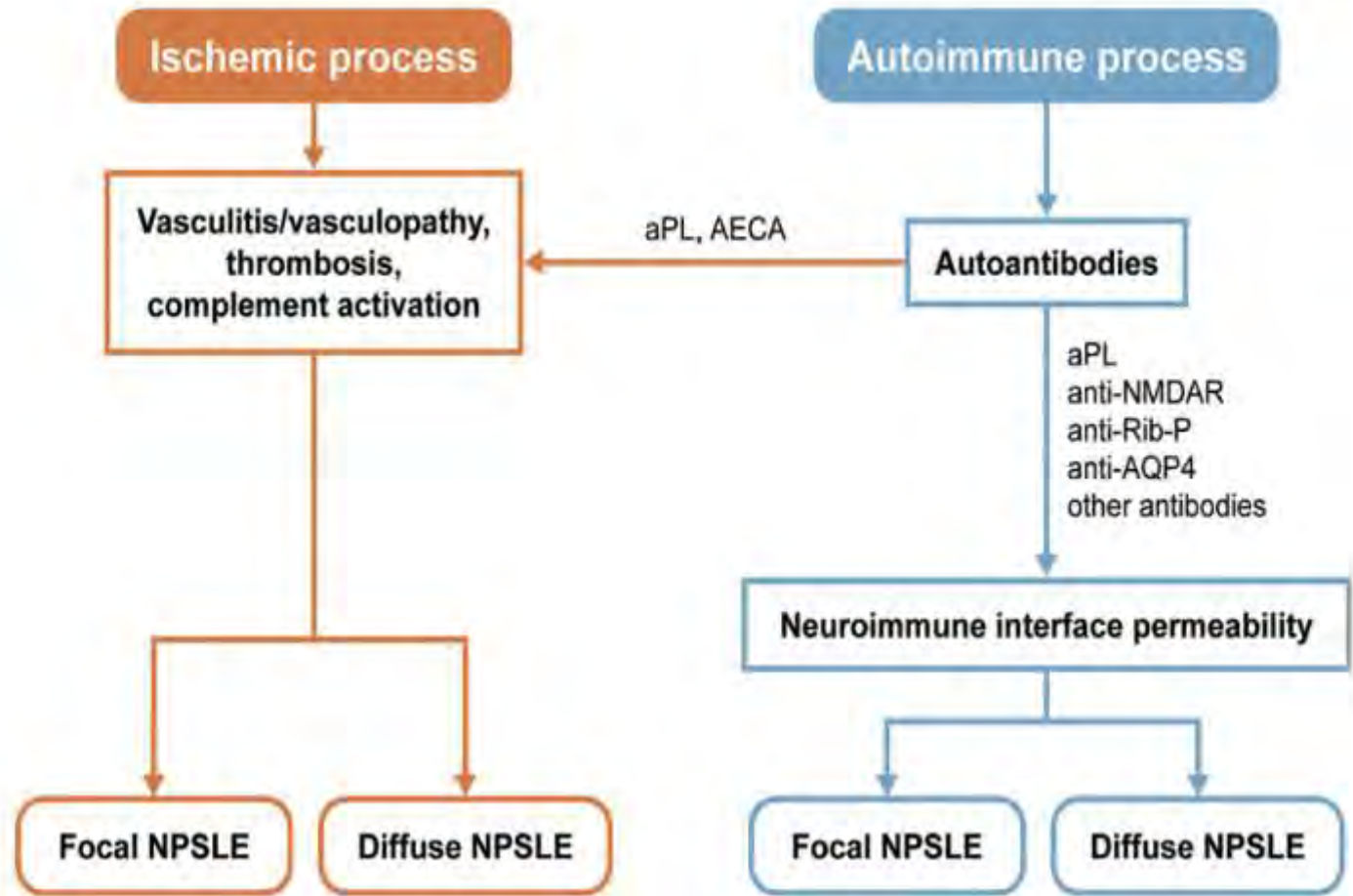
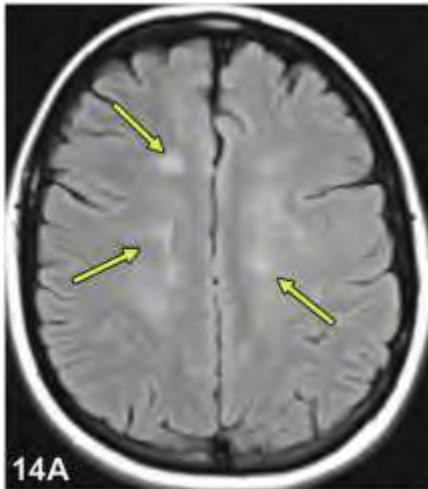
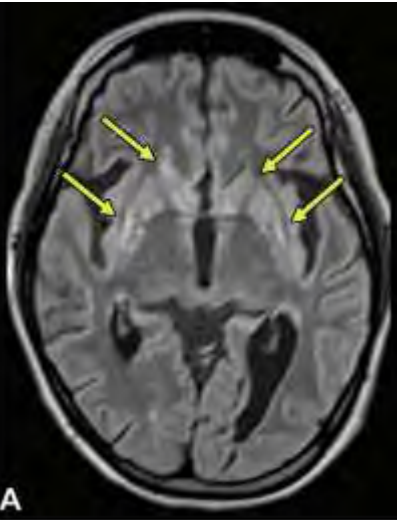
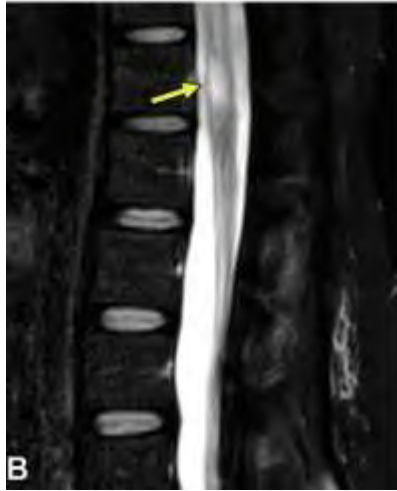
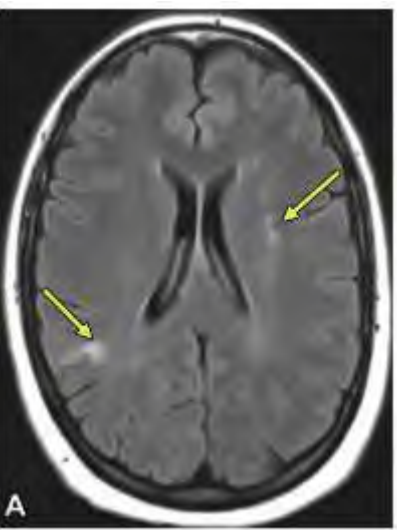
- Immunkomplex-mediált
- Anti-Ro/SSA antitestek
- Toxikus gyógyszerek pl. ciklofoszamid, klorogin

Perikarditisz ~ 11-54 %

- Akut – fibrinózus/szerofibrinózus
- Krónikus – fibrózus/fibrofibrinózus



Neuropsychiátriai tünetek



Neuropszichiátriai tünetek

(ACR ad hoc Committee, *Arthritis Rheum* 42:599-608,1999.)

CNS

- Asepticus meningitis
- Cerebrovascularis laesio
- Demyelinisatio syndroma
- Fejfájás (Migrén is)
- Chorea
- Myelopathia
- Epilepsia
- Psychosis (diff.dg: Steroid)
- Acut confusus állapot
- Cognitiv dysfunctio
- Szorongás
- Depresszió

PNS

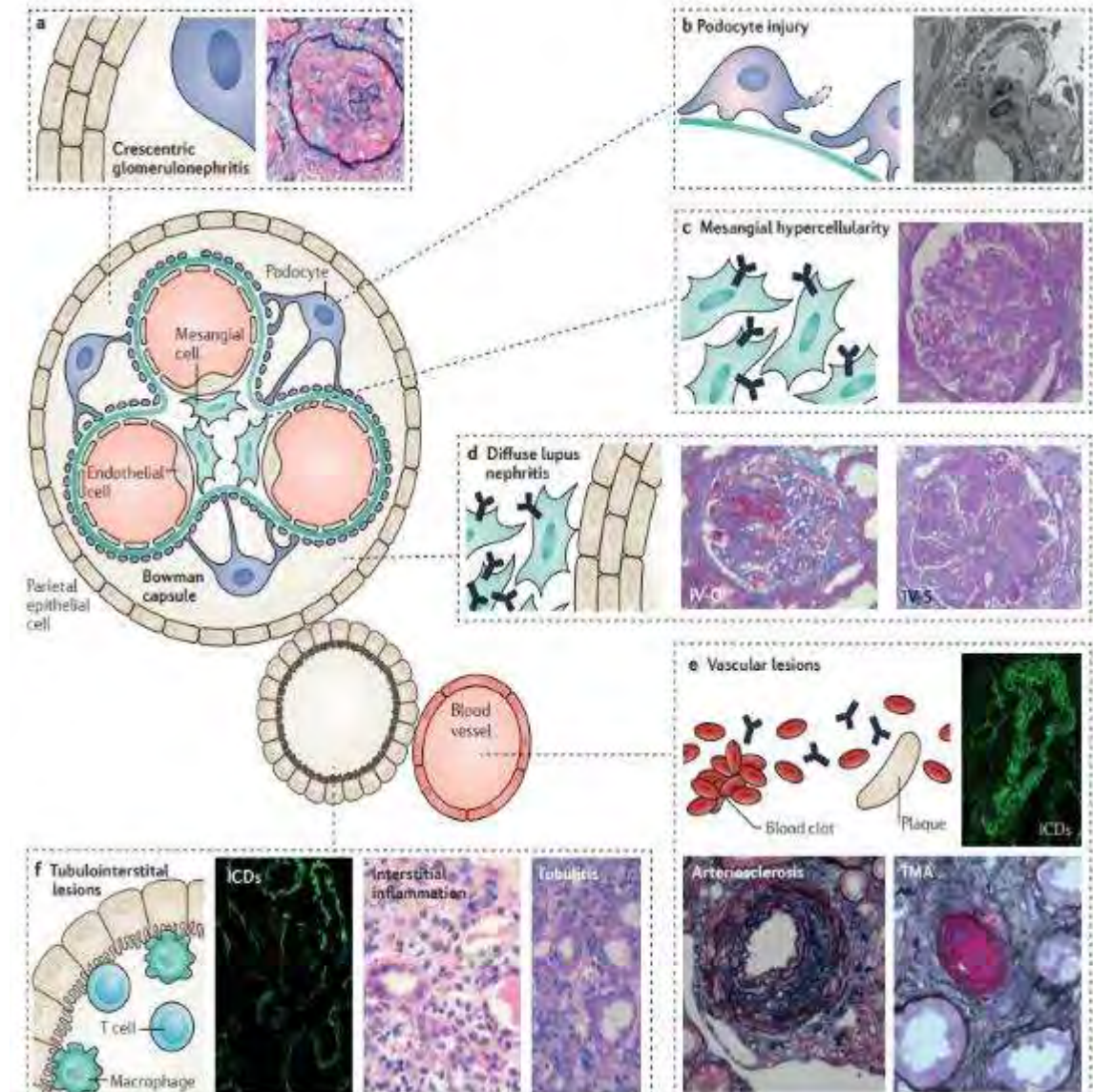
- Acut Guillain-Barré sy.
- Autonom idegrendszer zavarai
- Mononeuritis simplex/multiplex
- Myasthenia gravis like
- Cranialis neuropathia
- Polyneuropathia
- Plexopathia

NP clinical syndromes	Frequency range, %	
Cognitive dysfunction (mild) ^{a, c}	6.6–80	Frequent
Mood disorder ^a	7.4–65	
Anxiety ^a	6.4–40	
Headache ^a	12.2–28.3	
Seizures ^a	7.0–20	Common
Cerebrovascular disease ^a	8.0–15	
Psychosis ^a	0.6–11	Infrequent
Acute confusional status ^a	0.9–7	
Mononeuropathy ^b	0.9–6.9	
Polyneuropathy ^b	1.5–5.4	
Myelopathy ^a	0.9–3.9	
Demyelinating syndrome ^a	0.9–2.7	
Aseptic meningitis ^a	0.3–2.7	Rare
Autonomic disorder ^b	0.08–1.3	
AIDP (GBS) ^b	0.08–1.2	
Cranial neuropathy ^b	1.0	
Movement disorders (chorea) ^a	0.9	
Myasthenia gravis ^b	0.2	
Plexopathy ^b	NR	

- ✓ IC lerakódás, képződés helye szerint
 - ✓ Mesangiumban (Mesangiális)
 - ✓ Subendothelialisan (Proliferatív)
 - ✓ Subepitheliális (Membranosus)
- ✓ Crescent képződés
- ✓ Podocyta sérülés, podocytopathia
- ✓ Vasculáris károsodás: TMA, atherosclerosis
- ✓ Tubulointestinalis károsodás



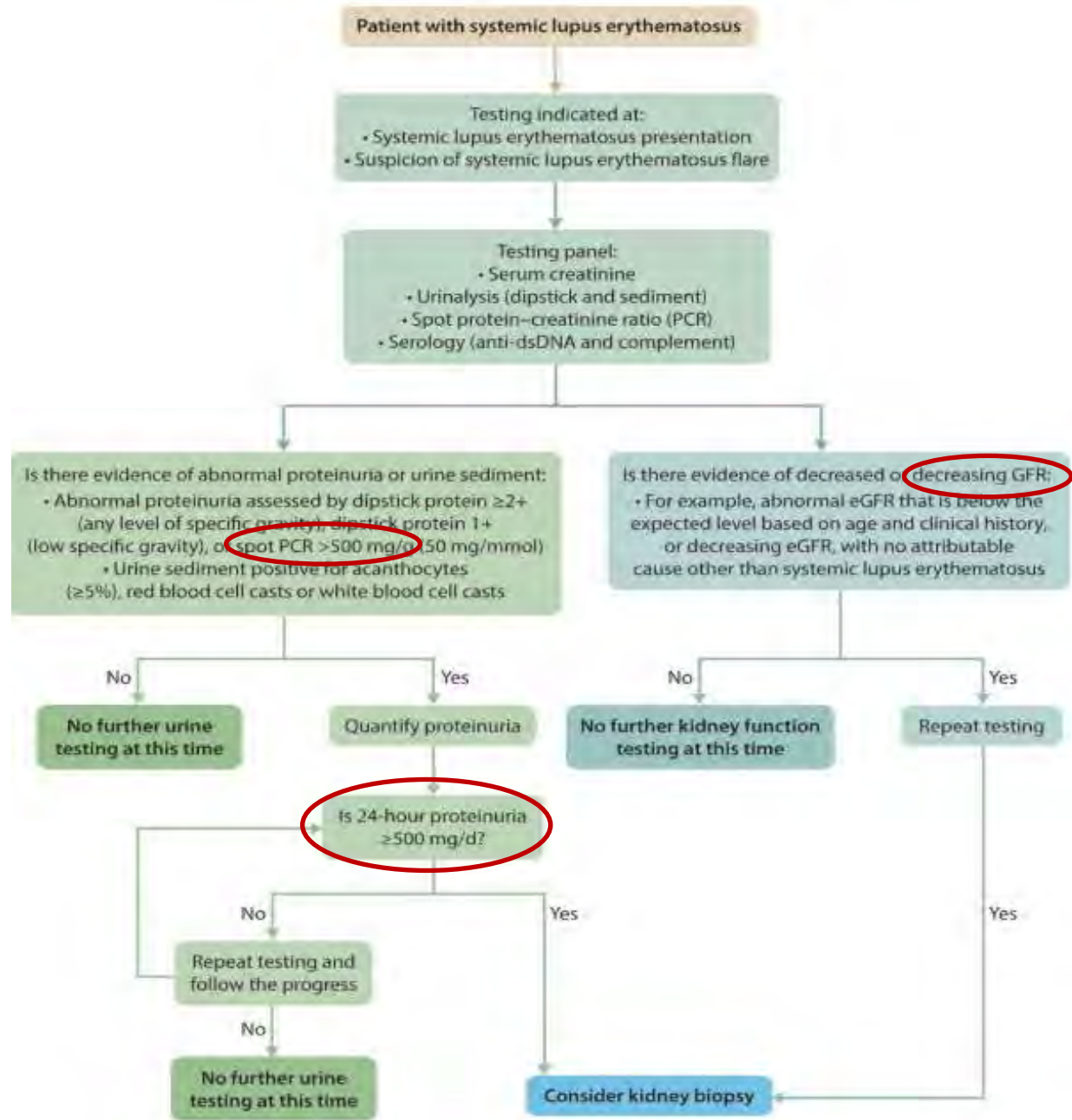
Lupus nephritis



Lupus nephritis diagnózisa

Klinikai tünetek:

✓ Proteinuria	100 %
✓ Haematuria	80 %
✓ Vvt cilinderek	30 %
✓ Egyéb cilinderek	30 %
✓ Nephrosis szindróma	50 %
✓ Veseelégtelenség	60 %
✓ Rapid progrediáló veseelégtelenség:	15 %
✓ Hypertonia:	30 %
✓ Tubularis eltérések	70 %



Lupus nephritis klasszifikációja

Table 3. The evolution of LN classifications (adapted after [21,37,38]).

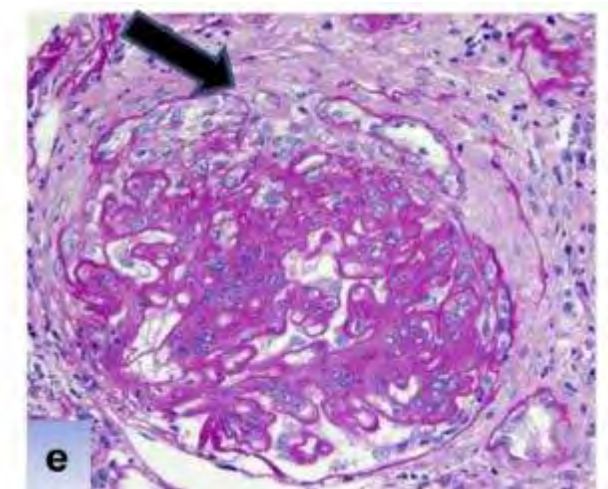
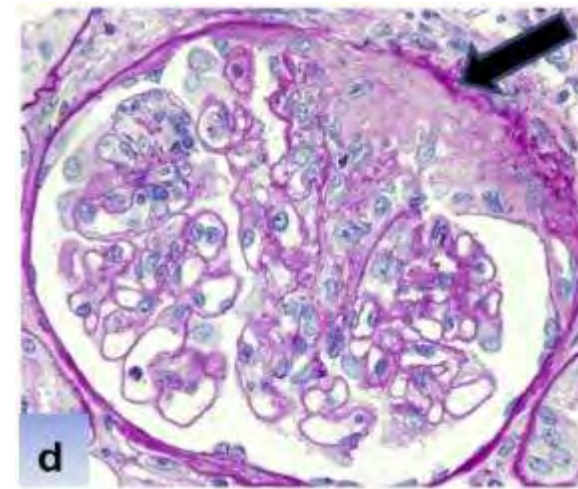
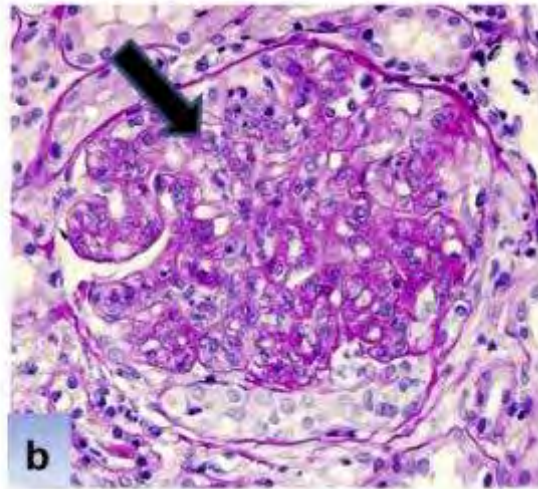
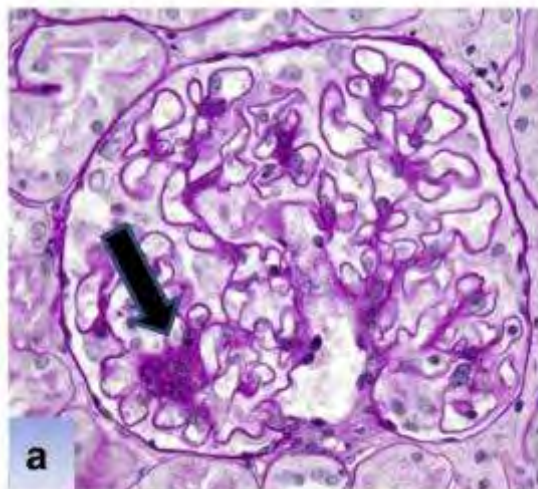
	WHO 1974	WHO 1982	ISN/RPS 2003	ISN/RPS 2018
Class I	Normal glomeruli	Normal glomeruli a. Nil (by LM/IF/EM) b. Normal by LM, but deposits by IF/EM	Minimal mesangial LN Normal by LM, mesangial deposits by IF/EM	Minimal mesangial LN Normal by LM, mesangial deposits by IF/EM
Class II	Purely mesangial disease a. Normocellular mesangium by LM but mesangial deposits by IF/EM b. Mesangial hypercellularity with mesangial deposits	Pure mesangial alterations a. Mild hypercellularity b. Moderate hypercellularity	Mesangial proliferative LN Mesangial hypercellularity with mesangial deposits by IF/EM	Mesangial proliferative LN Mesangial hypercellularity with mesangial deposits by IF/EM
Class III	Focal proliferative GN (<50%)	Focal segmental GN a. With "active" necrotizing lesion b. With "active" and sclerosing lesions c. With sclerosing lesions	Focal LN (<50%) Class III (A) Class III (A/C) Class III (C)	Focal LN (<50%) Modified NIH lupus nephritis activity and chronicity scoring system to be used instead of the A, C, and A/C parameters
Class IV	Diffuse proliferative GN (≥50%)	Diffuse GN a. Without segmental lesions b. With "active" necrotizing lesion c. With "active" and sclerosing lesions d. With sclerosing lesions	Diffuse LN (≥50%) Class IV-S (A) Class IV-G (A) Class IV-S (A/C) Class IV-G (A/C) Class IV-S (C) Class IV-G (C)	Diffuse LN (≥50%) Elimination of S and G subdivisions Modified NIH lupus nephritis activity and chronicity scoring system to be used instead of the A, C, and A/C parameters
Class V	Membranous GN	Diffuse membranous GN a. Pure membranous GN b. Associated with lesions of class II c. Associated with lesions of class III d. Associated with lesions of class IV	Membranous LN	Membranous LN
Class VI	Not defined	Advanced sclerosing GN	Advanced sclerosing LN	Advanced sclerosing LN

Lupus nephritis klasszifikációja

Table 2 | Proposed modified NIH lupus nephritis activity and chronicity scoring system

Modified NIH activity index	Definition	Score
Endocapillary hypercellularity	Endocapillary hypercellularity in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Neutrophils/karyorrhexis	Neutrophils and/or karyorrhexis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Fibrinoid necrosis	Fibrinoid necrosis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	(0–3) × 2
Hyaline deposits	Wire loop lesions and/or hyaline thrombi in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Cellular/fibrocellular crescents	Cellular and/or fibrocellular crescents in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	(0–3) × 2
Interstitial Inflammation	Interstitial leukocytes in <25% (1+), 25%–50% (2+), or >50% (3+) in the cortex	0–3
Total		0–24
Modified NIH chronicity index	Definition	Score
Total glomerulosclerosis score	Global and/or segmental sclerosis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Fibrous crescents	Fibrous crescents in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Tubular atrophy	Tubular atrophy in <25% (1+), 25%–50% (2+), or >50% (3+) of the cortical tubules	0–3
Interstitial fibrosis	Interstitial fibrosis in <25% (1+), 25%–50% (2+), or >50% (3+) in the cortex	0–3
Total		0–12

NIH, National Institutes of Health.

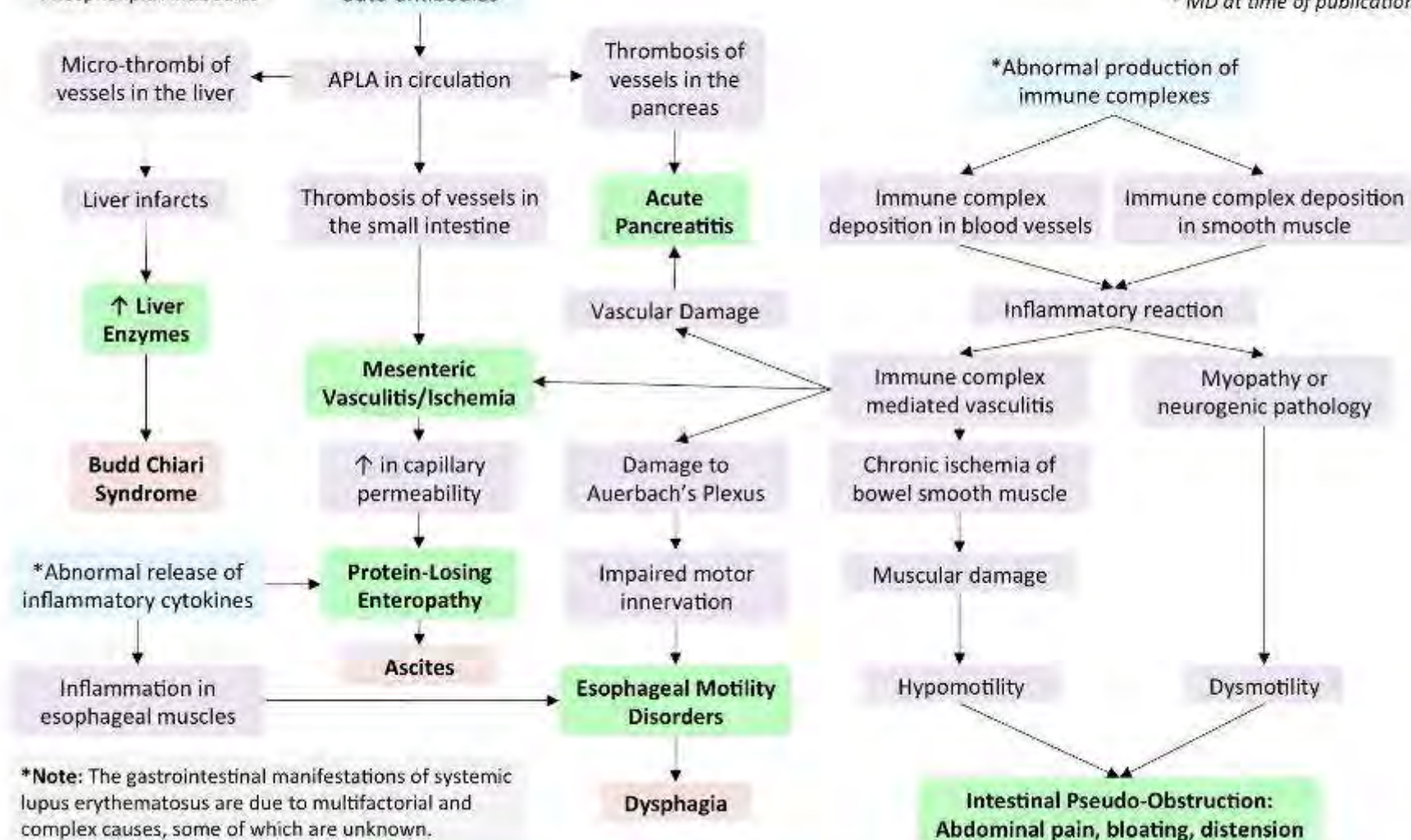


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time of publication

- **APLA** – Anti-Phospholipid Antibodies

*Production of auto-antibodies



***Note:** The gastrointestinal manifestations of systemic lupus erythematosus are due to multifactorial and complex causes, some of which are unknown.

Szemészeti manifesztációk

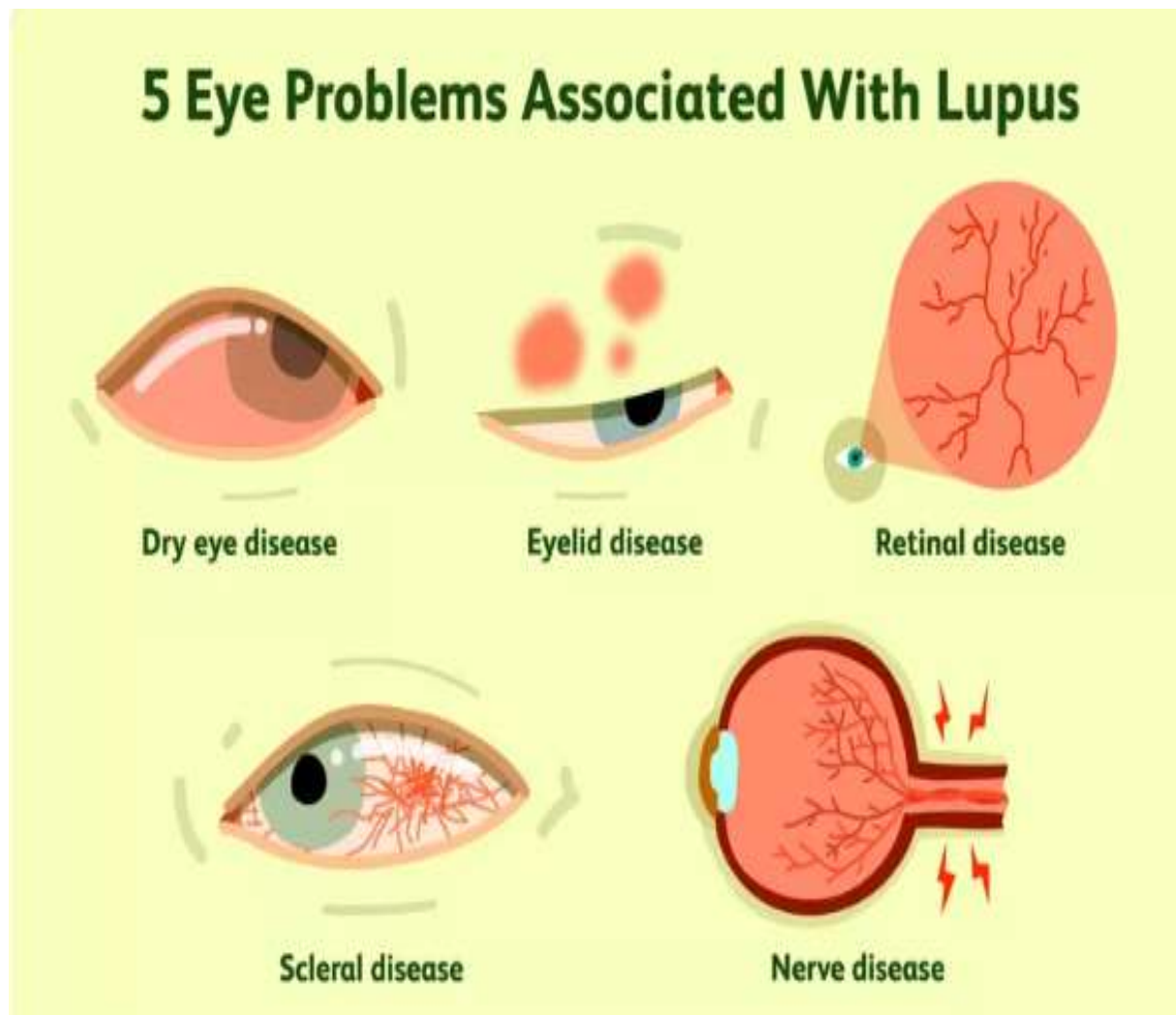
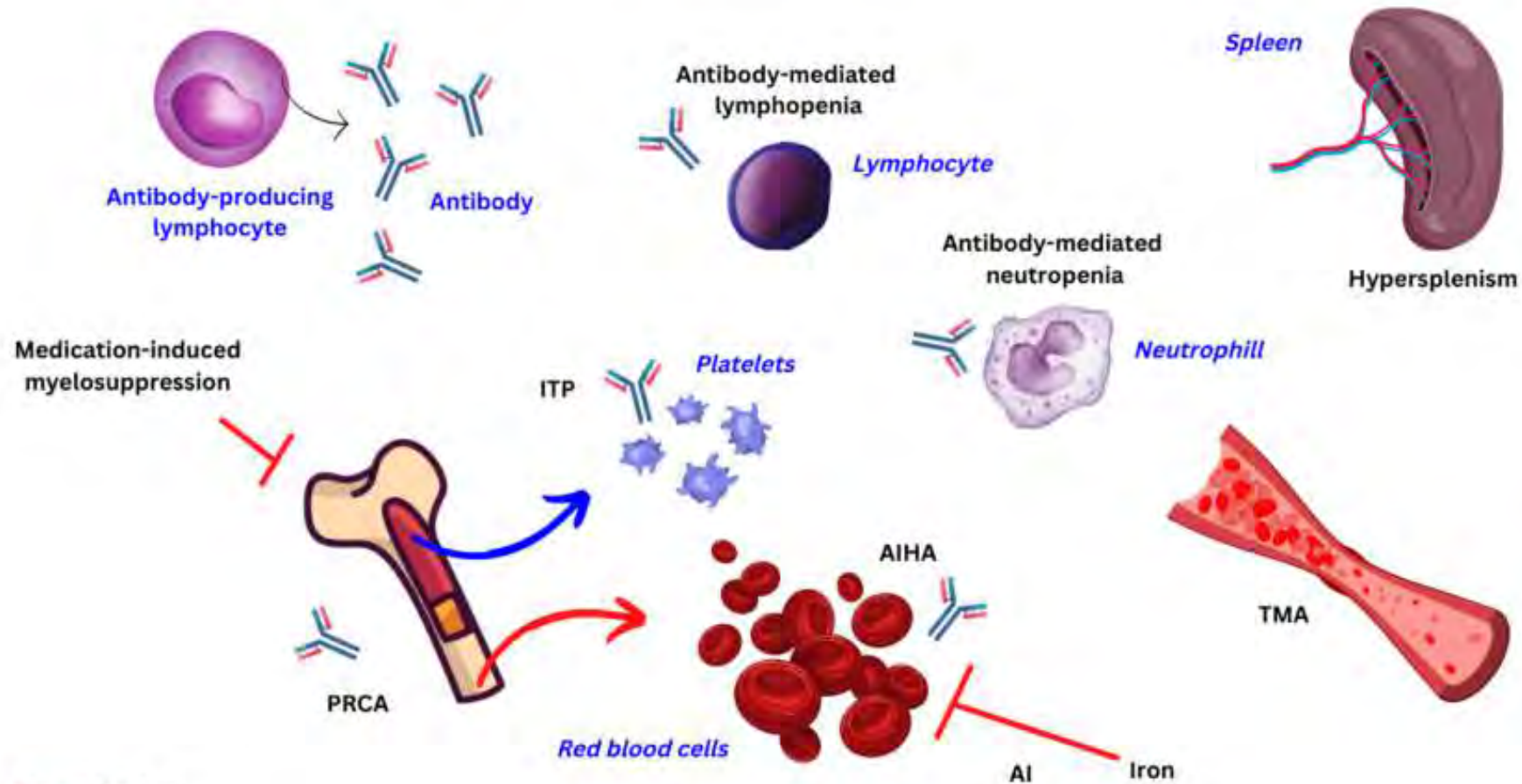


Table 1. Ocular manifestations of systemic lupus erythematosus (SLE)

Ocular Structure	Common ocular manifestations	Rare ocular manifestations
Cornea	Keratoconjunctivitis Sicca (most common)	Recurrent corneal erosion syndrome Peripheral ulcerative keratitis
Retina	Mild lupus retinopathy Mild retinal artery and vein occlusion	Severe vaso-occlusive retinopathy Vitreous hemorrhage Neovascular glaucoma Lupus choroidopathy
Uvea		Uveitis
Sclera		Scleritis Episcleritis
Neuro-ophthalmic	Sixth nerve palsy	Ischemic optic neuropathy Ischemic optic neuritis Blepharospasm
Orbit		Vasculitis Myositis Panniculitis

Mechanisms of hematologic manifestations in SLE





Systemic Lupus Erythematosus: Management strategies



Early SLE diagnosis

- ✓ Clinical suspicion
- ✓ Immunological tests
- ✓ ACR/EULAR 2019 Classification criteria
- ✓ SLERPI (ANA (-) patients)

Quantification of disease activity

- ✓ SLEDAI-2K
- ✓ BILAG 2004
- ✓ PGA
- ❖ in every visit



Assessment of organ damage



- SLICC Damage Index (SDI) yearly

Prevention of flares

- ✓ Detection of underlying risk factors for flares
- ✓ Assessment of changes in disease activity (BILAG Flare index/ SFI)

Health related quality of life

- Assessment PROs to evaluate the effect of an intervention on their life in every visit
 - ✓ LupusPRO
 - ✓ SF36
 - ✓ HRQoL



Treat to target strategies

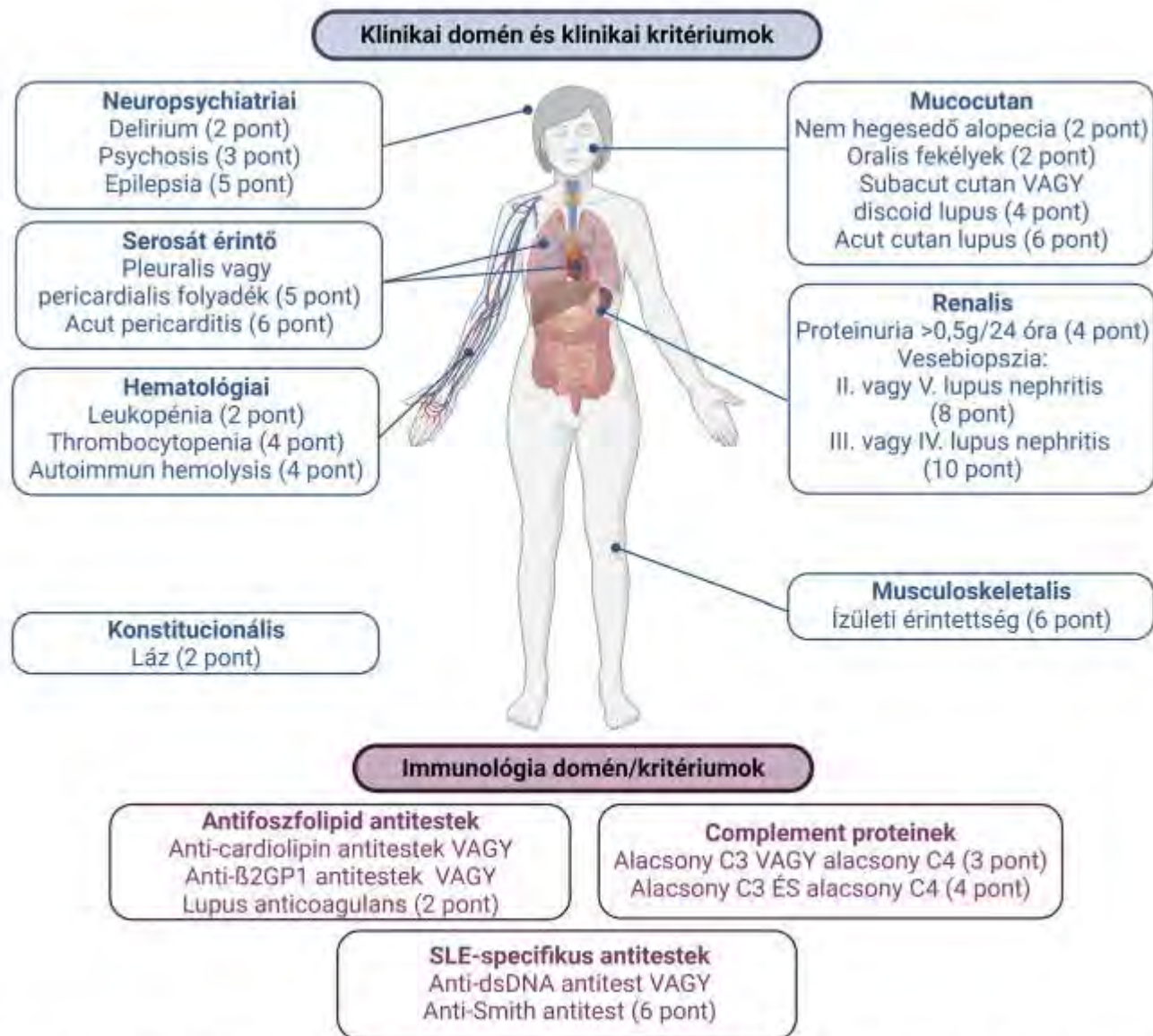
- Early use of biologic agents
- Minimization of treatment's toxicity
- Discontinuation of GCs first if possible
- Customization of therapy according to disease pattern



SLE management aims at sustained remission, prevention of organ damage and eventually improvement of quality of life

Klasszifikációs kritériumok

Korai diagnózis!



Kiindulási kritérium feltétel: **antinuclearis antitest (ANA) pozitivitás** $\geq 1:80$ titerben HEp-2 sejt kultúrán vagy ezzel egyenértékű vizsgálattal (most vagy korábban).
Kiegészítő kritériumok: **Létezik az SLE-nél valószínűbb magyarázat. Elegendő, ha egy adott kritérium egyszer észlelhető volt. Legalább egy klinikai kritérium jelen van és az összpontszám ≥ 10 pont.** Minden domén esetén csak a legmagasabb pontszám számít be az összpontszámába.

SLE aktivitás monitorozása

Weight	SLEDAI SCORE	Descriptor	Definition
8	_____	Seizure	Recent onset, exclude metabolic, infectious or drug causes.
8	_____	Psychosis	Altered ability to function in normal activity due to severe disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Exclude uremia and drug causes.
8	_____	Organic brain syndrome	Altered mental function with impaired orientation, memory, or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious, or drug causes.
8	_____	Visual disturbance	Retinal changes of SLE. Include cytoid bodies, retinal hemorrhages, serous exudate or hemorrhages in the choroid, or optic neuritis. Exclude hypertension, infection, or drug causes.
8	_____	Cranial nerve disorder	New onset of sensory or motor neuropathy involving cranial nerves.
8	_____	Lupus headache	Severe, persistent headache; may be migrainous, but must be nonresponsive to narcotic analgesia.
8	_____	CVA	New onset of cerebrovascular accident(s). Exclude arteriosclerosis.
8	_____	Vasculitis	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, or biopsy or angiogram proof of vasculitis.
4	_____	Arthritis	≥ 2 joints with pain and signs of inflammation (i.e., tenderness, swelling or effusion).
4	_____	Myositis	Proximal muscle aching/weakness, associated with elevated creatine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis.
4	_____	Urinary casts	Heme-granular or red blood cell casts.
4	_____	Hematuria	>5 red blood cells/high power field. Exclude stone, infection or other cause.
4	_____	Proteinuria	>0.5 gram/24 hours
4	_____	Pyuria	>5 white blood cells/high power field. Exclude infection.
2	_____	Rash	Inflammatory type rash.
2	_____	Alopecia	Abnormal, patchy or diffuse loss of hair.
2	_____	Mucosal ulcers	Oral or nasal ulcerations.
2	_____	Pleurisy	Pleuritic chest pain with pleural rub or effusion, or pleural thickening.
2	_____	Pericarditis	Pericardial pain with at least 1 of the following: rub, effusion, or electrocardiogram or echocardiogram confirmation.
2	_____	Low complement	Decrease in CH50, C3, or C4 below the lower limit of normal for testing laboratory.
2	_____	Increased DNA binding	Increased DNA binding by Farr assay above normal range for testing laboratory.
1	_____	Fever	>38° C. Exclude infectious cause.
1	_____	Thrombocytopenia	<100,000 platelets / x10 ⁹ /L, exclude drug causes.
1	_____	Leukopenia	< 3,000 white blood cells / x10 ⁹ /L, exclude drug causes.
TOTAL SLEDAI SCORE _____			

SLE-DAS disease activity categories



Treatment targets

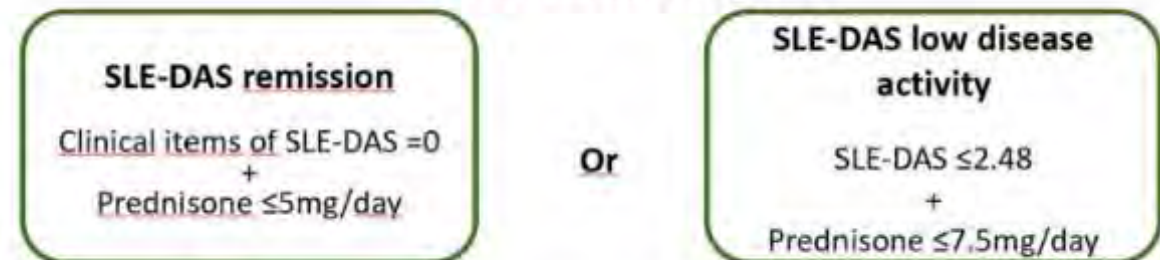
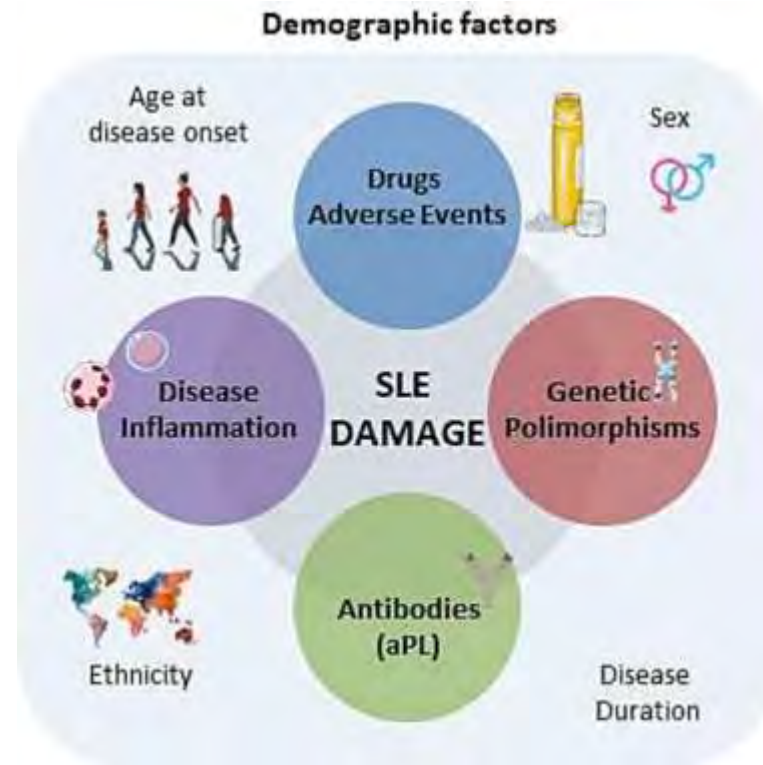
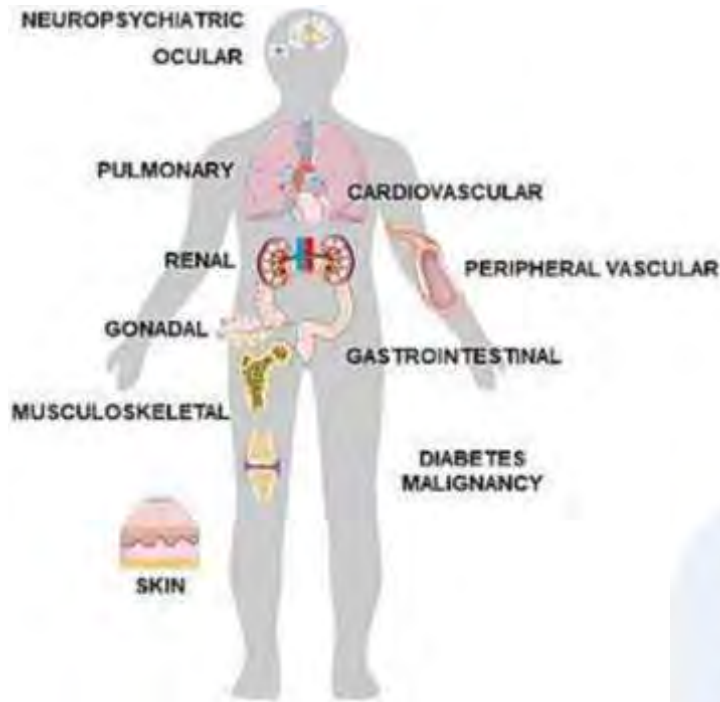


Fig. 2. SLE-DAS definitions of disease activity categories and treatment targets.

Krónikus károsodás és mérése



- Befolyásolható:
 - Aktivitás
 - Gyógyszeres terápia (GC)
 - Antifoszfolipid antitestek?

Organ (system)	Item	Score	Maximum score
Ocular (Either eye, by clinical assessment)	Any cataract, ever	1	
Neuropsychiatric	Retinal changes OR optic atrophy	1	2
	Cognitive impairment (e.g. memory deficits, difficulty with calculation, poor concentration, difficulty with spoken or written language, impaired performance level) OR Major psychosis	1	
	Seizures requiring therapy for at least six months	1	
	Stroke, ever (score 2 if more than 1) OR resection not for malignancy	1 (2)	
	Cranial OR peripheral neuropathy (excluding optic neuropathy)	1	
Renal	Transverse myelitis	1	6
	Estimated or measured glomerular filtration rate < 50%	1	
	Proteinuria 24h, ≥ 3.5 g	1	
Pulmonary	OR End-stage renal disease (regardless of dialysis or transplantation)	3	3
	Pulmonary hypertension (right ventricular prominence, or loud P2)	1	
	Pulmonary fibrosis (physical and chest radiograph)	1	
	Shrinking lung (chest radiograph)	1	
	Pleural fibrosis (chest radiograph)	1	
Cardiovascular	Pulmonary infarction (chest radiograph) OR resection not for malignancy	1	5
	Angina OR coronary artery bypass	1	
	Myocardial infarction, ever (score 2 if more than 1)	1 (2)	
	Cardiomyopathy (ventricular dysfunction)	1	
	Valvular disease (diastolic murmur, or a systolic murmur > 3/6)	1	
Peripheral vascular	Pericarditis for six months, OR Pericardiectomy	1	6
	Claudication for six months	1	
	Minor tissue loss (pulp space)	1	
	Significant tissue loss, ever (e.g. loss of digit or limb) (score 2 if more than 1 site)	1 (2)	
Gastrointestinal	Venous thrombosis with residual swelling, ulceration, OR venous stasis	1	5
	Infarction OR resection of bowel (below duodenum), spleen, liver, or gallbladder, ever, (score 2 if more than 1 site)	1 (2)	
	Mesenteric insufficiency	1	
	Chronic peritonitis	1	
	Stricture OR upper gastrointestinal tract surgery, ever	1	
Musculoskeletal	Pancreatic insufficiency requiring enzyme replacement or with pseudocyst	1	6
	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, ever (score 2 if more than one)	1 (2)	
	Osteomyelitis	1	
Skin	Ruptured tendons	1	7
	Scarring chronic alopecia	1	
	Extensive scarring of the skin or panniculus other than scalp and pulp space	1	
	Skin ulcers (excluding thrombosis) for more than 6 months	1	3
Gonadal	Premature gonadal failure (secondary amenorrhea, prior to age 40)	1	1
Endocrine	Diabetes (regardless of treatment)	1	1
Malignancy	Malignancy (exclude dysplasia) (score 2 if more than 1 site)	1 (2)	2

Gonzalez LA et al, Rev. colomb reumatol . (2 0 2 1); 28(S1):66–81

Ceccarelli F et al, Autoimmunity Rev., 2023, <https://doi.org/10.1016/j.autrev.2023.103374>

T2T SLE-ben és lupus nephritisben

Table 1 DORIS remission and LLDAS definitions

Criteria category	DORIS remission [7]	LLDAS [15]
Disease activity	Clinical SLEDAI-2K = 0 PGA < 0.5 Serological activity permitted	SLEDAI-2K ≤ 4, with no activity in major organ systems ^a PGA ≤ 1 No new lupus disease activity compared with the previous assessment Serological activity permitted
Permitted maintenance therapies	Low-dose GCs (≤ 5 mg/day) Antimalarials Stable doses of immunosuppressants including biologics	Prednisolone (or equivalent) dose ≤ 7.5 mg daily Well-tolerated standard maintenance doses of immunosuppressive drugs and approved biological agents

CNS central nervous system, DORIS Definition Of Remission In SLE, GC glucocorticoid, LLDAS Lupus Low Disease Activity State, PGA Physician's Global Assessment, SLE systemic lupus erythematosus, SLEDAI-2K SLE Disease Activity Index 2000

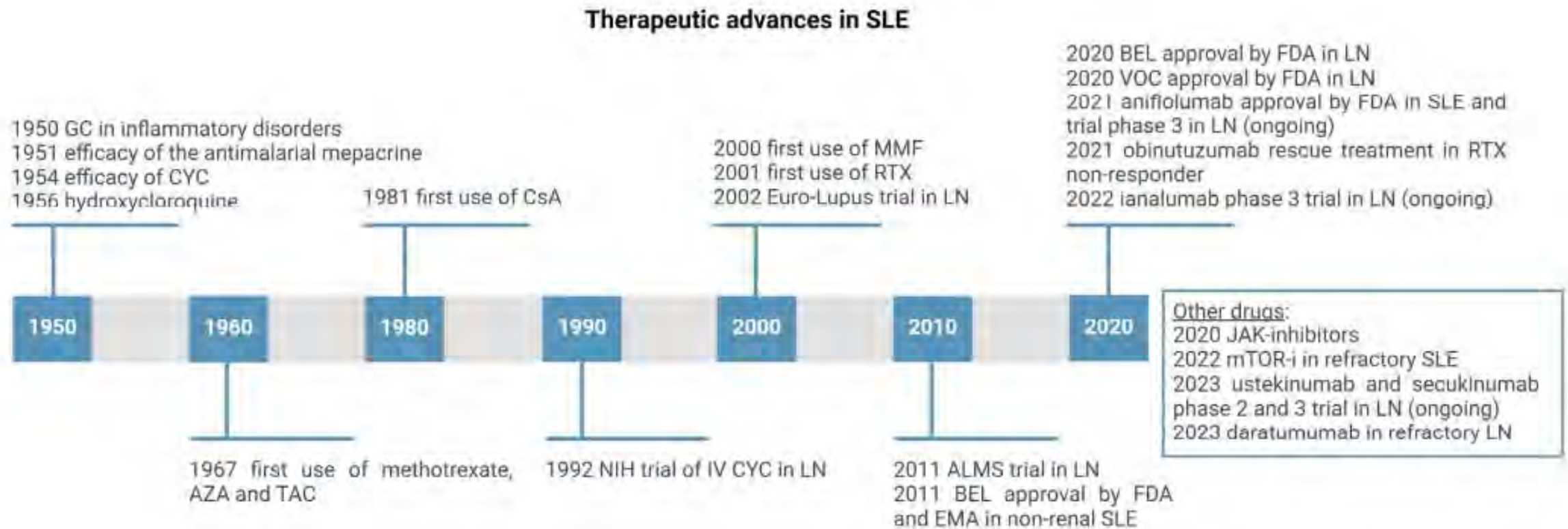
^aRenal, CNS, cardiopulmonary, vasculitis, and fever

Agner R. Parra Sa'nchez et al, *Rheumatol Ther* (2023) 10:1459–1477
 Nikolopoulos et al, *Mediterr J Rheumatol* 2024;35(Suppl 2):328-41
 S. TAKEYAMA AND M. KONO, *Immunological Medicine*, 2026.

Table 1. Comparing definition of clinical indicators among three recommendations and guidelines.

	2024 KDIGO guideline [13]	2024 ACR guideline [12]	2025 update of EULAR recommendations [11]
Treatment goals	Achieve CRR within 6–12 months of starting therapy, but could take >12 months	Achieve CRR within 6–12 months of starting therapy (may take >12 months)	Treatment should aim for optimization (preservation or improvement) of kidney function within 3 months, accompanied by a reduction in proteinuria of at least 25% by 3 months, 50% by 6 months, and a UPCR target <0.7 g/g by 12 months, and as low as possible afterwards
Complete renal response (CRR)	- Reduction in proteinuria <0.5 g/g measured as the UPCR from a 24-h urine collection - Stabilization or improvement in kidney function (±10–15% of baseline) - Within 6–12 months of starting therapy, but could take >12 months	- Reduction in proteinuria <0.5 g/g; AND - Stabilization or improvement in kidney function (+ 20% baseline i.e. at least 80% of baseline) - Within 6–12 months of starting therapy (may take >12 months)	- UPCR <0.5 g/g at any time point AND - Stabilization (if not improvement) of GFR to ≥80% of baseline value is desirable within the first 3 months
Primary efficacy renal response	- UPCR ≤0.7 g/g - eGFR that was no worse than 20% below the pre-flare value or ≥60 mL/min per 1.73 m² - No use of rescue therapy for treatment failure	-	-
Partial renal response (PRR)	- Reduction in proteinuria by at least 50% and to <3 g/g - Stabilization or improvement in kidney function (±10–15% of baseline) - Within 6–12 months of starting therapy	- Within 6–12 months of starting therapy; - Reduction in proteinuria by at least 50% and to <3 g/g; AND - Stabilization of kidney function (+ 20% baseline i.e. at least 80% baseline)	Proteinuria (with GFR normalization/stabilization) should be noted by 3 months, and at least 50% reduction in proteinuria
Inadequate renal response/ Nonresponse	Failure to achieve a partial or complete response within 6–12 months of starting therapy	Lack of achieving at least a PRR despite adherence to appropriate treatment for active LN of any class by 6–12 months	(Failure to achieve the treatment goals described above raises the possibility for non-responding or refractory disease)
Refractory disease / Persistently active or relapsing disease	No definition (Recommendation warned that the certainty of evidence on the management of LN "refractory" to standard initial therapy is marred by variable definitions of treatment response or refractoriness)	"Refractory disease" - Persistently active disease and absence of at least a PRR to at least two different appropriate 6-month courses of therapy for active LN of any class	"Persistently active or relapsing disease" - Disease not responding to initial immunosuppressive therapy

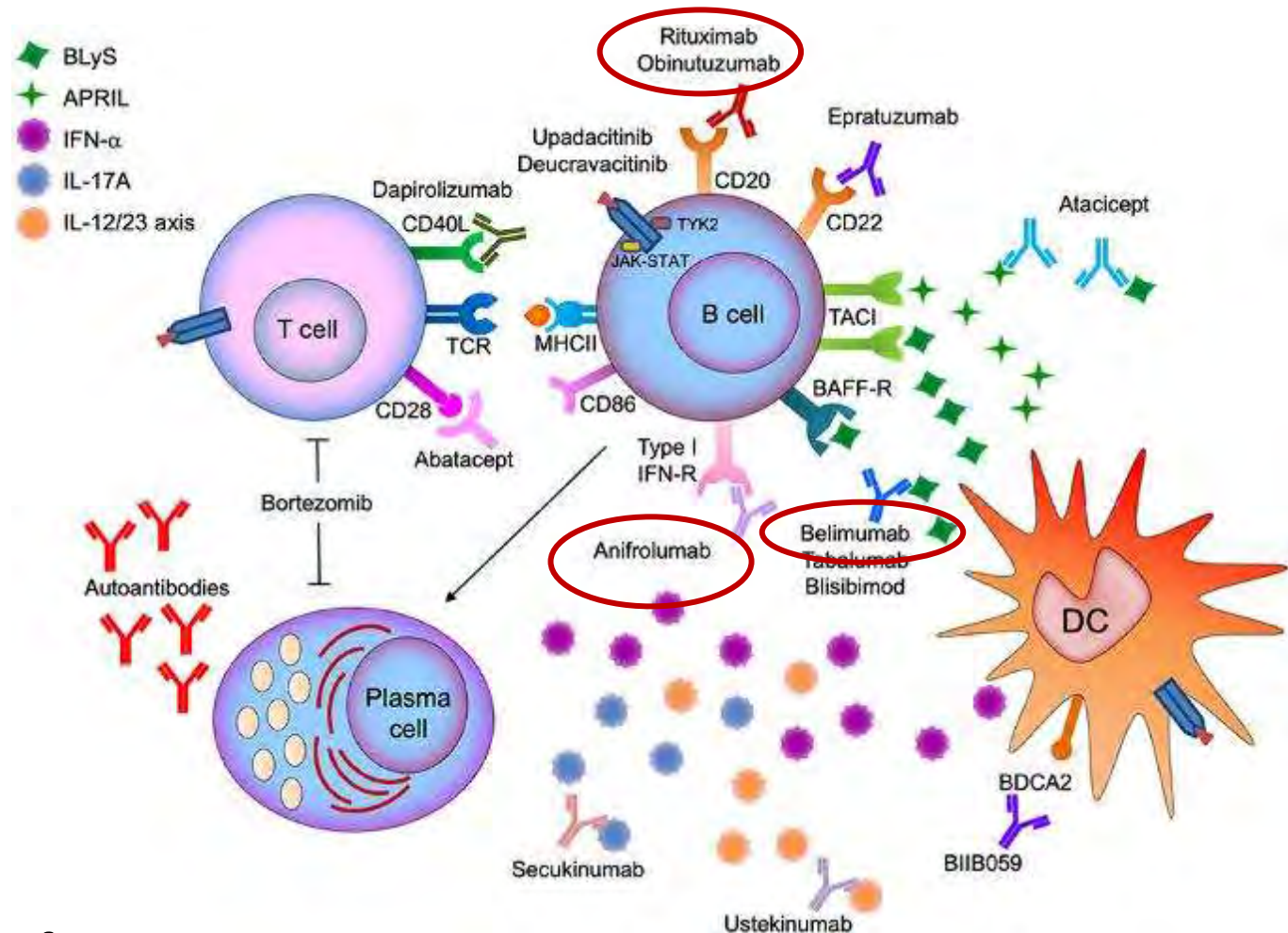
Terápiás lehetőségek fejlődése SLE-ben

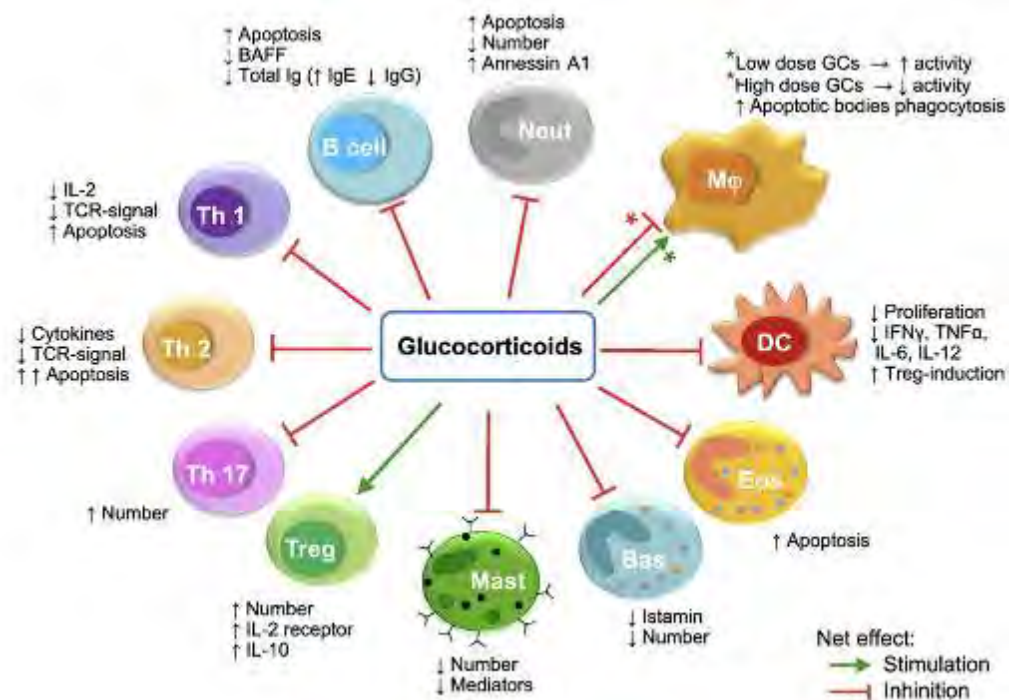
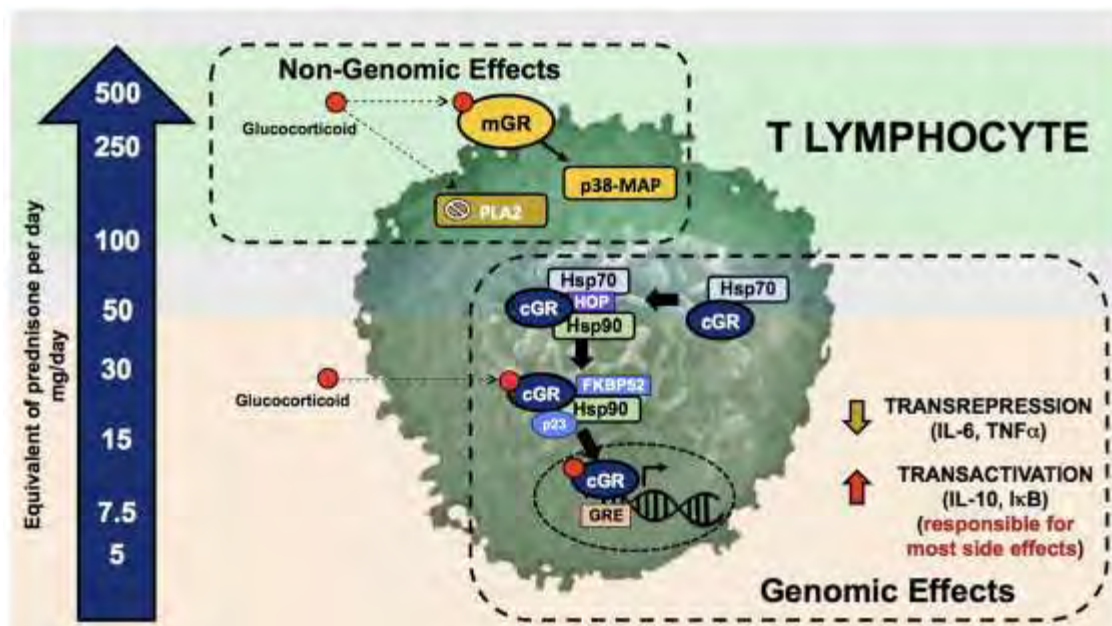


SLE terápiás lehetőségek, fejlesztések

- Kortikosteroid
- Chloroquin, HCQ
- Azathioprin
- Methotrexat
- Leflunomide
- Cyclophosphamid
- Cycloporine A
- Tacrolimus
- Voclosporin
- Mycophenolat mofetil

- IVIG
- Plazmaferézis
- CAR-T sejt kezelés
- Autológ őssejt transzplantáció





Glükokortikoidok hatásmechanizmusa

Glucocorticoid	Anti-Inflammatory Effect (Genomic Way)	Anti-Inflammatory Effect (Non-Genomic Way)
Cortisol/hydrocortisone	1	Low
Prednisone/prednisolone	4	4
Methylprednisolone	5	10–15
Dexamethasone	20–30	20
Betamethasone	20–30	<4

Table 2. Summary of the mechanisms of action of glucocorticoids.

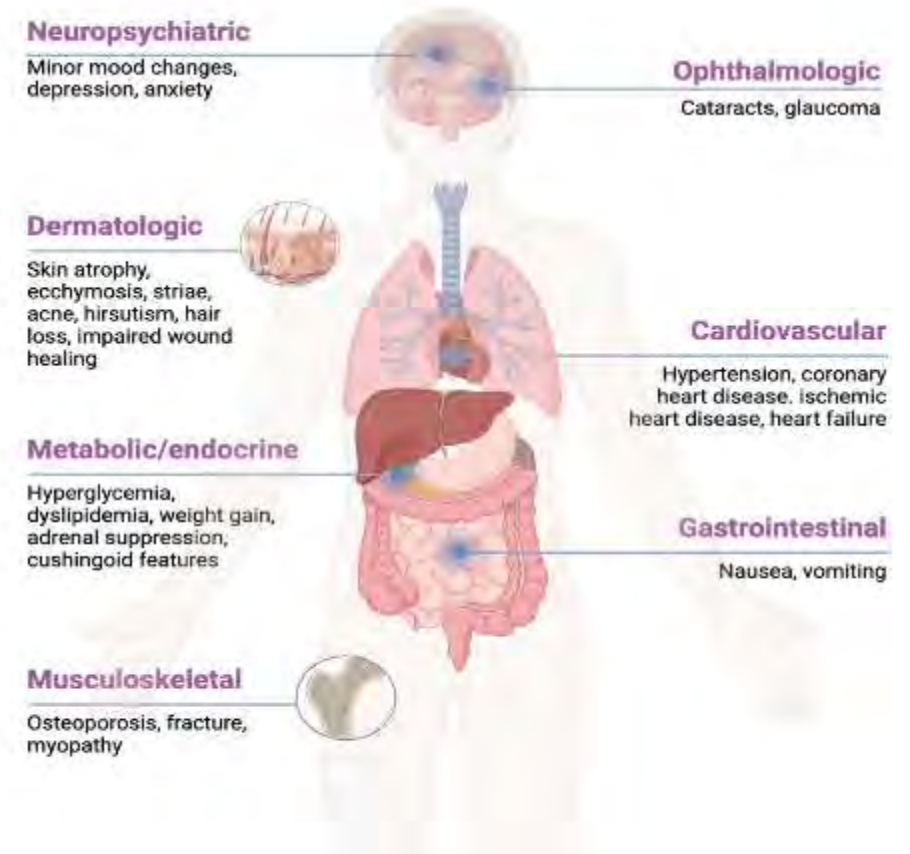
	Genomic Pathway	Non-Genomic Pathway
Cells targeted	All the organism	Inflammatory cells
Mechanism of action	Genomic modulation	Membrane receptor and intracellular inflammatory pathways
Start of action	~4 to 6 h	~15 min
Saturation dose of the immunosuppressive – anti-inflammatory effects	~100% at 30 to 40 mg/day of prednisone-equivalent	Unknown
Minimum effective dose	2.5 to 5 mg/day of prednisone-equivalent	Over 100 mg of prednisone-equivalent
Maximum effective doses that minimize adverse effects	30 to 40 mg/day of prednisone-equivalent (for trans-repression)	500/day mg of methylprednisolone
Damage accrual with cumulative doses	Proven	Not proven
Glucocorticoids acting by this way	All	Mainly methylprednisolone and dexamethasone

Mejía-Vilet and Ayoub, *Front.Med.*, 2021.
 Reichardt S.D et al, *Cells* 2021, 10, 2921
 M.Zen et al. *AutoimmunityReviews*10(2011)
 Porta S et al, *J. Clin. Med.* 2020, 9, 2709.

Kortikoszteroid terápia

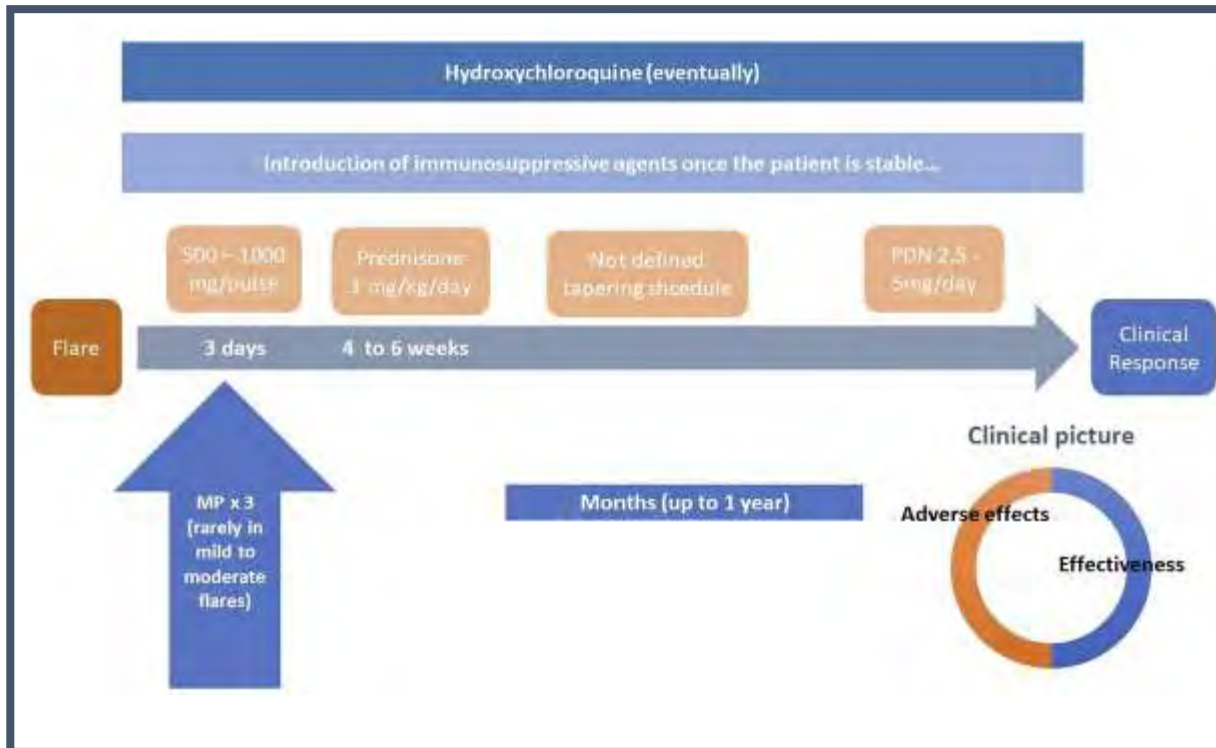
- Minimalizáció: **5 mg/nap** prednisolon equivalens
- Számos mellékhatás, krónikus károsodás
- Nincs kontrollált vizsgálat a különböző szteroid dózistra és csökkentésre
- Szteroid spórolás módjai
 - Nem mindenkinek szükséges
 - Pulzus iv. adás, majd alacsonyabb per os adag
 - Korai immunszuppresszív terápia
 - Multi-target terápia
 - Célzott terápiák
 - Ne felejtsük el elhagyni

Side effects of long-term systemic corticosteroid exposure

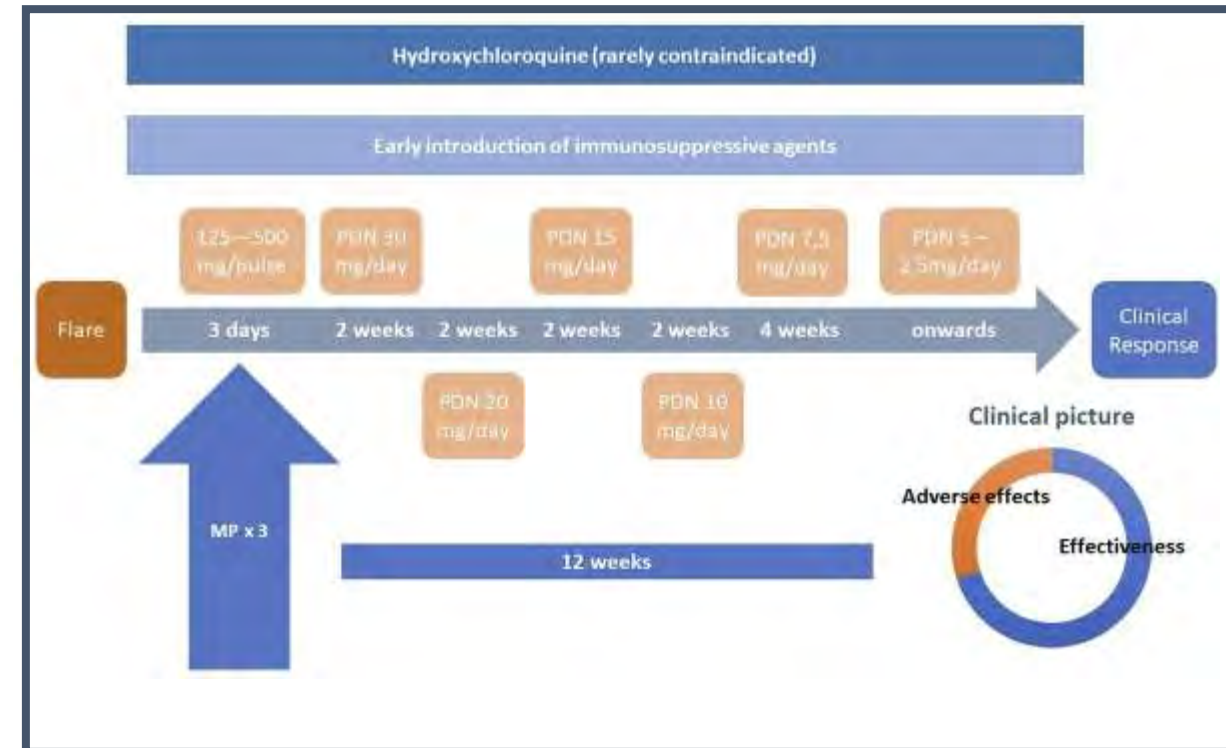


Paradigma váltás szteroid használatban SLE-ben

Régi paradigma

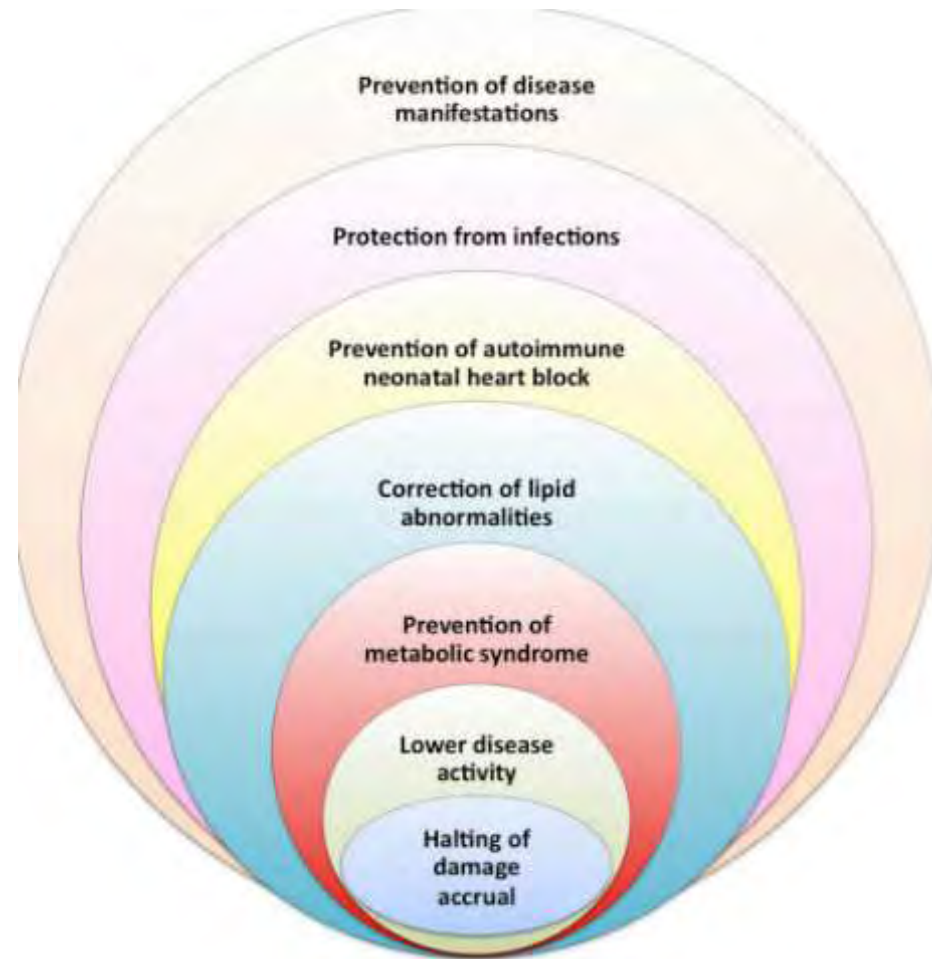


Új paradigma



Antimaláriás szerek

- Kontraindikáció hiányában minden betegnek: Chloroquin, hydroxichloroquin
- Alacsony dózis 2x emeli a flare-k, 6x a súlyos flare-k rizikóját
- Csökkenti lupus nephritisben a relapsust, ESRD-t
- Javítja a túlélést
- Csökkenti a krónikus szervi károsodások kialakulását
- Kedvező lipid és glikémiás kontroll
- Javítja az endothel sejtek funkcióját
- Kedvező cardiovasculáris hatás
- Véd a súlyos bakteriális és virális fertőzéstől
- Terhességben csökkenti a flare-ek gyakoriságát
- Dózis: HCQ-5 mg/tskg , szérum szint monitorozás?



Immunszuppresszánsok

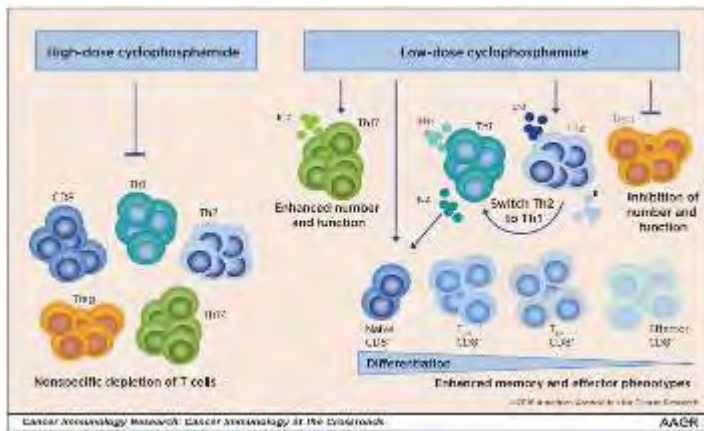
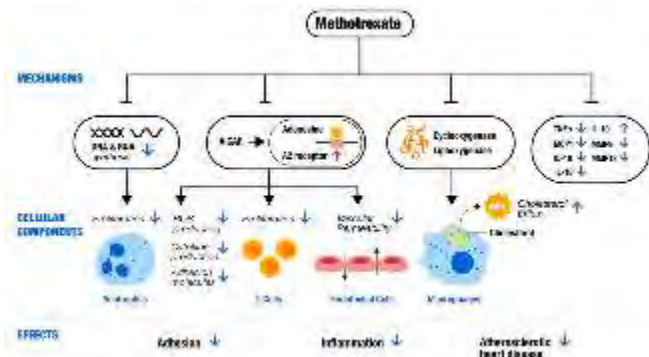


FIGURE 1. Mechanism of action of cyclophosphamide. Cyclophosphamide is converted to active metabolites (phosphoramide mustard and acrolein) which then target DNA and proteins, leading to cell death.



	Immunosuppressive agent	Dose	Main indications in SLE	Adverse events	Special issue
immuno-	CYC	Low dose 500 mg, iv, biweekly, 4 times High dose 0.75–1.0 mg/m ² , iv, monthly, 6 times	Severe organ involvement: LN NPSLE Vasculitis	Cystitis (especially high doses) Gastrointestinal Hematological	Teratogenic effect Premature ovarian failure Malignancies To prevent bladder toxicity—Mesna administration For overall less toxicity—regimen according to Euro-Lupus [51]
	MMF	2.0–3.0 g/day, orally	Hematologic Skin LN in induction and maintenance therapy	Gastrointestinal Hematological	Teratogenic effect
	AZA	1.0–5.0 mg/kg/day, orally Pregnancy and lactation: ≤ 2.0 mg/kg/day, orally	Hematologic Skin LN in maintenance therapy	Gastrointestinal Hepatotoxicity Hematological	Drug interactions with allopurinol Safe during pregnancy and lactation Mild GCs-sparing effect
	MTX	7.5–25 mg/week, orally/sc	Joints Skin Serositis	Gastrointestinal Hepatotoxicity Hematological	Teratogenic effect Mild GCs-sparing effect Use with caution in elderly patients and in patients with reduced GFR (< 30 ml/min)

Calcineurin inhibitorok

Efficacy and safety of voclosporin versus placebo for lupus nephritis (AURORA 1): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial

Brad H Rovin, Y K Onno Teng, Ellen M Ginzler, Cristina Amiens, Dawn J Caster, Juanita Romero-Diaz, Keisha Gibson, Joshua Kaplan, Laura Lisk, Sandra Navatra, Samir V Parikh, Simrat Randhawa, Neil Salomons, Robert B Huizinga

Calcineurin inhibitors

CsA 3.0—5.0 mg/kg/day, orally
LN
Skin
Hematologic
Safe during pregnancy and lactation
Continuing with folic acid during pregnancy

Voclosporin 23.7 mg, twice daily, orally
LN
Combination therapy with MMF in LN
Dose adjustment based on eGFR
Advantages compared with CsA and tacrolimus with respect to dosing and tolerability

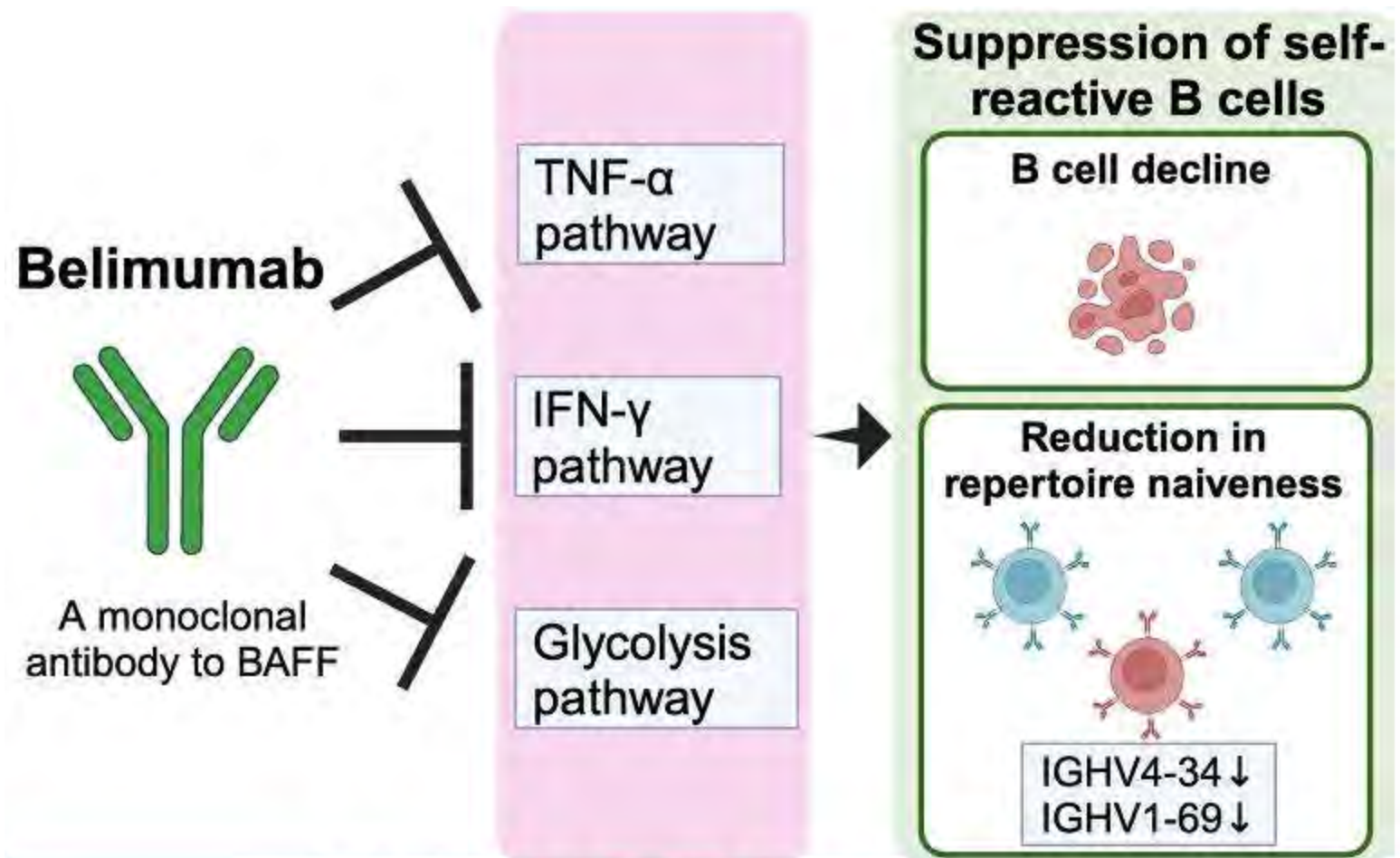
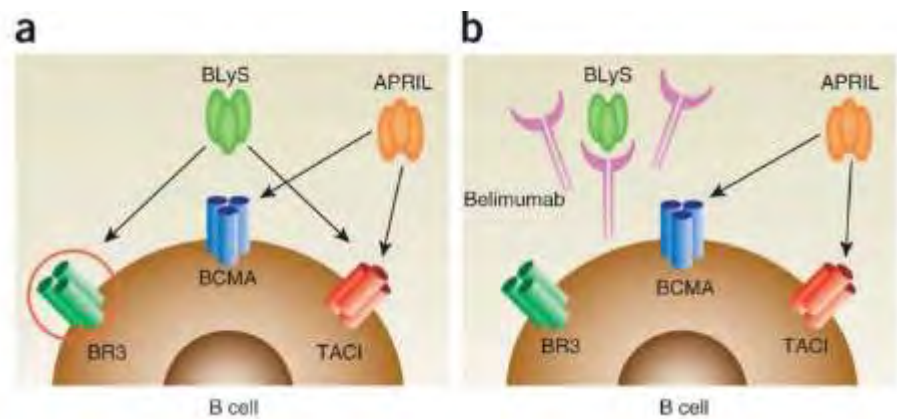
Tacrolimus 0.2–0.3 mg/kg/day, orally
LN
Combination therapy with MMF in LN with nephrotic proteinuria

	Voclosporin group (n=179)	Placebo group (n=178)	OR or HR (95% CI)	p value
Primary endpoint*				
Complete renal response at 52 weeks	73 (41%)	40 (23%)	OR 2.65 (1.64–4.27)	<0.0001
Secondary endpoints				
Complete renal response at 24 weeks	58 (32%)	35 (20%)	OR 2.23 (1.34–3.72)	0.002
Partial renal response at 24 weeks	126 (70%)	89 (50%)	OR 2.43 (1.56–3.79)	<0.001
Partial renal response at 52 weeks	125 (70%)	92 (52%)	OR 2.26 (1.45–3.51)	<0.001
Time to UPCR ≤0.5 mg/mg, days	169 (141–214)	372 (295–NC)	HR 2.02 (1.51–2.70)	<0.001
Time to 50% reduction in UPCR, days	29 (29–32)	63 (57–87)	HR 2.05 (1.62–2.60)	<0.001

Data are n (%) or median (95% CI), unless otherwise specified. OR=odds ratio. HR=hazard ratio. UPCR=urine protein creatinine ratio. NC=non-calculable. *The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, mycophenolate mofetil use at baseline, and region.

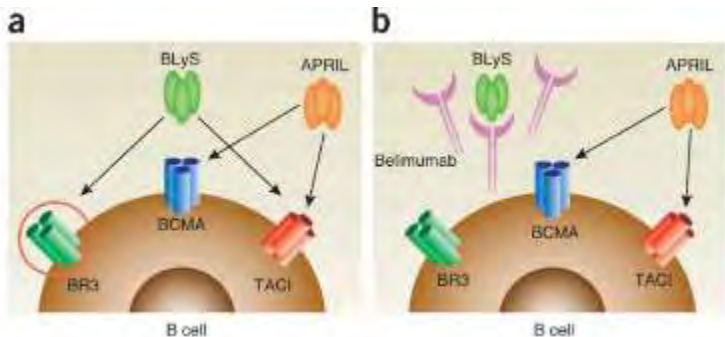
Table 2: Summary of complete and partial renal responses at weeks 24 and 52 (intention-to-treat population)

Belimumab SLE-ben és lupus nephritisben



Clinical efficacy and safety of belimumab			
Improvement of disease activity SRI-4 response ↑ The risk of flares ↓	Combination therapy MMF Rituximab Hydroxychloroquine	Low risk of infection	Adverse events Psychiatric events Infusion reaction

Belimumab SLE-ben és lupus nephritisben



Trial	Phase	Population	Primary Endpoint	Treatment Arms	Results	Year of Publication
BLISS-52	Phase III	Active SLE (SELENA-SLEDAI ≥ 6 and ANA and/or anti-dsDNA positive); n: 867; Latin America, Asia-Pacific, Eastern Europe	SRI-4 at Week 52	Belimumab 1 mg/kg + SOC; Belimumab 10 mg/kg + SOC vs. Placebo + SOC	Primary endpoint met: 51% 1 mg/kg ($p = 0.01$); 58% 10 mg/kg ($p = 0.0006$) vs. 44% placebo	2011
BLISS-76	Phase III	Active SLE (SELENA-SLEDAI ≥ 6 and ANA and/or anti-dsDNA positive); n: 819; North America and Europe	SRI-4 at Week 52	Belimumab 1 mg/kg + SOC; Belimumab 10 mg/kg + SOC vs. Placebo + SOC	Primary endpoint met for 10 mg/kg: 43% vs. 33.5% placebo ($p = 0.017$); 1 mg/kg: 40.6% ($p = 0.089$)	2011
BLISS-SC	Phase III	Active SLE (SELENA-SLEDAI ≥ 8 and ANA and/or anti-dsDNA positive); n: 836; multinational	SRI-4 at Week 52	Belimumab 200 mg SC weekly + SOC vs. Placebo + SOC	Primary endpoint met: 61.4% vs. 48.4% placebo ($p = 0.0006$); hypocomplementemic patients: 64.6% vs. 47.2% placebo ($p = 0.001$)	2017
BLISS-NEA	Phase III	Active SLE (SELENA-SLEDAI ≥ 8 and ANA positive); n: 677; Northeast Asia (China, Japan, South Korea)	SRI-4 at Week 52	Belimumab 10 mg/kg IV + SOC vs. Placebo + SOC	Primary endpoint met: 53.8% vs. 40.1% placebo ($p < 0.001$)	2018
BLISS-LN	Phase III	Active LN (biopsy-proven class III, IV, or V LN with proteinuria requiring induction therapy); n: 448; multinational	PERR at Week 104	Belimumab 10 mg/kg IV + SOC vs. Placebo + SOC	Primary endpoint met: 43% vs. 32% placebo ($p = 0.03$)	2020
EMBRACE	Phase III-IV	Active SLE (SELENA-SLEDAI ≥ 8 and ANA and/or anti-dsDNA positive); n: 448; patients of Black/African ancestry	SRI-SLEDAI-2K at Week 52	Belimumab 10 mg/kg IV + SOC vs. Placebo + SOC	Primary endpoint not met: 48.7% vs. 41.6% placebo ($p = 0.106$)	2022
BASE	Phase IV	Active SLE (ANA and/or anti-dsDNA positive); n: 4018; multinational	All-cause mortality and AESIs up to 52 weeks	Belimumab 10 mg/kg IV + SOC vs. Placebo + SOC	Primary endpoints: No excess mortality or major AESIs vs. placebo; higher rates of serious depression and suicidality with belimumab	2024

Fujio K et al., Rheumatol and Autoimm., 2025.

Xipell M. et al., J. Clin. Med. 2026, 15, 3173

Efficacy and Safety of Obinutuzumab in Active Lupus Nephritis

R.A. Furie,¹ B.H. Rovin,² J.P. Garg,³ M.B. Santiago,^{1,4} G. Aroca-Martinez,^{1,5} A.E. Zuta Santillán,⁶ D. Alvarez,^{1,6} C. Navarro Sandoval,¹ A.M. Lila,^{1,2} J.A. Tumlin,^{1,2} A. Saxena,^{1,4} I. Irujo Palazuelos,^{1,5} H. Raghu,⁷ B. Yoo,² I. Hassan,^{1,6} E. Martins,^{1,7} H. Sehgal,^{1,8} P. Kirchner,^{1,9} J. Ross Terres,² T.A. Omachi,² T. Schindler,^{1,4} W.F. Pendergraft III,¹ and A. Malvar,^{1,4} for the REGENCY Trial Investigators¹⁰

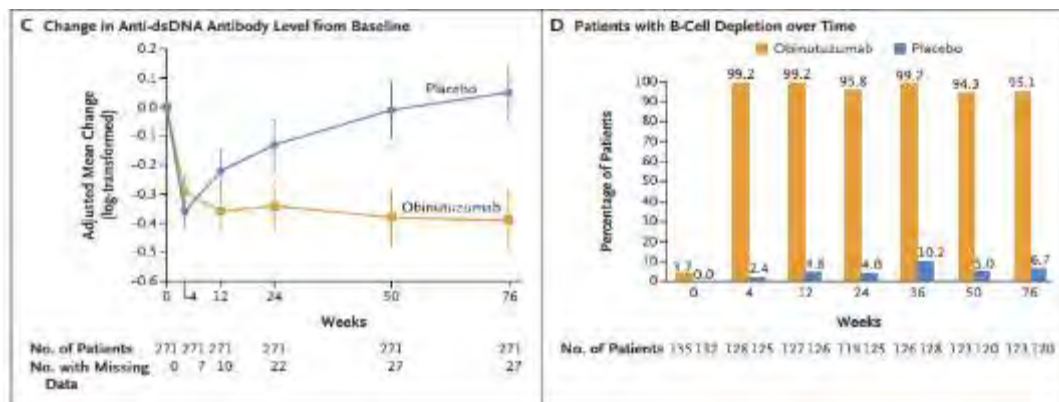
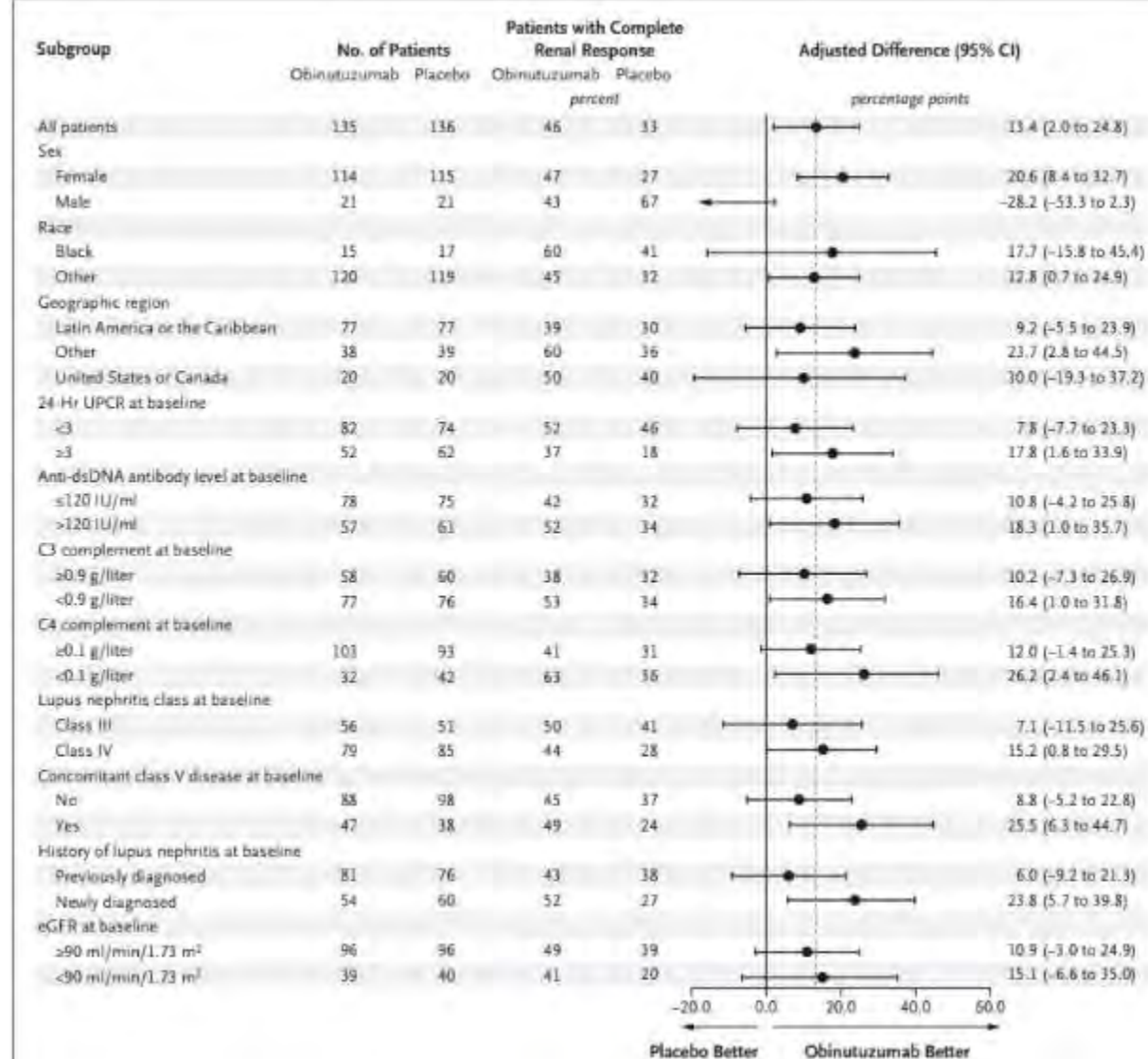


Table 2. Primary and Secondary End Point Results in the Intention-to-Treat Population.¹⁰

End Point	Obinutuzumab (N=135)	Placebo (N=136)	Adjusted Difference (95% CI) [†]	P Value [‡]
Primary end point				
Complete renal response at wk 76 — % (95% CI) ^{§¶}	46.4 (38.0 to 54.9)	33.1 (25.2 to 41.0)	13.4 (2.0 to 24.8)	0.02
Key secondary end points				
Complete renal response at wk 76 with prednisone taper to ≤7.5 mg/day between wks 64 and 76 — % (95% CI) ^{§¶} ***	42.7 (34.3 to 51.1)	30.9 (23.1 to 38.7)	11.9 (0.6 to 23.2)	0.04
UPCR <0.8 at week 76 with no intercurrent event — % (95% CI) ^{¶††}	55.5 (47.1 to 64.0)	41.9 (33.6 to 50.2)	13.7 (2.0 to 25.4)	0.02
Change in the eGFR from baseline to wk 76 — ml/min/1.73 m ² ^{‡‡}	2.31±2.71	-1.54±2.71	3.84 (-1.83 to 9.51)	
Death or renal-related event through wk 76 — % (95% CI) ^{¶¶}	18.9 (12.1 to 25.6)	35.6 (27.5 to 43.8)	-16.8 (-27.4 to -6.2)	
Overall renal response at wk 50 — % (95% CI) ^{¶¶}	59.1 (50.8 to 67.4)	50.7 (42.2 to 59.2)	8.4 (-3.4 to 20.1)	
Change in FACIT-F score from baseline to wk 76 — points ^{‡‡}	1.8±1.2	3.1±1.2	-1.4 (-3.9 to 1.2)	



ORIGINAL ARTICLE

Efficacy and Safety of Obinutuzumab in Active Systemic Lupus Erythematosus

R.A. Furie,^{1,2} M. Dall'Era,¹ E.M. Vital,^{4,5} J.P. Garg,⁶ F. Irazoque Palazuelos,¹ A.E. Zuta Santillán,⁸ J. Rayelo-Hernández,⁹ M.B. Santiago,^{10,12} B. Zazueta Montiel,¹¹ S. Botha,¹⁴ P. Leszczyński,¹⁵ V.A. de Souza,¹⁶ S.A. Sicsik,¹³ L. Bellatin,¹⁸ A. Naidoo,¹⁹ Z. Amoura,²⁰ M.A. D'Agostino,^{21,22} S. Kumar,¹¹ B. Workeneh,²⁴ J. Rae,⁸ H.A. Mao,²⁵ F. Erblang,²⁶ O. Meier,²⁸ J.C. Maller,⁴ and A.D. Askanase,²⁷ for the ALLEGORY Trial Investigators^{*}

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline (Intention-to-Treat Population).[‡]

Characteristic	Obinutuzumab (N=151)	Placebo (N=152)
Age — yr [§]	41.1±12.3	41.4±12.6
Female sex — no. (%)	139 (92.1)	135 (88.8)
Race or ethnic group — no. (%) [†]		
American Indian or Alaska Native	44 (29.1)	42 (27.6)
Asian	4 (2.6)	2 (1.3)
Black	22 (14.6)	25 (16.4)
Native Hawaiian or other Pacific Islander	0	1 (0.7)
White	64 (42.4)	62 (40.8)
Multiple	7 (4.6)	11 (7.2)
Unknown or not reported	10 (6.6)	9 (5.9)
Hispanic or Latino ethnic group — no. (%) [†]	75 (49.7)	86 (56.6)
SLEDAI-2K [§]		
Mean global score	13.1±4.4	13.2±4.0
Score of ≥12 — no. (%) [§]	98 (64.9)	99 (65.1)
BILAG-2004 domain A or B score — no. (%) [¶]		
Constitutional	4 (2.6)	4 (2.6)
Mucocutaneous	135 (89.4)	145 (95.4)
Neuropsychiatric	2 (1.3)	1 (0.7)
Musculoskeletal	139 (92.1)	144 (94.7)
Cardiorespiratory	7 (4.6)	7 (4.6)
Gastrointestinal	2 (1.3)	0
Ophthalmic	0	0
Renal	16 (10.6)	22 (14.5)
Hematologic	0	2 (1.3)
PGA score	1.9±0.4	1.9±0.4
Baseline treatment for SLE		
Antimalarial: hydroxychloroquine, chloroquine, or quinacrine — no. (%)	121 (80.1)	124 (81.6)
Conventional immunosuppressant — no. (%)	107 (70.9)	102 (67.1)
Azathioprine — no./total no. (%)	40/107 (37.4)	26/102 (25.5)
Methotrexate — no./total no. (%)	32/107 (29.9)	28/102 (27.5)
Mycophenolate mofetil or mycophenolic acid — no./total no. (%)	34/107 (31.8)	44/102 (43.1)
Prednisone (or equivalent) dose of ≥10 mg/day — no. (%)	86 (57.0)	85 (55.9)

Table 2. Results for Primary and Secondary Efficacy End Points (Intention-to-Treat Population).

End Point	Obinutuzumab (N=151) [*]	Placebo (N=152) [*]	Adjusted Difference or Hazard Ratio (95% CI) [*]	P Value [†]
Primary end point: SRI-4 response at wk 52 (95% CI) — % ^{‡§}	76.7 (69.8–83.5)	53.5 (45.3–61.6)	23.1 (12.5–33.6)	<0.001
Supplementary treatment policy analysis [¶]	85.4 (79.6–91.2)	68.5 (60.7–76.3)	16.8 (7.1–26.4)	<0.001
Key secondary end points [‡]				
BICLA response at wk 52 (95% CI) — %	62.0 (54.2–69.8)	40.1 (32.1–48.1)	21.9 (10.8–32.9)	<0.001
Reduction in glucocorticoid dose to ≤7.5 mg/day, sustained from wk 40 to wk 52 (95% CI) — % ^{***}	80.0 (71.5–88.5)	54.1 (43.5–64.7)	26.1 (12.7–39.5)	<0.001
SRI-4 response at wk 40, sustained to wk 52 (95% CI) — % ^{††}	72.0 (64.6–79.3)	46.4 (38.3–54.6)	25.4 (14.6–36.2)	<0.001
SRI-6 response at wk 52 (95% CI) — % ^{‡‡}	68.9 (61.4–76.5)	38.9 (31.0–46.9)	30.0 (19.2–40.7)	<0.001
Median time to first BILAG flare through wk 52 — wk ^{§§}	Could not be estimated	52.3	0.58 (0.40–0.82)	0.002
Additional secondary end points ^{¶¶}				
DORIS response at wk 52 — %	33.8	13.8	19.9 (10.6–29.2)	
LLDAS at wk 52 — % ^{***}	57.6	25.0	32.6 (22.3–43.0)	

Anifrolumab hatékonysága SLE-ben

Mechanism of action of anifrolumab in the context of SLE pathogenesis

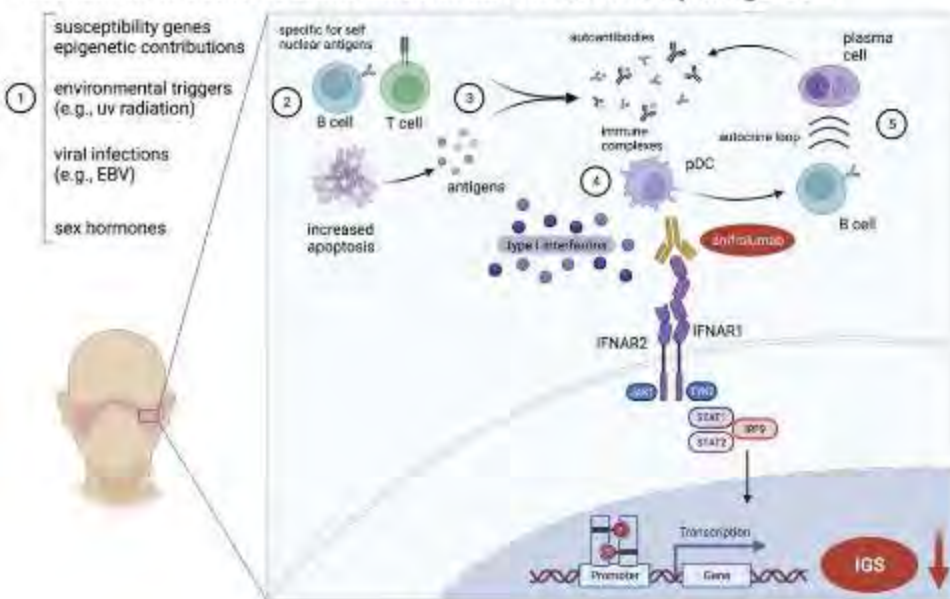


Table 2. Primary and Key Secondary Efficacy End Points.

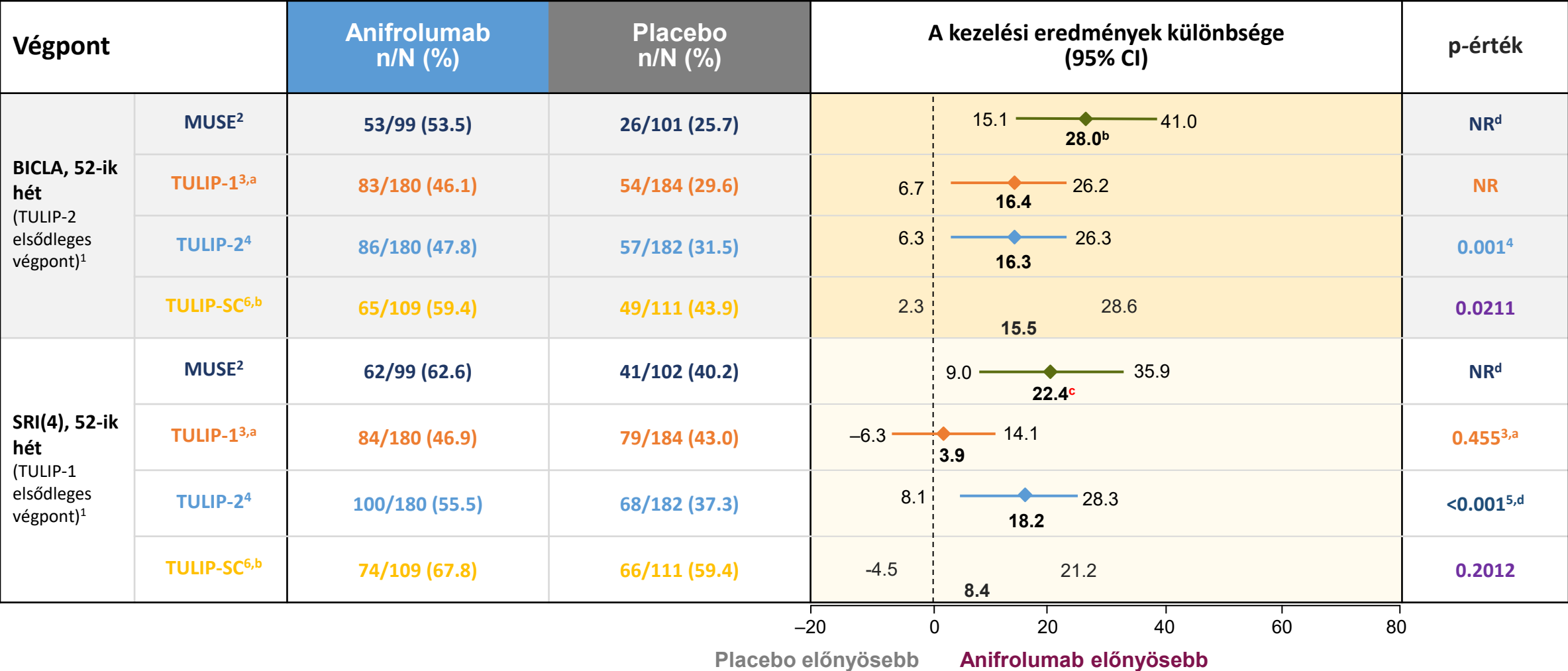
End Point	Placebo (N=182) [†]	Anifrolumab, 300 mg (N=180) [‡]	Difference (95% CI) [§]	Adjusted P Value [¶]
	number/total number (percent)		percentage points	
Primary end point: BICLA response at wk 52 [‡]	57/182 (31.5)	86/180 (47.8)	16.3 (6.3 to 26.3)	0.001
Key secondary end points				
BICLA response at wk 52 in patients with a high type I interferon gene signature	46/151 (30.7)	72/150 (48.0)	17.3 (6.5 to 28.2)	0.002
Glucocorticoid reduction to target dose, sustained from wk 40 to wk 52 [¶]	25/83 (30.2)	45/87 (51.5)	21.2 (6.8 to 35.7)	0.01
≥50% Reduction in CLASI activity from baseline to wk 12 [¶]	10/40 (25.0)	24/49 (49.0)	24.0 (4.3 to 43.6)	0.04
≥50% Reduction in both swollen and tender joints from baseline to wk 52 [¶]	34/90 (37.5)	30/71 (42.2)	4.7 (−10.6 to 20.0)	0.55 ^{**}
Annualized flare rate through wk 52 ^{††}	0.64	0.43	0.67 (0.48 to 0.94) ^{‡‡}	0.08 ^{**}

BICLA válasz: Minden kiindulási BILAG-2004 A és B domain változása B/C/D és C/D-re, nincs romlás egyik doménban sem
Nem romlik az SLEDAI-2K pontszám; és nincs ≥0.3 pont romlás a Physician's Global Assessment-be (range 0–3).

Az anifrolumab IV és SC adagolása konzisztens hatékonyságot mutatott az SLE

klinikai vizsgálati programjaiban

Elsődleges végpontok



Analytic methods and definitions differ across trials.
^aThe primary endpoint of TULIP-1, SRI-4 response at Week 52, was not statistically significant. Data shown are from the amended rules for restricted medications analysis, which corrected for inappropriately classified NSAID use early in the trial. Therefore, the presented p-value is nominal. ^bTULIP-SC data are from a pre-planned interim analysis of efficacy, which was conducted once 220 patients completed the double-blind treatment period or discontinued; only the primary endpoint was formally tested; secondary endpoints are descriptive only. ^cThe primary publication of MUSE² expressed these data as odds ratios rather than CIs.
^dp-value not adjusted for multiplicity.
1. Tanaka Y, Tummala R. *Mod Rheumatol*. 2020;1–12;doi:10.1080/14397595.2020.1812201. 2. Furie R, et al. *Arthritis Rheumatol*. 2017;69:376–386. 3. Furie RA, et al. *Lancet Rheumatol*. 2019;1:e208–219. 4. Morand EF, et al. *N Engl J Med*. 2020;382:211–221.
5. Morand EF, et al. Supplementary Appendix. *N Engl J Med*. 2020;382:211–221. 6. Manzi S et al. Poster presented at: ACR Convergence; October 24-29, 2025; Chicago, IL.

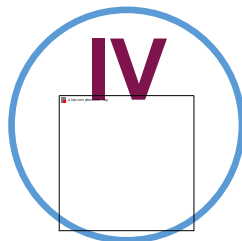
Anifrolumab alkalmazási és adagolási lehetőségei

Anifrolumab IV^{1,a}

 Ajánlott adagolás: **300 mg, 30 perc alatt, 4 hetente**

 Infúzió előtt **hígítani** kell

 **Egészségügyi szakembernek** kell beadnia

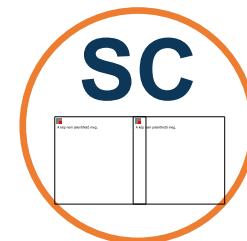


Anifrolumab SC¹

 Ajánlott adagolás: **120 mg, hetente**

 Autoinjektorként kisserelve

 **Beadhatja egy egészségügyi szakember, a beteg vagy gondozója**



Tárolás¹

Az anifrolumab intravénás és subkután injekciós formáját **hűtőszekrényben (2–8 °C)** kell tárolni.

Váltás az alkalmazási módok között¹

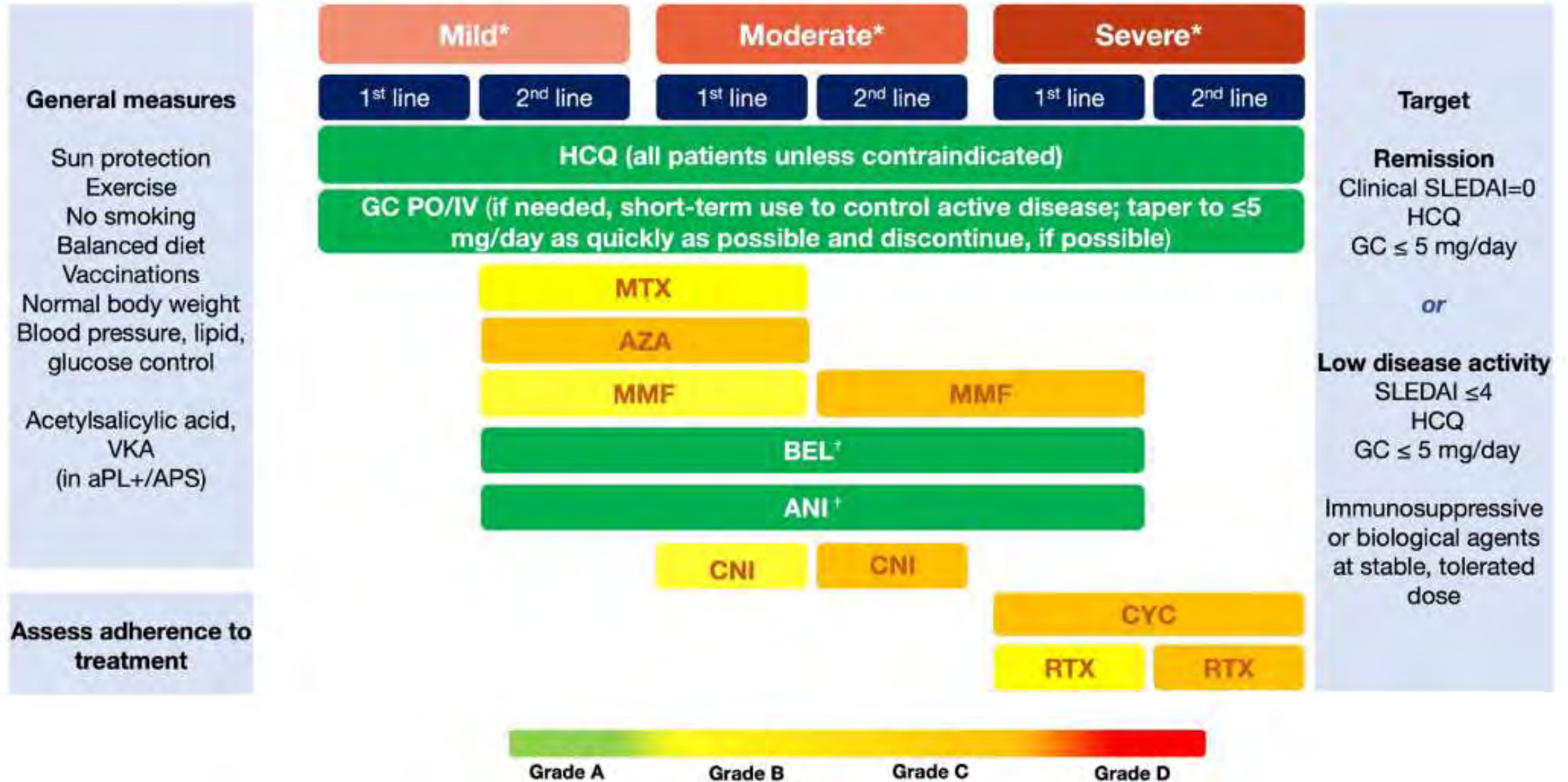
IV-ről SC-re: Az első SC injekciót **~2 héttel** az utolsó intravénás infúzió után kell beadni.

SC-ről IV-re: Az első IV infúziót **~3-4 héttel** az utolsó SC injekció után kell beadni.

^aIf a planned infusion is missed, anifrolumab should be administered as soon as possible. A minimum interval of 14 days between infusions should be maintained. Please see Prescribing Information for full dosing and administration information.

1. SAPHNELO® SmPC

Treatment of Non-Renal Systemic Lupus Erythematosus



SLE kezelésének ACR ajánlása

Systemic Lupus Erythematosus						
HCQ (unless contraindicated)						
Glucocorticoids: Only if necessary, at lowest effective dose for shortest possible duration*				Taper to ≤5 mg/day by 6 months (ideally to zero)		
Pulse glucocorticoid for organ- and life-threatening manifestations						
Escalation of therapy (any organ system) when refractory to initial treatment						
Early introduction of immunosuppressive agents to minimize glucocorticoid toxicity*						
Mucocutaneous	Musculoskeletal	Serositis	Hematologic	Neuropsychiatric	Cardiac	Vasculitis
Sunscreen /Topicals	Arthritis	Pleuropericarditis	Leukopenia	Psychosis/seizures	Myocarditis	• Azathioprine • IV CYC • MPAA • Anti-CD20 • Anifrolumab • Belimumab Severe • IV CYC • Anti-CD20 Life-threatening Addition of: • PLEX and/or IVIG
ACLE, SCLE, CCLE	• Azathioprine • Methotrexate[§] • MPAA[±] Low threshold to add/substitute for • Anifrolumab • Belimumab	Initial treatment, mild • Colchicine • NSAIDs • and/or IVIG	Asymptomatic • No IS treatment unless other SLE activity present	Anti-psychotic / anti-seizure therapy	• IV CYC • MPAA • Anti-CD20 and/or IVIG	
Mild • Add quinacrine • Switch HCQ to CQ**		Ongoing/recurrent • Azathioprine • MPAA[±] • Anifrolumab • Belimumab • IL-1 blockade	Thrombocytopenia	Optic neuritis, acute confusional state, mononeuritis multiplex • IV CYC[†] • MPAA • Anti-CD20	Libman-Sacks Endocarditis • Anticoagulation • IS therapy	
Moderate-Severe [†] • Methotrexate • MPAA • Anifrolumab • Belimumab		Asymptomatic <30,000 platelets/ mCL • Azathioprine • CNI • MPAA[±] • Belimumab • Anti-CD20 and/or IVIG	Myelitis • IV CYC			
Refractory • Lenalidomide			Symptomatic • Anti-CD20 and/or IVIG	Cognitive Dysfunction		
Bullous LE			Hemolytic anemia	Cognitive therapy		
Mild • Dapsone			Symptomatic • Anti-CD20 and/or IVIG	• No IS treatment		
Severe • Azathioprine • Methotrexate • MPAA • Anti-CD20						
Chilblain LE						
• CCB • PDE5i • Pentoxifylline						
LCV						
• Colchicine • Dapsone						

Strong recommendation for

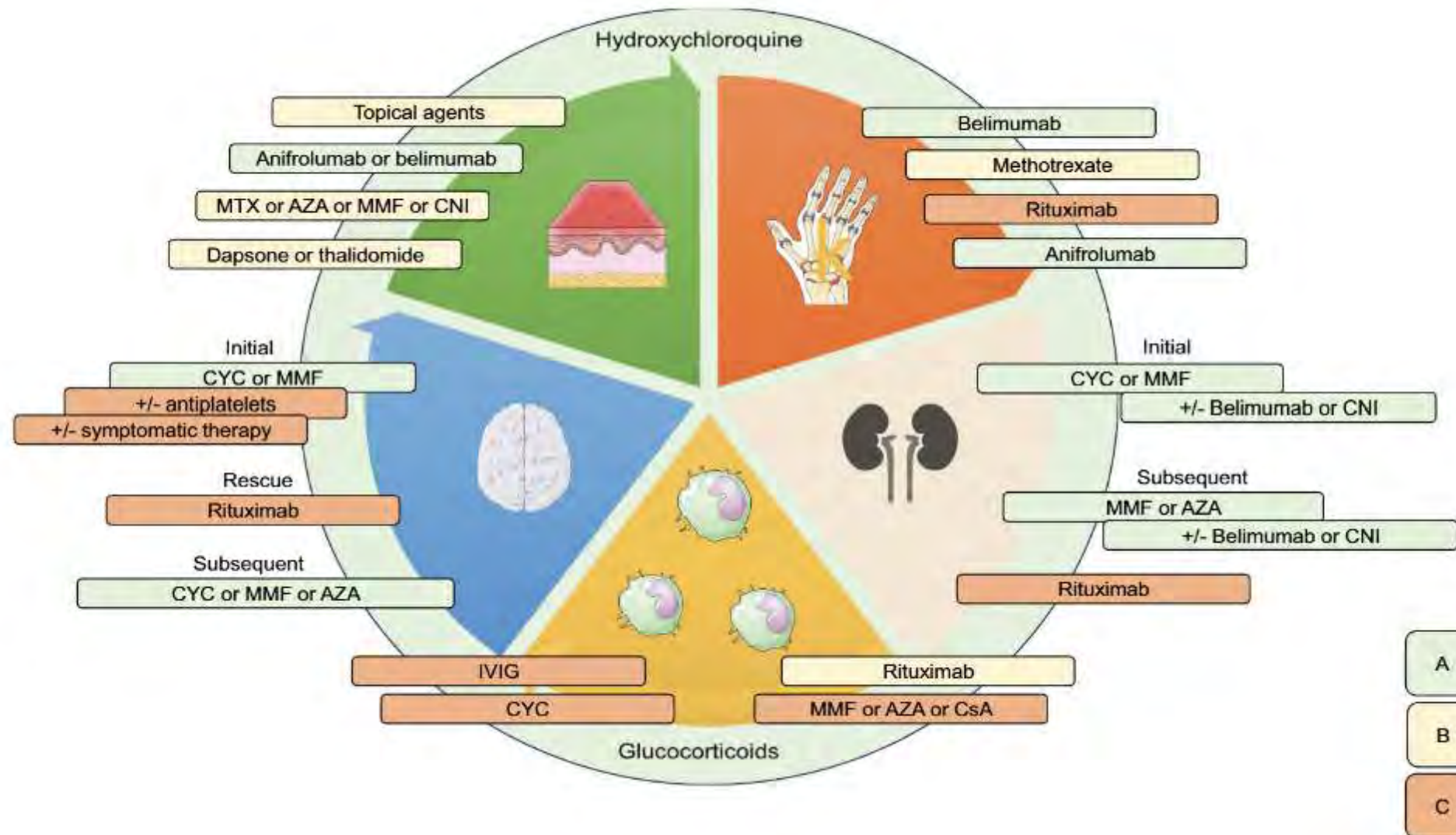
Conditional recommendation for

Conditional recommendation against

*Good practice statements

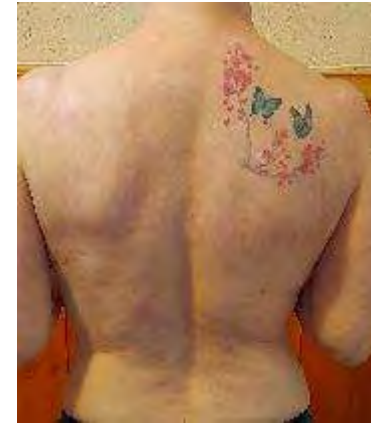
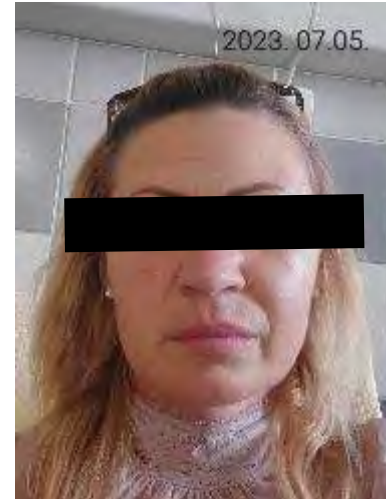
Strong recommendation for
 Conditional recommendation for
 Conditional recommendation against
 *Good practice statements

Immunszuppresszáns terápia a szervi manifesztációk függvényében



Bőrtünetek kezelése

- Lokális kezelés (glükokortikoid, calcineurin inhibitorok)
- Antimaláriás készítmények (chloroquin, HCQ) és/vagy szisztémás glükokortikoid ha szükséges
- Másodvonalbeli kezelésként:
 - Anifrolumab
 - Belimumab
 - Methotrexate
 - MMF
- Harmadik vonal:
 - Dapsone
 - Retinoidok
 - Calcineurin gátló
 - Azathioprin
 - Cyclophosphamid
 - Rituximab



SLE arthritis kezelése



NONDEFORMING NONEROSIVE (NDNE) ARTHRITIS



Prevalence: 80%-85%
Biomarkers: type I IFN signature
MRI findings: capsular and tendon inflammation

DEFORMING ARTHRITIS (JACCOUD'S ARTHROPATHY)



Prevalence: 3%-13%
Biomarkers: ↑MMP-3, ↓MMP-12
MRI findings: capsular and tendon inflammation

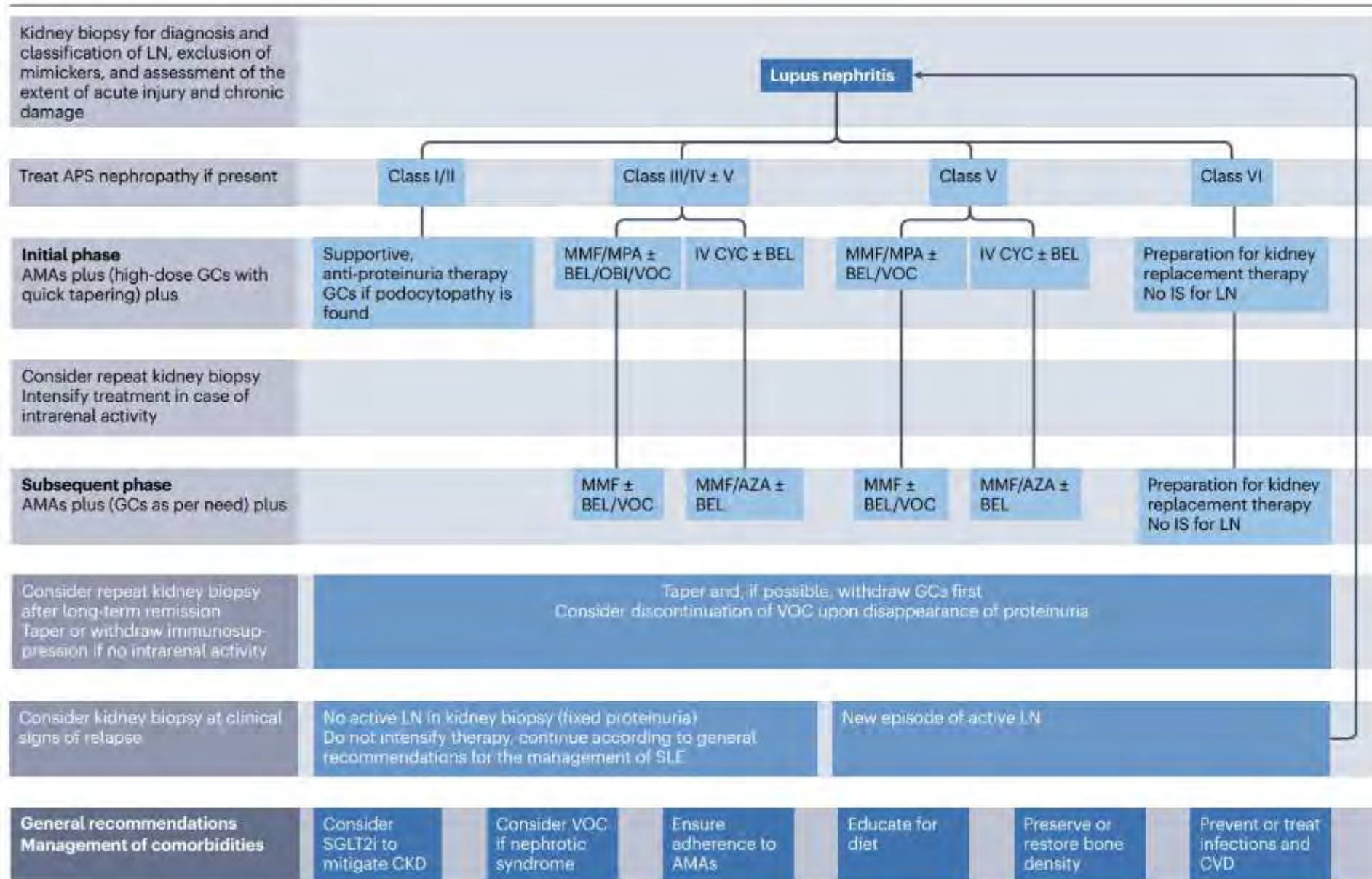
RHEUMATOID-LIKE EROSIVE ARTHRITIS (RHUPUS)



Prevalence: 3%-5%
Biomarkers: RF, ACPA, aCarP
MRI findings: synovial hyperplasia and bone erosions

Phenotypes	Prevalence According to Traditional X-ray	Prevalence According to Ultrasound	Biomarkers Available	Treatment
Nondeforming nonerosive arthritis	80–85%	40–60%	Type I interferon signature	First-line treatment: GCs, HCQ, MTX Second-line treatment: belimumab, anifrolumab
Deforming arthritis (Jaccoud's arthropathy)	3–13%	2–47%	MMP3, MMP12	First-line treatment: GCs, HCQ, MTX Second-line treatment: belimumab, anifrolumab
Rheumatoid-like erosive arthritis (rhumus)	3–5%	about 5%	RF, ACPA Anti-CarP	First-line treatment: GCs, HCQ, MTX Second-line treatment: belimumab Third-line treatment: rituximab Tocilizumab JAKi

Lupus nephritis kezelése



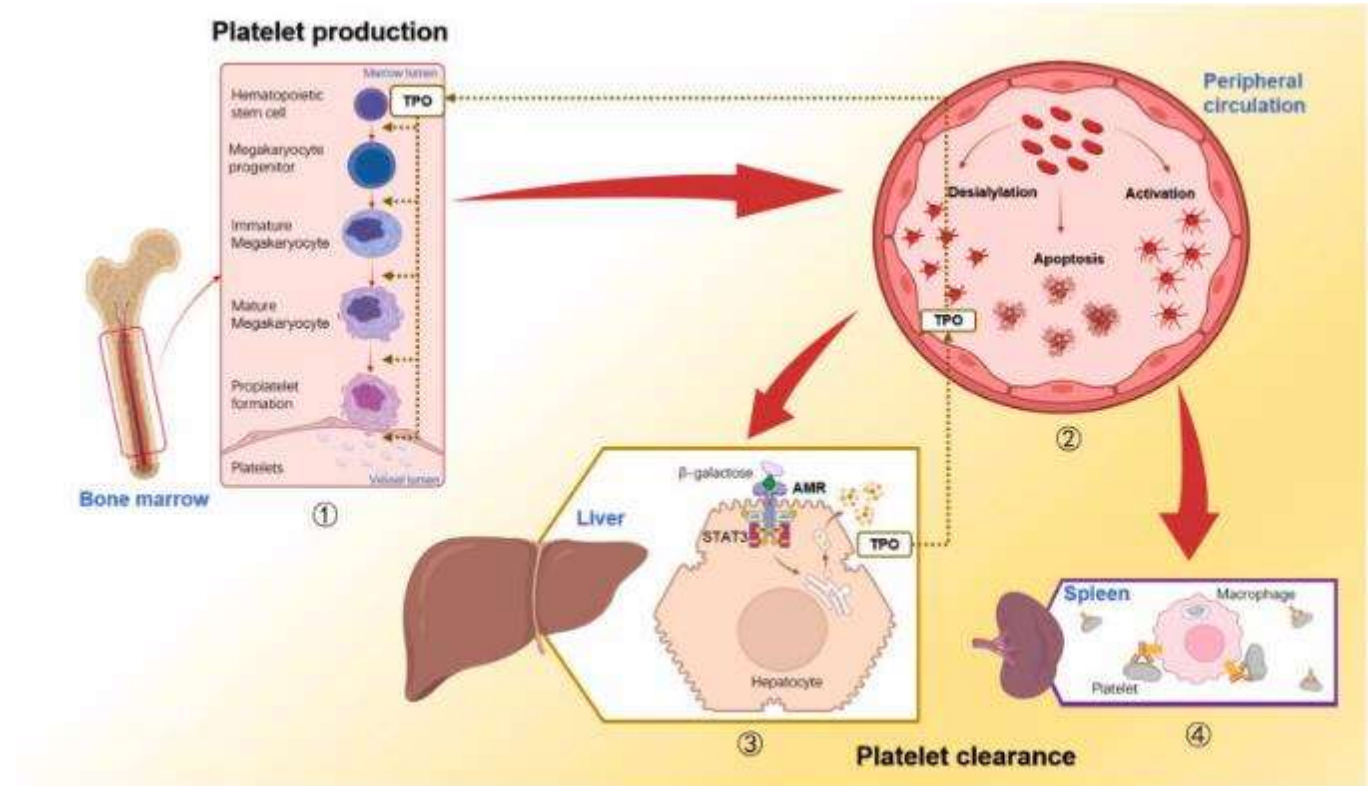
Súlyos autoimmun cytopenia kezelése

- Nagy dózisú glükokortikoid
- Nagy dózisú IVIG
- és/vagy rituximab
- és/vagy iv. cyclophosphamid

Fenntartó kezelés:

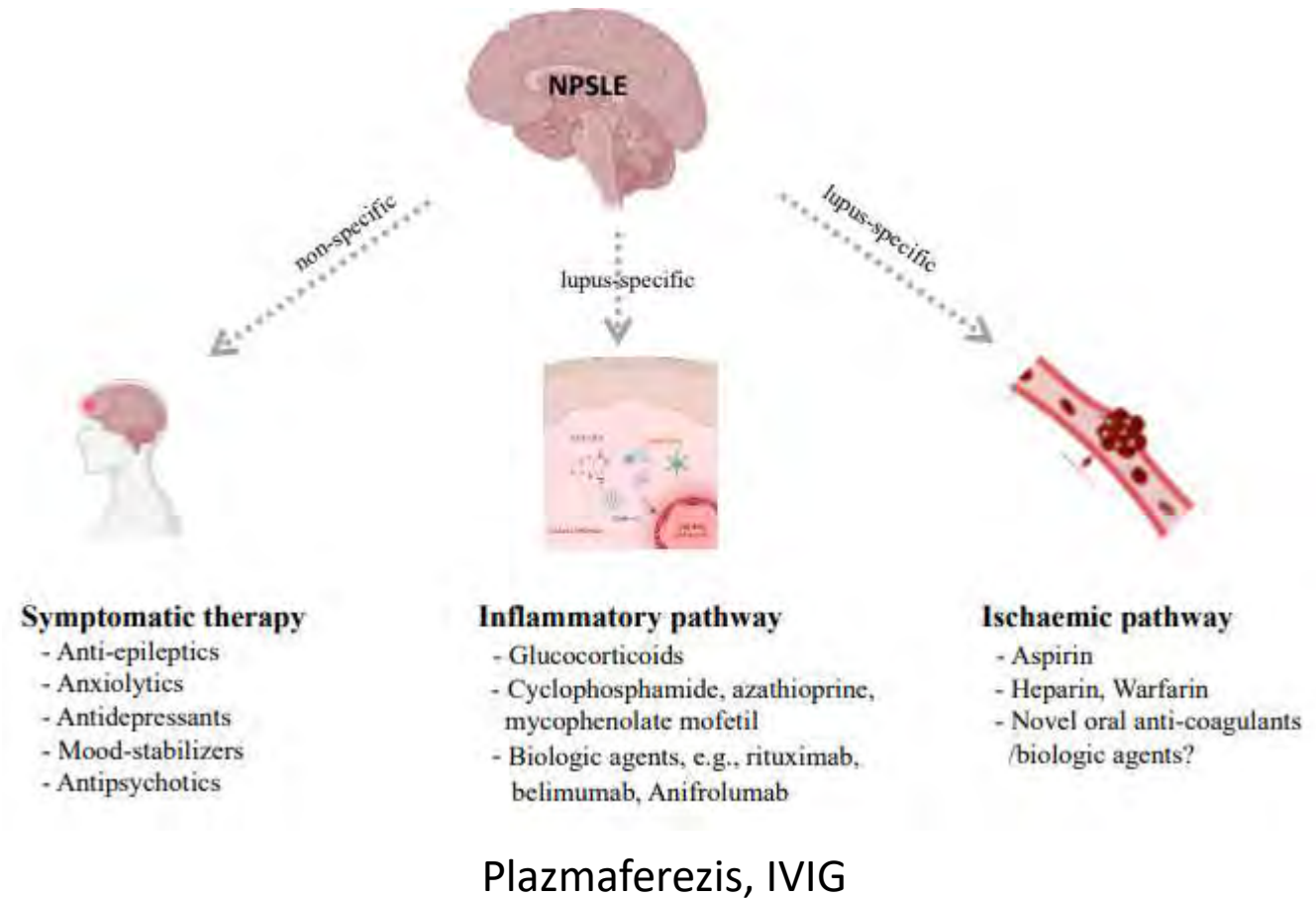
- Rituximab
- Azathioprine
- Mycophenolat mofetil
- Cyclosporine A

Fostamatinib: lép tirozin kináz inhibitor krónikus ITP-ben törzskönyvezett
TPO receptor agonista, APA pozitív betegben óvatosan!

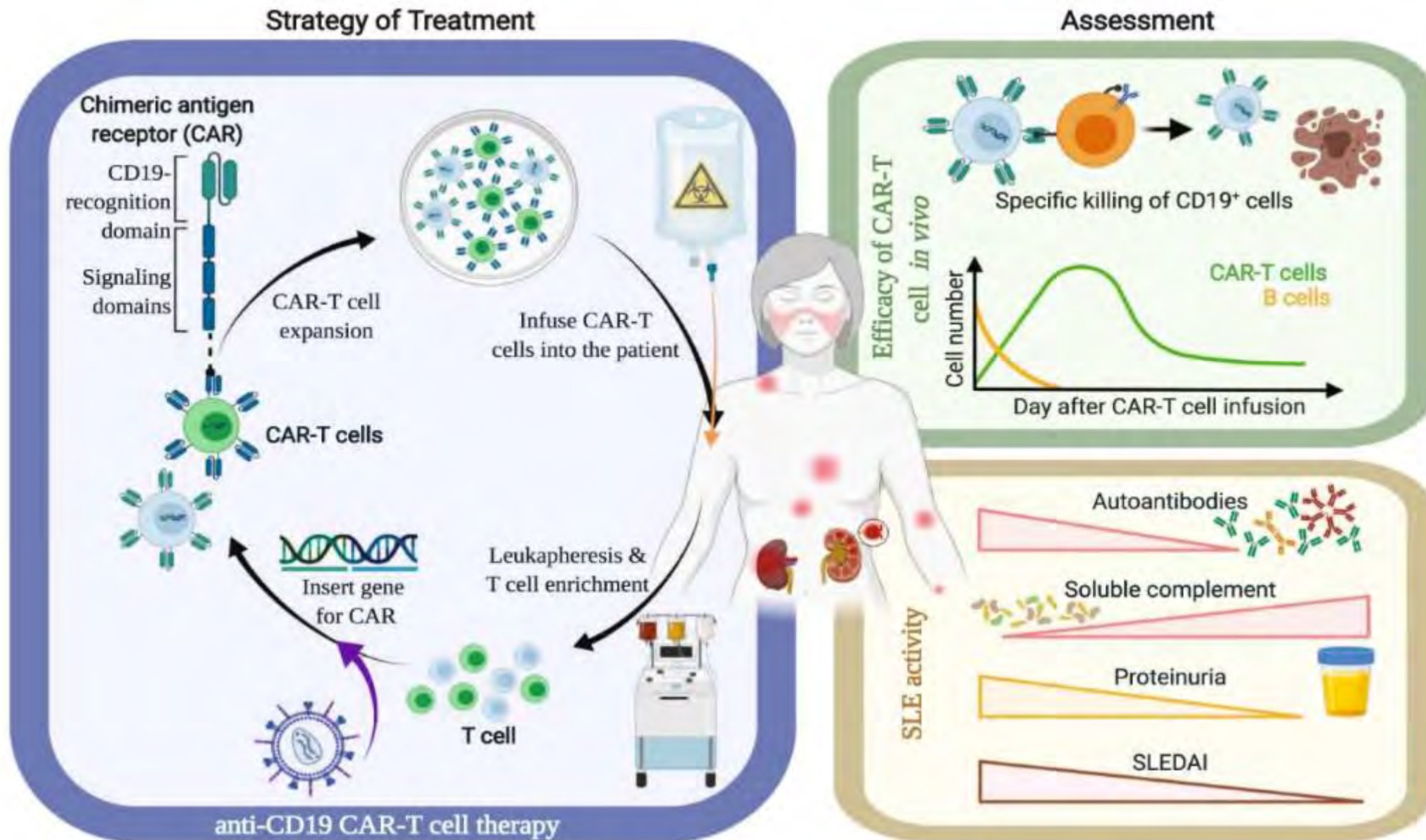


Aktív neuropszichiátriai manifestáció esetén

- Szimptomatikus terápia
- Gyulladásos manifestáció esetén:
glükokortikoid és immunszuppresszáns (1b/A)
- Atherosclerotikus vagy APS-hez társuló
thrombotikus manifestáció esetén
antikoaguláns/thrombocyta aggregáció
kezelés megfontolandó

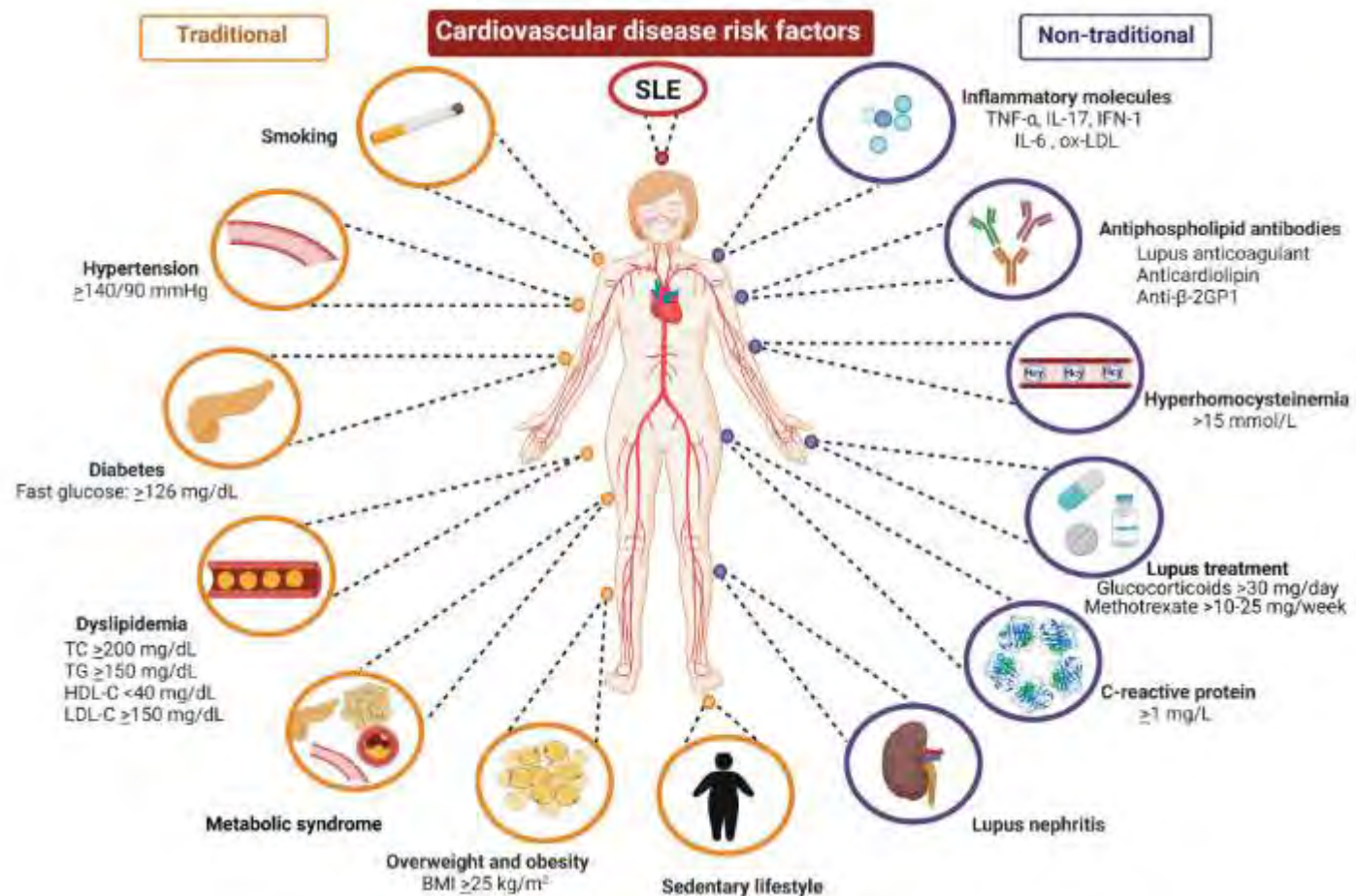


CAR-T sejt kezelés SLE-ben



Egyéb teendők

- Immunszuppresszáns csökkentés GC kezeléssel kezdve
- APS társulása esetén KVA adása
- Magas rizikójú APA profil esetén ASA profilaxis
- Védőoltások
- Osteoporosis megelőzés
- Kardiovasculáris rizikó management
- Tumorok szűrése



Fanouriakis A, et al. *Ann Rheum Dis* 2023;0:1–15. doi:10.1136/ard-2023-224762

Pesqueda-Cendejas K et al, *Nutrients* 2023, 15, 1036. <https://doi.org/10.3390/nu15041036>

Köszönöm a figyelmet!

