# EULAR/ERA-EDTA Lupus Nephritis Recommendations

*Written by Toni Rizzo*

George Bertsias, MD, University of Crete Medical School, Heraklion, Greece, presented the new European League Against Rheumatism/European Renal Association European Dialysis and Transplant Association recommendations for the management of adult lupus nephritis, based on expert opinion and a systematic review of 887 published articles. The level of agreement among experts was excellent, with average scores ranging from 8.6 to 9.7 on a 10-point scale.

The resulting recommendations are summarized as follows:

1. Indications for first renal biopsy in systemic lupus erythematosus: any sign of renal involvement.
2. Pathological assessment: follow International Society of Nephrology/Renal Pathology Society 2003 classification system; include not only active and chronic glomerular and tubulointerstitial changes but also vascular lesions that are associated with antiphospholipid antibodies/syndrome.

3a. Indications for immunosuppressive treatment: Class $III_A$ or $III_{A/C}$ (± V) and $IV_A$ or $IV_{A/C}$ (± V) nephritis; pure class V nephritis if proteinuria >1 g/24 hours despite optimal use of renin-angiotensin-aldosterone system blockers.

3b. Goals of immunosuppressive treatment: long-term preservation of renal function, prevention of disease flares, avoidance of treatment-related harms, improved quality of life and survival; complete renal response; partial renal response by 6 to 12 months.

4a. Initial treatment: Class $III/IV_A$ or $III/IV_{A/C}$ (± V)—mycophenolic acid (MPA) or low-dose intravenous cyclophosphamide (3 g over 3 months); adverse prognostic factors (acute deterioration of renal function, substantial cellular crescents, and/or fibrinoid necrosis)—consider monthly higher-dose cyclophosphamide; initially combine regimens with 3 consecutive pulses of intravenous methylprednisolone, followed by oral prednisone; pure class V with nephrotic-range proteinuria—MPA with oral prednisone; cyclophosphamide or calcineurin inhibitors or rituximab as alternative or for nonresponders; Class III-IV or V—azathioprine as alternative in selected patients.

4b. Subsequent treatment: for improving patients, use lower-dose MPA with low-dose prednisone for 3 years; then, attempt gradual drug withdrawal; if pregnancy is contemplated, switch to azathioprine; consider calcineurin inhibitors.

4c. MPA or cyclophosphamide failure: switch from MPA to cyclophosphamide or vice versa, or give rituximab.

5. Adjunctive treatment: angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers for urine protein-creatinine ratio >50 mg/mmol or hypertension; statins for persistent dyslipidemia; hydroxychloroquine; acetylsalicylic acid for antiphospholipid antibodies; calcium and vitamin D; nonlive vaccine immunizations; anticoagulants for nephrotic syndrome or antiphospholipid antibodies.

6a. Monitoring and prognosis: body weight, blood pressure, serum creatinine and estimated glomerular filtration rate, serum albumin, proteinuria, urinary sediment examination, serum C3 and C4, anti-dsDNA, complete blood count each visit; antiphospholipid antibodies and lipids at baseline and intermittently.

6b. Monitoring and prognosis: Repeat renal biopsy if worsening or refractory to immunosuppressive or biologic treatment or at relapse.

7. End-stage renal disease: renal replacement therapy (dialysis, transplantation) can be used.
8. Antiphospholipid syndrome-associated nephropathy: consider hydroxychloroquine and/or antiplatelet/anticoagulant treatment.
9. Pregnancy: may be planned in stable lupus patients; hydroxychloroquine, and when needed, low-dose prednisone, azathioprine, and/or calcineurin inhibitors are acceptable; treatment intensity should not be reduced; consider acetylsalicylic acid to reduce risk of preeclampsia.
10. Pediatric lupus: lupus nephritis is more severe in children; diagnosis, management, and monitoring similar to that for adults; coordinated transition program to adult specialists is important in assessing concordance to therapies and optimizing long-term outcomes.

Prof. Bertsias concluded that these recommendations can facilitate medical care of patients with lupus without restricting the autonomy of their physicians.