American College of Rheumatology (ACR) 2024 Lupus Nephritis Guideline–Treatment Overview

Class III/IV ± V
Active, newly diagnosed, or flare

FIRST LINE (CONTINUOUS) THERAPY
Preferred:

TRIPLE THERAPY
GC pulse/oral taper to ≤5 mg/day by 6 mo.
+
MPAA
+
BEL[a] *or* CNI[b]

Alternatives:

TRIPLE THERAPY
GC pulse/oral taper to ≤5 mg/d by 6 mo.
+
Low-dose CYC‡ + BEL

DUAL THERAPY if TRIPLE THERAPY is not available or not tolerated

Pure Class V*
Active, newly diagnosed, or flare

FIRST LINE (CONTINUOUS) THERAPY
Preferred:

TRIPLE THERAPY
GC pulse/oral taper to ≤5 mg/day by 6 mo.
+
MPAA
+
CNI

Alternatives:

TRIPLE THERAPY
GC pulse/oral taper to ≤5 mg/d by 6 mo.
+
MPAA + BEL *or* Low-dose CYC‡ + BEL

DUAL THERAPY if TRIPLE THERAPY is not available or not tolerated

Hydroxychloroquine and RAAS-I†

Lack of Response

If initial TRIPLE THERAPY: Change to ALTERNATE TRIPLE THERAPY
If initial DUAL THERAPY: Escalate to TRIPLE THERAPY

Refractory Disease
Consider adherence and/or other diagnoses (e.g., aPL nephropathy) or advanced chronicity

Escalate to a more intensive regimen, including addition of anti-CD20 agents, combination therapy with 3 immunosuppressives (i.e., MPAA, belimumab and CNI), or referral for investigational therapy.

* For ≥1 g protein; for less than 1 g, treat with GC and/or immunosuppression
† Discuss adjunctive treatment with systemic anticoagulation with nephrology for patients with LN and significant risk factors for thrombosis (e.g., low serum albumin in context of severe proteinuria)
‡ Substitute MPAA once low-dose CYC cycle is completed
a: Recommended preferentially when significant extrarenal manifestations present
b: Recommended preferentially when proteinuria ≥3.0 g

Goal: Complete renal response (CRR)
■ Within 6-12 mo, reduction in proteinuria to ≤0.5 g/g and ■ Stabilization or improvement in kidney function (±20% baseline)
Duration of therapy: at least 3-5 years after achievement of CRR

RAAS-I, renin-angiotensin-aldosterone system inhibitors; GC, glucocorticoid; MPAA, mycophenolic acid analogs (including mycophenolate mofetil, or MMF); BEL, belimumab; CNI, calcineurin inhibitor; CYC, cyclophosphamide.
GC pulse/oral taper: Pulse intravenous glucocorticoids (250-1000 mg methylprednisolone daily x 1-3 days) followed by oral glucocorticoid ≤0.5 mg/kg/day (maximum dose 40 mg/day) and taper.
Low-dose cyclophosphamide: as per ELNT protocol[a], 500 mg IV CYC every 2 weeks for 6 doses.
DUAL THERAPY: GC pulse/oral taper plus one immunosuppressive agent, usually MPAA or low-dose CYC .

[a]Houssiau FA, Vasconcelos C, D'Cruz D, et al. Immunosuppressive therapy in lupus nephritis: the Euro-Lupus Nephritis Trial, a randomized trial of low-dose versus high-dose intravenous cyclophosphamide. *Arthritis Rheum* 2002;46:2121-2131.